PTO/SB/81 (01-09)
Approved for use through 11/30/2011. OMB 0651-0035
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

POWER OF ATTORNEY OR REVOCATION OF POWER OF ATTORNEY WITH A NEW POWER OF ATTORNEY AND CHANGE OF CORRESPONDENCE ADDRESS

Application Number	11/844,440
Filing Date	August 24, 2007
First Named Inventor	Alan H. Auerbach
Title	Methods and Compositions for Treating Cance
Art Unit	1628 - Confirmation No. 6850
Examiner Name	HUI, San Ming R.
Attorney Docket Number	11515-004-999

I hereby revoke all previous powers of attorney given in the above-identified application.

☐ A Power of Attorney is submitted herewith.

OR

☒ I hereby appoint Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s) to prosecute the application identified above, and to transact all business in the United States Patent and Trademark Office connected therewith:

27777

OR

☐ I hereby appoint Practitioner(s) named below as my/our attorney(s) or agent(s) to prosecute the application identified above, and to transact all business in the United States Patent and Trademark Office connected therewith:

Practitioner(s) Name	Registration Number

Please recognize or change the correspondence address for the above-identified application to:

☒ The address associated with the above-mentioned Customer Number.

OR

☐ The address associated with Customer Number:

OR

☐ Firm or Individual Name					
Address					
City		State		Zip	
Country					
Telephone		Email			

I am the:

☐ Applicant/Inventor.

OR

☒ Assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) (Form PTO/SB/96) submitted herewith or filed on _____.

SIGNATURE of Applicant or Assignee of Record

Signature	Andrea Kamage	Date	2/22/11
Name	Andrea Kamage, Esq.	Telephone	(732) 524-3957
Title and Company	Asst. Secretary, Cougar Biotechnology, Inc./Johnson & Johnson		

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

This collection of information is required by 37 CFR 1.31, 1.32 and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/SB/96 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(b)

Applicant/Patent Owner: Cougar Biotechnology, Inc.

Application No./Patent No.: 11/844,440 Filed/Issue Date: August 24, 2007

Titled: METHODS AND COMOSITIONS FOR TREATING CANCER

Cougar Biotechnology, Inc. , a Corporation

(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.

states that it is:

1. [X] the assignee of the entire right, title, and interest in;

2. [ ] an assignee of less than the entire right, title, and interest in (The extent (by percentage) of its ownership interest is _____ %); or

3. [ ] the assignee of an undivided interest in the entirety of (a complete assignment from one of the joint inventors was made) the patent application/patent identified above, by virtue of either:

A. [ ] An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel _____, Frame _____, or for which a copy therefore is attached.

OR

B. [X] A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: Alan H. Auerbach and Arie S. Belldegrun To: Cougar Biotechnology, Inc.

The document was recorded in the United States Patent and Trademark Office at
Reel 018839, Frame 0027, or for which a copy thereof is attached.

2. From: Alan H. Auerbach To: Cougar Biotechnology, Inc.

The document was recorded in the United States Patent and Trademark Office at
Reel 020040, Frame 0635, or for which a copy thereof is attached.

3. From: Arie S. Belldegrun To: Cougar Biotechnology, Inc.

The document was recorded in the United States Patent and Trademark Office at
Reel 020040, Frame 0690, or for which a copy thereof is attached.

[ ] Additional documents in the chain of title are listed on a supplemental sheet(s).

[X] As required by 37 CFR 3.73(b)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (*i.e.*, a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Andrea Kamage — Signature

9/22/11 — Date

Andrea Kamage, Esq. — Printed or Typed Name

Assistant Secretary — Title

Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Andrea J. Kamage/Laurie Phillips
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Utility application filing	1011	1	330	330
Utility Search Fee	1111	1	540	540
Utility Examination Fee	1311	1	220	220
Pages:				
Claims:				
Claims in excess of 20	1202	16	52	832
Independent claims in excess of 3	1201	1	220	220
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**2142**

Electronic Acknowledgement Receipt

EFS ID:	9527423
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Andrea J. Kamage/Laurie Phillips
Filer Authorized By:	Andrea J. Kamage
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	24-FEB-2011
Filing Date:	
Time Stamp:	16:49:59
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$2142
RAM confirmation Number	3721
Deposit Account	100750
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Application Data Sheet	CGR5001USCNTAPPLICATIONDATASHEET.pdf	1031200 0997e1bece1ad81a95897fd4e7556e09e9173a7b	no	5
Warnings:					
Information:					
2		CGR5001USNPAPPLNASORIGINALLYFILED.pdf	1649829 9b0f93c22c6b033155e73cc04a189006792dc563	yes	30

Multipart Description/PDF files in .zip description		
Document Description	**Start**	**End**
Specification	1	23
Claims	24	29
Abstract	30	30

Warnings:					
Information:					
3	Oath or Declaration filed	CGR5001DECLARATION.pdf	129278 c044f69ffb40b471b2e4909aacd40d0055911ee1	no	2
Warnings:					
Information:					
4	Change of Address	11844440POA.pdf	41818 54aa33facc8b7b9c0cfe4bdf11e9d6bb0c154771	no	1
Warnings:					
Information:					
5	Assignee showing of ownership per 37 CFR 3.73(b).	11844440STATEMENT373B.pdf	46773 b7bfddbc2b3dbba4b04935ef24ce3e0c69110307	no	1
Warnings:					
Information:					
6	Fee Worksheet (PTO-875)	fee-info.pdf	37686 2aa3ea7e51ac8b33a96fbf7bee79bde5f4d7589e	no	2
Warnings:					

Information:	
Total Files Size (in bytes):	2936584

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Electronic Acknowledgement Receipt

EFS ID:	9527423
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Andrea J. Kamage/Laurie Phillips
Filer Authorized By:	Andrea J. Kamage
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	24-FEB-2011
Filing Date:	
Time Stamp:	16:49:59
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$2142
RAM confirmation Number	3721
Deposit Account	100750
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Application Data Sheet	CGR5001USCNTAPPLICATIONDATASHEET.pdf	1031200 0997e1bece1ad81a95897fd4e7556e09e9173a7b	no	5
Warnings:					
Information:					
2		CGR5001USNPAPPLNASORIGINALLYFILED.pdf	1649829 9b0f93c22c6b033155e73cc04a189006792dc563	yes	30

Multipart Description/PDF files in .zip description		
Document Description	**Start**	**End**
Specification	1	23
Claims	24	29
Abstract	30	30

Warnings:					
Information:					
3	Oath or Declaration filed	CGR5001DECLARATION.pdf	129278 c044f69ffb40b471b2e4909aacd40d0055911ee1	no	2
Warnings:					
Information:					
4	Change of Address	11844440POA.pdf	41818 54aa33facc8b7b9c0cfe4bdf11e9d6bb0c154771	no	1
Warnings:					
Information:					
5	Assignee showing of ownership per 37 CFR 3.73(b).	11844440STATEMENT373B.pdf	46773 b7bfddbc2b3dbba4b04935ef24ce3e0c69110307	no	1
Warnings:					
Information:					
6	Fee Worksheet (PTO-875)	fee-info.pdf	37686 2aa3ea7e51ac8b33a96fbf7bee79bde5f4d7589e	no	2
Warnings:					

Information:	
Total Files Size (in bytes):	2936584

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	CGR5001USCNT1
	Application Number	
Title of Invention	Methods and Compositions for Treating Cancer	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Applicant Information:

Applicant 1 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Alan	H.	Auerbach	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	Hermosa Beach	State/Province	CA	Country of Residence i	US

Citizenship under 37 CFR 1.41(b) i: US

Mailing Address of Applicant:

Address 1	One Johnson & Johnson Plaza
Address 2	

City	New Brunswick	State/Province	NJ
Postal Code	08933	Country i	US

Applicant 2 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Arie	S.	Belldegrum	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	Los Angeles	State/Province	CA	Country of Residence i	US

Citizenship under 37 CFR 1.41(b) i: US

Mailing Address of Applicant:

Address 1	One Johnson & Johnson Plaza
Address 2	

City	New Brunswick	State/Province	NJ
Postal Code	08933	Country i	US

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

☐ **An Address is being provided for the correspondence Information of this application.**

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	CGR5001USCNT1
	Application Number	
Title of Invention	Methods and Compositions for Treating Cancer	

Customer Number	27777		
Email Address	jnjuspatent@corus.jnj.com	Add Email	Remove Email

Application Information:

Title of the Invention	Methods and Compositions for Treating Cancer		
Attorney Docket Number	CGR5001USCNT1	Small Entity Status Claimed	☐
Application Type	Nonprovisional		
Subject Matter	Utility		
Suggested Class (if any)		Sub Class (if any)	
Suggested Technology Center (if any)			
Total Number of Drawing Sheets (if any)		Suggested Figure for Publication (if any)	

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S. C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Enter either Customer Number or complete the Representative Name section below. If both sections are completed the Customer Number will be used for the Representative Information during processing.

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	27777		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) or indicate National Stage entry from a PCT application. Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78(a)(2) or CFR 1.78(a)(4), and need not otherwise be made part of the specification.

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
	non provisional of	60/921506	2006-08-25
Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
	Continuation of	11/844440	2007-08-24

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	CGR5001USCNT1
	Application Number	
Title of Invention	Methods and Compositions for Treating Cancer	

Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button. Add

Foreign Priority Information:

This section allows for the applicant to claim benefit of foreign priority and to identify any prior foreign application for which priority is not claimed. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(a).

Remove

Application Number	Country [i]	Parent Filing Date (YYYY-MM-DD)	Priority Claimed
			(•) Yes ( ) No

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button. Add

Assignee Information:

Providing this information in the application data sheet does not substitute for compliance with any requirement of part 3 of Title 37 of the CFR to have an assignment recorded in the Office.

Assignee 1 Remove

If the Assignee is an Organization check here. ☐

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information:

Address 1			
Address 2			
City		**State/Province**	
Country [i]		Postal Code	
Phone Number		Fax Number	
Email Address			

Additional Assignee Data may be generated within this form by selecting the **Add** button. Add

Signature:

A signature of the applicant or representative is required in accordance with 37 CFR 1.33 and 10.18. Please see 37 CFR 1.4(d) for the form of the signature.

Signature	/Andrea Jo Kamage/			Date (YYYY-MM-DD)	2011-02-24
First Name	Andrea Jo	Last Name	Kamage	Registration Number	43703

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	CGR5001USCNT1
	Application Number	
Title of Invention	Methods and Compositions for Treating Cancer	

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

METHODS AND COMPOSITIONS FOR TREATING CANCER

FIELD OF THE INVENTION

[0001] Methods and compositions for treating cancer are described herein. More particularly, the methods for treating cancer comprise administering a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate (*i.e.*, 3β-acetoxy-17-(3-pyridyl) androsta-5, 16-diene), in combination with at least one additional therapeutic agent, such as an anti-cancer agent or a steroid. Furthermore, disclosed are compositions comprising a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, and at least one additional therapeutic agent such as an anti-cancer agent or a steroid, *e.g.*, a corticosteroid or, more specifically, a glucocorticoid.

BACKGROUND

[0002] The number of people diagnosed with cancer has significantly increased. Of special interest are individuals diagnosed with androgen-dependent disorders, such as prostate cancer, and estrogen-dependent disorders, such as breast cancer since such diagnoses are increasing in number at an alarming rate.

[0003] Prostate cancer is currently the most common non-skin cancer and the second leading cause of cancer-related death in men after lung cancer. The primary course of treatment for patients diagnosed with organ-confined prostate cancer is usually prostatectomy or radiotherapy. Not only are these treatments highly invasive and have undesirable side effects, such localized treatments are not effective on prostate cancer after it has metastasized. Moreover, a large percent of individuals who receive localized treatments will suffer from recurring cancer.

[0004] Additionally, breast cancer incidence in women has increased from one out of every 20 women in 1960 to one out of every eight women in 2005. Moreover, it is the most common cancer among white and African-American women. Similar to treating prostate cancer, most options for women diagnosed with breast cancer are highly invasive and have significant side-effects. Such treatments include surgery, radiation and chemotherapy.

[0005] Hormone therapy is another treatment option for individuals diagnosed with prostate or breast cancer. Hormone therapy is a form of systemic treatment for prostate or breast cancer wherein hormone ablation agents are used to suppress the production or block

the effects of hormones, such as estrogen and progesterone in the body, which are believed to promote the growth of breast cancer, as well as testosterone and dihydrotestosterone, which are believed to promote the growth of prostate cancer. Moreover, hormone therapy is less invasive than surgery and does not have many of the side effects associated with chemotherapy or radiation. Hormone therapy can also be used by itself or in addition to localized therapy and has shown to be effective in individuals whose cancer has metastasized.

[0006] Even though hormone therapy is less invasive and can be used on more advanced stages of cancer, some individuals administered current hormone therapy treatments may not show a significant response or may not show any response at all to such treatments. Additionally, some patients treated with current hormone therapy treatments may also suffer from relapsing or recurring cancer. Currently, such refractory cancer patients are left with very few treatment options.

[0007] Despite the progress made in the treatment of cancer, there remains a need for more effective ways to treat cancer such as, but not limited to, prostate cancer and breast cancer. Additionally, there is a need for effective anti-cancer treatment options for patients who are not responding to current anti-cancer treatments. Also, there is a need for effective anti-cancer treatment options for patients whose cancer has recurred.

SUMMARY OF THE INVENTION

[0008] Described herein are methods for treating a cancer in which a therapeutically effective amount of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate (*i.e.* 3β-acetoxy-17-(3-pyridyl)androsta-5,16-diene), is administered to a patient, *e.g.*, a patient in need thereof, in combination with a therapeutically effective amount of at least one additional therapeutic agent including, but not limited to, an anti-cancer agent or steroid. Such methods can also provide an effective treatment for individuals with a refractory cancer, including individuals who are currently undergoing a cancer treatment. Therefore, in certain embodiments, the method is directed to treating a refractory cancer in a patient, in which a therapeutically effective amount of 17α-hydroxylase/$C_{17,20}$-lyase inhibitor is administered to a patient currently receiving an anti-cancer agent.

[0009] For example, in certain embodiments, the method for the treatment of a cancer in a mammal comprises administering an amount of about 0.01 mg/kg/day to about

100 mg/kg/day of abiraterone acetate and an amount of about 0.1 mg/m^2 to about 20 mg/m^2 of mitoxantrone.

[0010] In another embodiment, the method for the treatment of a cancer in a mammal comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/m^2 to about 175 mg/m^2 of paclitaxel.

[0011] In still other embodiments, the method for the treatment of a cancer in a mammal comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/m^2 to about 100 mg/m^2 of docetaxel.

[0012] Furthermore, described herein is a method for the treatment of a cancer in a mammal comprising administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate; and an amount of about 0.01 mg to about 200 mg of leuprolide, wherein the leuprolide is administered over a period of about 3 days to about 12 months.

[0013] In other embodiments, the method for the treatment of a cancer in a mammal comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 0.01 mg to about 20 mg of goserelin, wherein the goserelin is administered over a period of about 28 days to about 3 months.

[0014] Additionally, in another embodiment, the method for the treatment of a cancer in a mammal comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 0.01 mg to about 20 mg of triptorelin, wherein the triptorelin is administered over a period of about 1 month.

[0015] The method for the treatment of a cancer in a mammal can also comprise administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 0.1 μg/day to about 500 μg/day of seocalcitol, such as about 100 μg/day of seocalcitol.

[0016] Also, the method for the treatment of a cancer in a mammal can comprise administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/day to about 300 mg/day of bicalutamide.

[0017] In yet another embodiment, the method for the treatment of a cancer in a mammal can comprise administering an amount of about 0.01 mg/kg/day to about 100

mg/kg/day of abiraterone acetate and an amount of about 1 mg/day to about 2000 mg/day of flutamide.

[0018] Moreover, the method for the treatment of a cancer in a mammal can comprise administering an amount of about 50 mg/day to about 2000 mg/day of abiraterone acetate and an amount of about 0.01 mg/day to about 500 mg/day of a glucocorticoid including, but not limited to, hydrocortisone, prednisone or dexamethasone.

[0019] Also described herein are compositions for the treatment of cancer that comprise a combination of a therapeutically effective amount of at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and a therapeutically effective amount of at least one additional anti-cancer agent, such as, but not limited to, mitoxantrone, paclitaxel, docetaxel, leuprolide, goserelin, triptorelin, seocalcitol, bicalutamide, flutamide, or a steroid including, but not limited to, hydrocortisone, prednisone, or dexamethasone.

[0020] Finally, single unit dosage forms comprising abiraterone acetate and a glucocorticoid, optionally with carriers, diluents or excipients, are contemplated. Also, kits comprising at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and an additional anti cancer agent or steroid are contemplated. For example, the kit may include a vial containing abiraterone acetate and another vial containing a glucocorticoid.

Definitions

[0021] As used herein and unless otherwise defined the word "cancer," refers to the growth, division or proliferation of abnormal cells in the body. Cancers that can be treated with the methods and the compositions described herein include, but are not limited to, prostate cancer, breast cancer, adrenal cancer, leukemia, lymphoma, myeloma, Waldenström's macroglobulinemia, monoclonal gammopathy, benign monoclonal gammopathy, heavy chain disease, bone and connective tissue sarcoma, brain tumors, thyroid cancer, pancreatic cancer, pituitary cancer, eye cancer, vaginal cancer, vulvar cancer, cervical cancer, uterine cancer, ovarian cancer, esophageal cancer, stomach cancer, colon cancer, rectal cancer, liver cancer, gallbladder cancer, cholangiocarcinoma, lung cancer, testicular cancer, penal cancer, oral cancer, skin cancer, kidney cancers, Wilms' tumor and bladder cancer.

[0022] As used herein, and unless otherwise defined, the terms "treat," "treating" and "treatment" include the eradication, removal, modification, management or control of a

tumor or primary, regional, or metastatic cancer cells or tissue and the minimization or delay of the spread of cancer.

[0023] As used herein, and unless otherwise defined, the term "patient" means an animal, including but not limited to an animal such as a human, monkey, cow, horse, sheep, pig, chicken, turkey, quail, cat, dog, mouse, rat, rabbit, or guinea pig. In one embodiment, the patient is a mammal and in another embodiment the patient is a human. In certain embodiments, the patient can be an adult male or female. In some embodiments, the patient is a male of age about 30 years to about 85 years. In other embodiments, the patient is a female of age about 30 years to about 85 years. In a particular embodiment, the patient has or is susceptible to having (*e.g.*, through genetic or environmental factors) cancer. In a further embodiment, the patient has or is susceptible to having (*e.g.*, through genetic or environmental factors) a tumor. In other embodiments, the patient can be castrated or non-castrated.

[0024] The term "17α-hydroxylase/$C_{17,20}$-lyase inhibitor" as used herein refers to an inhibitor of 17α-hydroxylase/$C_{17,20}$-lyase, (which is an enzyme in testosterone synthesis), an analog thereof, derivative thereof, metabolite thereof or pharmaceutically acceptable salt thereof. Also, unless otherwise noted, reference to a particular 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can include analogs, derivatives, metabolites or pharmaceutically acceptable salts of such particular 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0025] The term "anti-cancer agent" as used herein refers to any therapeutic agent that directly or indirectly kills cancer cells or directly or indirectly prohibits stops or reduces the proliferation of cancer cells. It should be noted that even though throughout this specification and in the claims the phrase "anti-cancer agent" is written as a singular noun, for example; "an anti-cancer agent" or "the anti-cancer agent," the phrase "anti-cancer agent" should not be interpreted as being limited to the inclusion of a single anti-cancer agent.

[0026] As used herein, and unless otherwise defined, the phrase "therapeutically effective amount" when used in connection with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor or therapeutic agent means an amount of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor or therapeutic agent effective for treating a disease or disorder disclosed herein, such as cancer.

[0027] As used herein and unless otherwise defined the phrase "refractory cancer," means cancer that is not responding to an anti-cancer treatment or cancer that is not

responding sufficiently to an anti-cancer treatment. Refractory cancer can also include recurring or relapsing cancer.

[0028] As used herein and unless otherwise defined the phrase "refractory patient," means a patient who has refractory cancer.

[0029] As used herein and unless otherwise defined the phrase "relapse cancer," means cancer that was at one time responsive to an anti-cancer treatment but has become no longer responsive to such treatment or is no longer responding sufficiently to such treatment.

[0030] As used herein and unless otherwise defined the phrase "recurring cancer," means cancer that has returned after a patient has been earlier diagnosed with cancer, under gone treatment or had been previously diagnosed as cancer-free.

[0031] As used herein and unless otherwise defined the term "derivative" refers to a chemically modified compound wherein the chemical modification takes place at one or more functional groups of the compound. The derivative may retain or improve the pharmacological activity of the compound from which it is derived.

[0032] As used herein and unless otherwise defined the term "analog" refers to a chemical compound that is structurally similar to another but differs slightly in composition (as in the replacement of one atom by an atom of a different element or in the presence of a particular functional group).

[0033] As used herein and unless otherwise defined the phrase "pharmaceutically acceptable salt" refers to any salt of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor which retains the biological effectiveness of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor. Examples of pharmaceutically acceptable salts include, but are not limited to, acetates, sulfates, pyrosulfates, bisulfates, sulfites, bisulfites, phosphates, monohydrogenphosphates, dihydrogenphosphates, metaphosphates, pyrophosphates, chlorides, bromides, iodides, acetates, propionates, decanoates, caprylates, acrylates, formates, isobutyrates, caproates, heptanoates, propiolates, oxalates, malonates, succinates, suberates, sebacates, fumarates, maleates, butyne-1,4-dioates, hexyne-1,6-dioates, benzoates, chlorobenzoates, methylbenzoates, dinitrobenzoates, hydroxybenzoates, methoxybenzoates, phthalates, sulfonates, xylenesulfonates, phylacetates, phenylpropionates, phenylbutyrates, citrates, lactates, gamma-hydroxybutyrates, glycollates, tartarates, alkanesulfonates (*e.g.* methane-sulfonate or mesylate), propanesulfonates, naphthalene-1-sulfonates, naphthalene-2-

sulfonates, and mandelates. Several of the officially approved salts are listed in Remington: The Science and Practice of Pharmacy, Mack Publ. Co., Easton.

DETAILED DESCRIPTION OF THE INVENTION

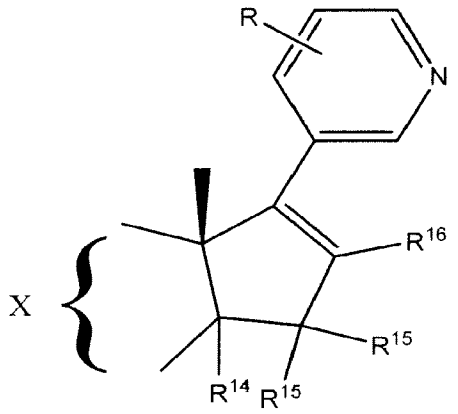
[0034] The methods described herein for treating cancer comprise administering to a mammal, preferably a human, a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor in addition to at least one therapeutic agent, such as an anti-cancer agent or steroid, particularly a glucocorticoid. The compositions described herein comprise a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and at least one additional therapeutic agent, such as an anti-cancer agent or steroid, particularly a corticosteroid or glucocorticoid. Other anti-cancer treatments such as, administration of yet another anti-cancer agent, radiotherapy, chemotherapy, photodynamic therapy, surgery or other immunotherapy, can be used with the methods and compositions.

17α-hydroxylase/$C_{17,20}$-lyase Inhibitors

[0035] 17α-hydroxylase/$C_{17,20}$-lyase inhibitors have been shown to be useful in the treatment of cancer, specifically hormone-dependent disorders such as, androgen-dependent and estrogen-dependent disorders like prostate cancer and breast cancer respectively, as described in United States Patent No. 5,604,213 to Barrie *et al.*, which is herein incorporated by reference in its entirety.

[0036] In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be 17-(3-pyridyl)androsta-5,16-dien-3β-ol; 17-(3-pyridyl)androsta-3,5,16-triene; 17-(3-pyridyl)androsta-4,16-dien-3-one; 17-(3-pyridyl)estra-1,3,5[10],16-tetraen-3-ol; 17-(3-pyridyl)-5α-androst-16-en-3α-ol; 17-(3-pyridyl)-5α -androst-16-en-3-one; 17-(3-pyridyl)-androsta-4,16-diene-3,11-dione; 17-(3-pyridyl)-androsta-3,5,16-trien-3-ol; 6α-and 6β-fluoro-17-(3-pyridyl)androsta-4,16-dien-3-one; 17-(3-pyridyl)androsta-4,16-dien-3,6-dione; 3α-trifluoromethyl-17-(3-pyridyl)androst-16-en-3β-ol or their acid addition salts and 3-esters as well as metabolites, analogs, derivatives or a pharmaceutically acceptable salt thereof.

[0037] In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can have the structure of formula (I):



(I)

wherein X represents the residue of the A, B and C rings of a steroid which can be, without limitation, androstan-3α- or 3β-ol; androst-5-en-3α- or 3β-ol; androst-4-en-3-one; androst-2-ene; androst-4-ene; androst-5-ene; androsta-5,7-dien-3α or 3β-ol ; androsta-1,4-dien-3-one; androsta-3,5-diene; androsta-3,5-diene-3-ol; estra-1,3,5[10]-triene; estra-1,3,5[10]-trien-3-ol; 5α -androstan-3-one; androst-4-ene-3,11-dione; 6-fluoroandrost-4-ene-3-one; or androstan-4-ene-3,6-dione; each of which, where structurally permissible, can be further derivatized in one or more of the following ways, including, but not limited to, to form 3-esters; to have one or more carbon or carbon ring double bonds in any of the 5,6-, 6,7-, 7,8-, 9,11- and 11,12-positions; as 3-oximes; as 3-methylenes; as 3-carboxylates; as 3-nitriles; as 3-nitros; as 3-desoxy derivatives; to have one or more hydroxy, halo, C_{1-4} -alkyl, trifluoro-methyl, C_{1-4} -alkoxy, C_{1-4} -alkanoyloxy, benzoyloxy, oxo, methylene or alkenyl substituents in the A, B, or C-ring; or to be 19-nor;

R represents a hydrogen atom or an alkyl group of 1-4 carbon atoms;

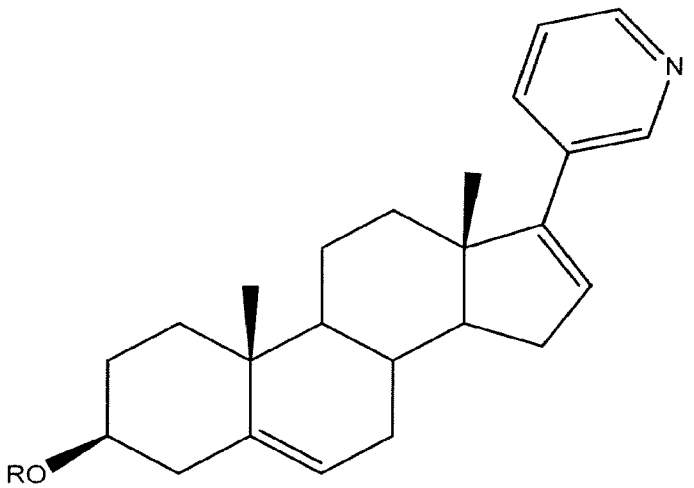
R^{14} represents a hydrogen atom, a halogen atom or an alkyl group of 1 to 4 carbon atoms;

each of the R^{15} substituents independently represents a hydrogen atom or an alkyl or alkoxy group of 1-4 carbon atoms, a hydroxy group or an alkylcarbonyloxy group of 2 to 5 carbon atoms or together represent an oxo or methylene group or R^{14} and one of the R^{15} groups together represent a double bond and the other R^{15} group represents a hydrogen atom or an alkyl group of 1 to 4 carbon atoms; and

R^{16} represents a hydrogen atom, halogen atom, or an alkyl group of 1 to 4 carbon atoms, in the form of the free bases or pharmaceutically acceptable acid addition salts, but excluding 3β-acetoxy-17-(3-pyridyl)androsta-5,14,16-triene, 3β,15α- and 3β,15β-diacetoxy-17-(3-pyridyl)androsta-5,16-diene and 3β-methoxy-17-(3-pyridyl-5α-androst-16-ene.

Suitable inhibitors also include metabolites, derivatives, analogs, or pharmaceutically acceptable salts of formula (I).

[0038] In another embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can have the structure of formula (I):

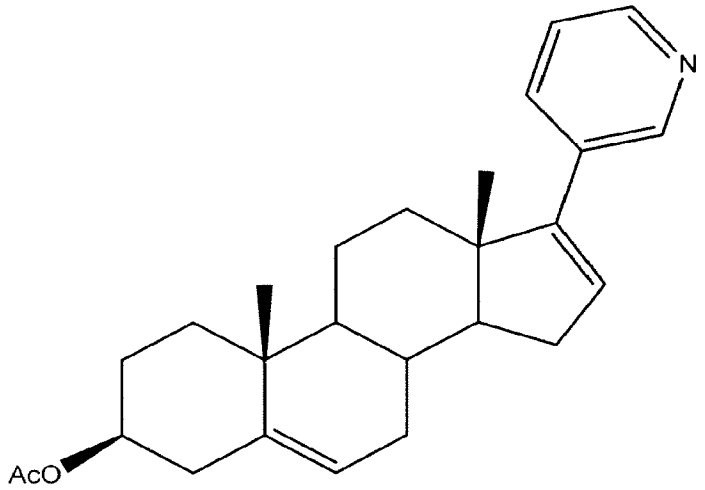


(I)

wherein R represents hydrogen or a lower acyl group having 1 to 4 carbons. Suitable inhibitors also include derivatives, analogs, or pharmaceutically acceptable salts of formula (I).

[0039] In still another embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be a 3β-alkanoyloxy-17-(3-pyridyl) androsta-5, 16-diene in which the alkanoyloxy group has from 2 to 4 carbon atoms.

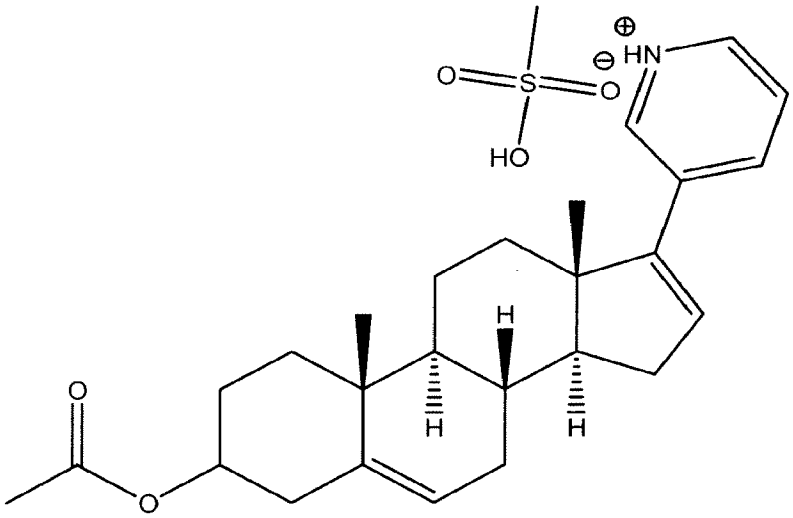
[0040] In a preferred embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises abiraterone acetate or 3β-acetoxy-17-(3-pyridyl)androsta-5,16-diene which has the following structural formula:



(II)

and pharmaceutically acceptable salts thereof.

[0041] Preferred salts of abiraterone acetate and methods of making such salts are also disclosed in United States Provisional Application No. 60/603,559 to Hunt, which is incorporated by reference in its entirety. Preferred salts include, but are not limited to, acetates, citrates, lactates, alkanesulfonates (e.g. methane-sulfonate or mesylate) and tartarates. Of special interest is the abiraterone acetate mesylate salt (*i.e.* 3β-acetoxy-17-(3-pyridyl)androsta-5,16-diene mesylate salt) which has the following structural formula:



(III)

[0042] The 17α-hydroxylase/$C_{17,20}$-lyase inhibitors can be made according to any method known to one skilled in the art. For example, such inhibitors can be synthesized according to the method disclosed in United States Patent Nos. 5,604,213 and 5,618,807 to Barrie *et al.*, herein incorporated by reference. Another method of making 17α-

hydroxylase/$C_{17,20}$-lyase inhibitors is disclosed in United States provisional application 60/603,558 to Bury, herein incorporated by reference.

[0043] The amount of 17α-hydroxylase/$C_{17,20}$-lyase inhibitor administered to a mammal having cancer is an amount that is sufficient to treat the cancer, whether the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor is administered alone or in combination with an additional anti-cancer treatment, such as an additional anti-cancer agent.

Additional Therapeutic Agents

[0044] Suitable compounds that can be used in addition to 17α-hydroxylase/$C_{17,20}$-lyase inhibitors as an anti-cancer agent include, but are not limited to, hormone ablation agents, anti-androgen agents, differentiating agents, anti-neoplastic agents, kinase inhibitors, anti-metabolite agents, alkylating agents, antibiotic agents, immunological agents, interferon-type agents, intercalating agents, growth factor inhibitors, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response modifiers, mitotic inhibitors, matrix metalloprotease inhibitors, genetic therapeutics, and anti-androgens. The amount of the additional anti-cancer agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor. Below are lists of examples of some of the above classes of anti-cancer agents. The examples are not all inclusive and are for purposes of illustration and not for purposes of limitation. Many of the examples below could be listed in multiple classes of anti-cancer agents and are not restricted in any way to the class in which they are listed in.

[0045] Suitable hormonal ablation agents include, but are not limited to, androgen ablation agents and estrogen ablation agents. In preferred embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor is administered with a hormonal ablation agent, such as deslorelin, leuprolide, goserelin or triptorelin. Even though throughout this specification and in the claims the phrase "hormonal ablation agent" is written as a singular noun, for example; "a hormonal ablation agent" or "the hormonal ablation agent," the phrase "hormonal ablation agent" should not be interpreted as being limited to the inclusion of a single hormonal ablation agent. The amount of the hormonal ablation agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0046] Suitable anti-androgen agents include but are not limited to bicalutamide, flutamide and nilutamide. The amount of the anti-androgen agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0047] In another embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor may be administered with a differentiating agent. Suitable differentiating agents include, but are not limited to, polyamine inhibitors; vitamin D and its analogs, such as, calcitriol, doxercalciferol and seocalcitol; metabolites of vitamin A, such as, ATRA, retinoic acid, retinoids; short-chain fatty acids; phenylbutyrate; and nonsteroidal anti-inflammatory agents. The amount of the differentiating agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0048] In another preferred embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor may be administered with an anti-neoplastic agent, including, but not limited to, tubulin interacting agents, topoisomerase inhibitors and agents, acitretin, alstonine, amonafide, amphethinile, amsacrine, ankinomycin, anti-neoplaston, aphidicolin glycinate, asparaginase, baccharin, batracylin, benfluron, benzotript, bromofosfamide, caracemide, carmethizole hydrochloride, chlorsulfaquinoxalone, clanfenur, claviridenone, crisnatol, curaderm, cytarabine, cytocytin, dacarbazine, datelliptinium, dihaematoporphyrin ether, dihydrolenperone, dinaline, distamycin, docetaxel, elliprabin, elliptinium acetate, epothilones, ergotamine, etoposide, etretinate, fenretinide, gallium nitrate, genkwadaphnin, hexadecylphosphocholine, homoharringtonine, hydroxyurea, ilmofosine, isoglutamine, isotretinoin, leukoregulin, lonidamine, merbarone, merocyanlne derivatives, methylanilinoacridine, minactivin, mitonafide, mitoquidone, mitoxantrone, mopidamol, motretinide, N-(retinoyl)amino acids, N-acylated-dehydroalanines, nafazatrom, nocodazole derivative, ocreotide, oquizanocine, paclitaxel, pancratistatin, pazelliptine, piroxantrone, polyhaematoporphyrin, polypreic acid, probimane, procarbazine, proglumide, razoxane, retelliptine, spatol, spirocyclopropane derivatives, spirogermanium, strypoldinone, superoxide dismutase, teniposide, thaliblastine, tocotrienol, topotecan, ukrain, vinblastine sulfate, vincristine, vindesine, vinestramide, vinorelbine, vintriptol, vinzolidine, and withanolides. The amount of the anti-neoplastic agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0049] The 17α-hydroxylase/$C_{17,20}$-lyase inhibitors may also be used with a kinase inhibitor including p38 inhibitors and CDK inhibitors, TNF inhibitors, metallomatrix proteases inhibitors (MMP), COX-2 inhibitors including celecoxib, rofecoxib, parecoxib, valdecoxib, and etoricoxib, SOD mimics or $\alpha_v\beta_3$ inhibitors. The amount of the kinase inhibitor administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0050] In another embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor may be administered with an anti-metabolite agent. Suitable anti-metabolite agents may be selected from, but not limited to, 5-FU-fibrinogen, acanthifolic acid, aminothiadiazole, brequinar sodium, carmofur, cyclopentyl cytosine, cytarabine phosphate stearate, cytarabine conjugates, dezaguanine, dideoxycytidine, dideoxyguanosine, didox, doxifluridine, fazarabine, floxuridine, fludarabine phosphate, 5-fluorouracil, N-(2'-furanidyl)-5-fluorouracil, isopropyl pyrrolizine, methobenzaprim, methotrexate, norspermidine, pentostatin, piritrexim, plicamycin, thioguanine, tiazofurin, trimetrexate, tyrosine kinase inhibitors, and uricytin. The amount of the anti-metabolite agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0051] In another embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor may be administered with an alkylating agent. Suitable alkylating agents may be selected from, but not limited to, aldo-phosphamide analogues, altretamine, anaxirone, bestrabucil, budotitane, carboplatin, carmustine, chlorambucil, cisplatin, cyclophosphamide, cyplatate, diphenylspiromustine, diplatinum cytostatic, elmustine, estramustine phosphate sodium, fotemustine, hepsul-fam, ifosfamide, iproplatin, lomustine, mafosfamide, mitolactol, oxaliplatin, prednimustine, ranimustine, semustine, spiromustine, tauromustine, temozolomide, teroxirone, tetraplatin and trimelamol. The amount of the alkylating agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0052] In another preferred embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor may be administered with an antibiotic agent. Suitable antibiotic agents may be selected from, but not limited to, aclarubicin, actinomycin D, actinoplanone, adriamycin, aeroplysinin derivative, amrubicin, anthracycline, azino-mycin-A, bisucaberin, bleomycin

sulfate, bryostatin-1, calichemycin, chromoximycin, dactinomycin, daunorubicin, ditrisarubicin B, dexamethasone, doxorubicin, doxorubicin-fibrinogen, elsamicin-A, epirubicin, erbstatin, esorubicin, esperamicin-Al, esperamicin-Alb, fostriecin, glidobactin, gregatin-A, grincamycin, herbimycin, corticosteroids such as hydrocortisone, idarubicin, illudins, kazusamycin, kesarirhodins, menogaril, mitomycin, neoenactin, oxalysine, oxaunomycin, peplomycin, pilatin, pirarubicin, porothramycin, prednisone, prednisolone, pyrindanycin A, rapamycin, rhizoxin, rodorubicin, sibanomicin, siwenmycin, sorangicin-A, sparsomycin, talisomycin, terpentecin, thrazine, tricrozarin A, and zorubicin. The amount of the antibiotic agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0053] Alternatively, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitors may also be used with other anti-cancer agents, including but not limited to, acemannan, aclarubicin, aldesleukin, alemtuzumab, alitretinoin, altretamine, amifostine, amsacrine, anagrelide, anastrozole, ancestim, bexarotene, broxuridine, capecitabine, celmoleukin, cetrorelix, cladribine, clotrimazole, daclizumab, dexrazoxane, dilazep, docosanol, doxifluridine, bromocriptine, carmustine, cytarabine, diclofenac, edelfosine, edrecolomab, eflornithine, emitefur, exemestane, exisulind, fadrozole, filgrastim, finasteride, fludarabine phosphate, formestane, fotemustine, gallium nitrate, gemcitabine, glycopine, heptaplatin, ibandronic acid, imiquimod, iobenguane, irinotecan, irsogladine, lanreotide, leflunomide, lenograstim, lentinan sulfate, letrozole, liarozole, lobaplatin, lonidamine, masoprocol, melarsoprol, metoclopramide, mifepristone, miltefosine, mirimostim, mitoguazone, mitolactol, molgramostim, nafarelin, nartograstim, nedaplatin, nilutamide, noscapine, oprelvekin, osaterone, oxaliplatin, pamidronic acid, pegaspargase, pentosan polysulfate sodium, pentostatin, picibanil, pirarubicin, porfimer sodium, raloxifene, raltitrexed, rasburicase, rituximab, romurtide, sargramostim, sizofiran, sobuzoxane, sonermin, suramin, tasonermin, tazarotene, tegafur, temoporfin, temozolomide, teniposide, tetrachlorodecaoxide, thalidomide, thymalfasin, thyrotropin alfa, topotecan, toremifene, trastuzumab, treosulfan, tretinoin, trilostane, trimetrexate, ubenimex, valrubicin, verteporfin, vinorelbine. The amount of the anti-cancer agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0054] The 17α-hydroxylase/$C_{17,20}$-lyase inhibitors may also be administered or combined with steroids, such as corticosteroids or glucocorticoids. The 17α-hydroxylase/$C_{17,20}$-lyase inhibitors and the steroid may be administered in the same or in different compositions. Non-limiting examples of suitable steroids include hydrocortisone, prednisone, or dexamethasone. The amount of the steroid administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0055] In one embodiment, provided herein are methods and compositions comprising both abiraterone acetate and a steroid particularly a corticosteroid, or more particularly a glucocorticoid. Steroids within the scope of the disclosure include, but are not limited to, (1) hydrocortisone (cortisol; cyprionate (*e.g.*, CORTEF), oral; sodium phosphate injection (HYDROCORTONE PHOSPHATE); sodium succinate (*e.g.*, A-HYDROCORT, Solu-CORTEF); cortisone acetate oral or injection forms, etc.), (2) dexamethasone (*e.g.*, Decadron, oral; Decadron-LA injection, etc.), (3) prednisolone (*e.g.*, Delta-CORTEF, prednisolone acetate (ECONOPRED), prednisolone sodium phosphate (HYDELTRASOL), prednisolone tebutate (HYDELTRA-TBA, etc.)), or (4) prednisone (*e.g.*, DELTASONE, etc.) and combinations thereof. See, *e.g.*, GOODMAN & GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, 10TH EDITION 2001.

[0056] In a specific embodiment, single unit solid oral dosage forms which comprise an amount from about 50 mg to about 300 mg of abiraterone acetate and an amount from about 0.5 mg to about 3.0 mg of a steroid, *e.g.*, glucocorticoid in a single composition, optionally with excipients, carriers, diluents, etc. is contemplated. For instance, the single unit dosage form can comprise about 250 mg of abiraterone acetate and about 1.0 mg, 1.25 mg, 1.5 mg, or 2.0 mg of a steroid, such as but not limited to corticosteroids or glucocorticoids.

Administration of the 17α-hydroxylase/$C_{17,20}$-lyase Inhibitor and an Additional Therapeutic Agent

[0057] The 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the additional therapeutic agent, such as an anti-cancer agent or a steroid can be administered by any method known to one skilled in the art. In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the additional therapeutic agent can be in separate compositions prior to administration.

In the alternative, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the additional therapeutic agent can be combined into a single composition for administration.

[0058] The 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the additional therapeutic agent can be administered sequentially or simultaneously. If administered sequentially, the order of administration is flexible. For instance, 17α-hydroxylase/$C_{17,20}$-lyase inhibitor acetate can be administered prior to administration of the additional therapeutic agent. Alternatively, administration of the additional therapeutic agent can precede administration of 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0059] Whether they are administered as separate compositions or in one composition, each composition is preferably pharmaceutically suitable for administration. Moreover, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the therapeutic agent, if administered separately, can be administered by the same or different modes of administration. Examples of modes of administration include parenteral (*e.g.*, subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, intradermal, intraperitoneal, intraportal, intra-arterial, intrathecal, transmucosal, intra-articular, and intrapleural,), transdermal (*e.g.*, topical), epidural, and mucosal (*e.g.*, intranasal) injection or infusion, as well as oral, inhalation, pulmonary, and rectal administration. In specific embodiments, both are oral.

[0060] For example, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be administered transdermally and the additional therapeutic agent can be administered parenterally. Alternatively, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be administered orally, such as in a tablet, caplet or capsule, while the additional therapeutic agent can be administered intravenously. Such intravenous administered therapeutic agents include, but are not limited to, docetaxel injections, such as Taxotere®; paclitaxel injections, such as Paclitaxel® and mitoxantrone injections, such as Novantrone®. Also, the additional therapeutic agent can be in the form of depots or implants such as leuprolide depots and implants, *e.g.* Viadur® and Lupron Depot®; triptorelin depots, *e.g.* Trelstar®; goserelin implants, *e.g.* Zoladex®.

[0061] The suitable daily dosage of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor depends upon a number of factors, including, the nature of the severity of the condition to be treated, the particular inhibitor, the route of administration and the age, weight, and response of the individual patient. Suitable daily dosages of 17α-hydroxylase/$C_{17,20}$-lyase inhibitors can generally range from about 0.0001 mg/kg/day to about 1000 mg/kg/day, or

from about 0.001 mg/kg/day to about 200 mg/kg/day, or from about 0.01 mg/kg/day to about 200 mg/kg/day, or from about 0.01 mg/kg/day to about 100 mg/kg/day in single or multiple doses.

[0062] In some embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be administered in an amount from about 0.004 mg/day to about 5,000 mg/day, or from about 0.04 mg/day to about 3,000 mg/day, or from about 0.4 mg/day to about 1500 mg/day. In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be administered in an amount from about 0.1 mg/day to about 2000 mg/day or from about 1 mg/day to about 2000 mg/day or from about 50 mg/day to about 2000 mg/day or from about 100 mg/day to about 1500 mg/day or from about 5 mg/day to about 1,000 mg/day or from about 5 mg/day to about 900 mg/day or from about 10 mg/day to about 800 mg/day or from about 15 mg/day to about 700 mg/day or from about 20 mg/day to about 600 mg/day or from about 25 mg/day to about 500 mg/day in single or multiple doses.

[0063] In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor is co-administered with an additional anti-cancer agent such as mitoxantrone, paclitaxel or docetaxel. For example, a method for the treatment of a cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of mitoxantrone. For example, the abiraterone acetate can be administered in an amount of about 0.01 mg/kg/day to about 100 mg/kg/day and the mitoxantrone can be administered in an amount of about 0.1 mg/m^2 to about 20 mg/m^2. Preferably, the mitoxantrone is administered over a period of between about 10 to about 20 minutes once every 21 days.

[0064] Also, a method for the treatment of a cancer in a mammal can comprise administering an amount of abiraterone acetate and an amount of paclitaxel. In one embodiment, the abiraterone acetate can be administered in an amount of about 0.01 mg/kg/day to about 100 mg/kg/day and the paclitaxel can be administered in the amount of about 1 mg/m^2 to about 175 mg/m^2. Preferably, the paclitaxel is administered over a period of between about 2 to about 5 hours once every three months.

[0065] Additionally, a method for the treatment of a cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of docetaxel. For example, the abiraterone acetate can be administered in an amount of about 0.01 mg/kg/day to about 100 mg/kg/day and the docetaxel can be administered in an amount of about 1 mg/m^2 to about 100 mg/m^2. Preferably, the docetaxel is administered over a period of between about 1 to about 2 hours once every three weeks.

[0066] In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor is administered along with an anti-cancer agent that comprises a hormonal ablation agent, including, but not limited to, leuprolide, goserelin, or triptorelin. For example, one method for the treatment of a cancer in a mammal also comprises administering an amount of abiraterone acetate and an amount of leuprolide. The amount of abiraterone acetate can be about 0.01 mg/kg/day to about 100 mg/kg/day and the amount of leuprolide can be about 0.01 mg to about 200 mg over a period of about 3 days to about 12 months. Preferably, the leuprolide is administered in the amount of about 3.6 mg of leuprolide over a period of about 3 days to about 12 months.

[0067] Additionally, the methods for the treatment of cancer in a mammal include administering an amount of abiraterone acetate and an amount of goserelin. For example, the amount of abiraterone acetate can be about 0.01 mg/kg/day to about 100 mg/kg/day and the amount of goserelin can be about 0.01 mg to about 20 mg over a period of about 28 days to about 3 months. Preferably, the goserelin is administered in the amount of about 3.6 mg to about 10.8 mg over a period of about 28 days to about 3 months.

[0068] In certain embodiments the methods for the treatment of cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of triptorelin. For example, the amount of abiraterone acetate can be about 0.01 mg/kg/day to about 100 mg/kg/day and the amount of triptorelin can be about 0.01 mg to about 20 mg, over a period of about 1 month, preferably the triptorelin is administered in the amount of about 3.75 mg over a period of about 1 month.

[0069] Also, in one embodiment, the method for the treatment of a cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of seocalcitol. For instance, the method involves administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 0.1 μg/day to about 500 μg/day of seocalcitol, such as about 100 μg/day of seocalcitol.

[0070] In another embodiment, the method for the treatment of a cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of bicalutamide. For instance, the method involves administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/day to about 300 mg/day of bicalutamide.

[0071] In yet another embodiment, the method for the treatment of a cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of

flutamide. For example, the method comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/day to about 2000 mg/day of flutamide.

[0072] Moreover, the method for the treatment of a cancer in a mammal can comprise administering an amount of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor such as abiraterone acetate and an amount of a glucocorticoid including, but not limited to, hydrocortisone, prednisone or dexamethasone. For example, the method can comprise administering an amount of about 50 mg/day to about 2000 mg/day of abiraterone acetate and an amount of about 0.01 mg/day to about 500 mg/day of hydrocortisone. In other instances, the method can comprise administering an amount of about 500 mg/day to about 1500 mg/day of abiraterone acetate and an amount of about 10 mg/day to about 250 mg/day of hydrocortisone.

[0073] The method for the treatment of a cancer can also comprise administering an amount of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate, and an amount of a glucocorticoid, such as prednisone. For example, the method can comprise administering an amount of about 50 mg/day to about 2000 mg/day of abiraterone acetate and an amount of about 0.01 mg/day to about 500 mg/day of prednisone. Also, the method can comprise administering an amount of about 500 mg/day to about 1500 mg/day of abiraterone acetate and an amount of about 10 mg/day to about 250 mg/day of prednisone.

[0074] In addition, the method for the treatment of a cancer can also comprise administering an amount of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate, and an amount of a glucocorticoid, such as dexamethasone. For example, the method can comprise administering an amount of about 50 mg/day to about 2000 mg/day of abiraterone acetate and an amount of about 0.01 mg/day to about 500 mg/day of dexamethasone. Also, the method can comprise administering an amount of about 500 mg/day to about 1500 mg/day of abiraterone acetate and an amount of about 0.5 mg/day to about 25 mg/day of dexamethasone.

Compositions Containing a 17α-hydroxylase/$C_{17,20}$-lyase Inhibitor and an Additional Therapeutic Agent

[0075] In certain embodiments, the compositions can contain a combination of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, preferably abiraterone acetate, and any of the therapeutic agents recited above. Whether the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and

the additional therapeutic agent are administered in separate compositions or as a single composition, the compositions can take various forms. For example, the compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders or sustained-release formulations, depending on the intended route of administration.

[0076] For topical or transdermal administration, the compositions can be formulated as solutions, gels, ointments, creams, suspensions or salves.

[0077] For oral administration, the compositions may be formulated as tablets, pills, dragees, troches, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated.

[0078] The composition may also be formulated in rectal or vaginal compositions such as suppositories or retention enemas that contain conventional suppository bases such as cocoa butter or other glycerides.

[0079] In addition to the formulations described previously, the composition may also be formulated as a depot preparation. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the therapeutic agents may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

[0080] Additionally, the composition may be delivered using a sustained-release system, such as semi-permeable matrices of solid polymers containing the composition. Various forms of sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature can release the composition over a period of hours, days, weeks, months. For example a sustained release capsule can release the compositions over a period of 100 days or longer. Depending on the chemical nature and the biological stability of the composition, additional strategies for stabilization may be employed.

[0081] The compositions can further comprise a pharmaceutically acceptable carrier. The term "carrier" refers to a diluent, adjuvant (*e.g.*, Freund's adjuvant (complete and incomplete)), excipient, or vehicle with which the therapeutic is administered.

[0082] For parenteral administrations, the composition can comprise one or more of the following carriers: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerin, propylene glycol or other synthetic solvents; antibacterial

agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The parenteral preparation can be enclosed in ampules, disposable syringes or multiple dose vials made of glass or plastic.

[0083] For oral solid formulations suitable carriers include fillers such as sugars, *e.g.*, lactose, sucrose, mannitol and sorbitol; cellulose preparations such as maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, fats and oils; granulating agents; and binding agents such as microcrystalline cellulose, gum tragacanth or gelatin; disintegrating agents, such as cross-linked polyvinylpyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate, Primogel, or corn starch; lubricants, such as magnesium stearate or Sterotes; glidants, such as colloidal silicon dioxide; a sweetening agent, such as sucrose or saccharin; or flavoring agents, such as peppermint, methyl salicylate, or orange flavoring. If desired, solid dosage forms may be sugar-coated or enteric-coated using standard techniques.

[0084] For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy injectability with a syringe. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars; polyalcohols such as mannitol, sorbitol; sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

[0085] Also for intravenous administration, the compositions may be formulated in solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. The solution may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. In a preferred embodiment, the compositions are formulated in sterile solutions.

[0086] For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories.

[0087] For administration by inhalation, the compositions may be formulated as an aerosol spray from pressurized packs or a nebulizer, with the use of a suitable propellant, *e.g.*, dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol, the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the composition and a suitable powder base such as lactose or starch.

[0088] The pharmaceutical compositions may be manufactured by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes.

[0089] One example of a composition comprising a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and an additional therapeutic agent is an oral composition or composition suitable for oral administration comprising abiraterone acetate in combination with a steroid. For example, the oral composition can be a solid dosage form such as a pill, a tablet or a capsule. The oral composition can comprise about 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, 450 mg, 500 mg, 550 mg, 600 mg, 650 mg, 700 mg, 750 mg, 800 mg, 850 mg, 900 mg, 950 mg, or 1000 mg of abiraterone acetate. The oral composition can comprises about 0.25 mg, 0.5 mg, 0.75 mg, 1.0 mg, 1.25 mg, 1.5 mg, 1.75 mg, 2.0 mg, 2.25 mg, 2.5 mg, 2.75 mg, 3.0 mg, 3.25 mg, 3.5 mg, 3.75 mg, 4.0 mg, 4.25 mg, 4.5 mg, 4.75 mg, 5.0 mg, 7.5 mg, 10 mg, 20 mg, 30 mg, 40 mg or 50 mg of a steroid, such as a glucocorticoid.

[0090] In one embodiment, the oral composition can comprise about 50 mg to about 500 mg of abiraterone acetate and an amount of about 0.25 mg to about 3.5 mg of the

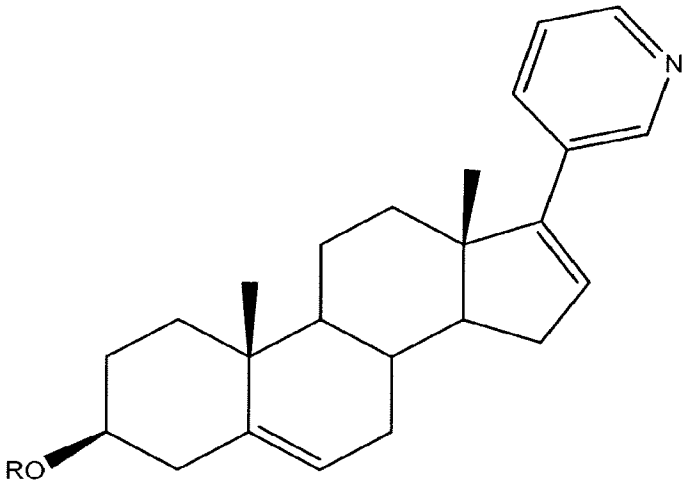
steroid, such as hydrocortisone, prednisone or dexamethasone. In other instances, the composition can comprise about 50 mg to about 300 mg of abiraterone acetate and an amount of about 1.0 mg to about 2.5 mg of the steroid, such as hydrocortisone, prednisone or dexamethasone. In another embodiment the composition can comprise about 50 mg to about 300 mg of abiraterone acetate and about 0.5 mg to about 3.0 mg of a steroid. For example, the oral composition can be a tablet containing 250 mg of abiraterone acetate; 1.25 mg or 2.0 mg of a steroid, such as hydrocortisone, prednisone or dexamethasone; and one or more carriers, excipients, diluents or additional ingredients. Additionally, the oral composition can be a capsule containing 250 mg of abiraterone acetate; 1.25 mg or 2.0 mg of a steroid, such as hydrocortisone, prednisone or dexamethasone; and one or more carriers, excipients, diluents or additional ingredients.

[0091] The description contained herein is for purposes of illustration and not for purposes of limitation. The methods and compositions described herein can comprise any feature described herein either alone or in combination with any other feature(s) described herein. Changes and modifications may be made to the embodiments of the description. Furthermore, obvious changes, modifications or variations will occur to those skilled in the art. Also, all references cited above are incorporated herein, in their entirety, for all purposes related to this disclosure.

THE CLAIMS

What is claimed is:

1. A method for the treatment of a cancer in a mammal comprising administering a therapeutically effective amount of at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and a therapeutically effective amount of at least one additional therapeutic agent to a patient having a cancer; wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises a compound of the formula (I) or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

2. The method of claim 1, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises abiraterone acetate or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof.

3. The method of claim 2, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises the mesylate salt of abiraterone acetate.

4. The method of claim 1, wherein the therapeutically effective amount of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg/day to about 2000 mg/day.

5. The method of claim 1, wherein the additional therapeutic agent comprises an anti-neoplastic agent, an alkylating agent, an anti-metabolite agent, an antibiotic agent, a hormonal ablation agent, an androgen ablation agent, an anti-androgen agent, or a steroid.

6. The method of claim 1, wherein the additional therapeutic agent comprises mitoxantrone, paclitaxel, docetaxel, leuprolide, goserelin, triptorelin, seocalcitol, bicalutamide, flutamide, hydrocortisone, prednisone or dexamethasone.

7. The method of claim 1, wherein the 17α-hydroxylase/$C_{17,20}$ lyase inhibitor and the additional therapeutic agent are administered to the mammal in a single composition comprising the 17α-hydroxylase/$C_{17,20}$ lyase inhibitor and the additional therapeutic agent.

8. The method of claim 1, wherein the 17α-hydroxylase/$C_{17,20}$ lyase inhibitor and the additional therapeutic agent are administered separately to the mammal.

9. The method of claim 1, wherein the cancer is prostate cancer or breast cancer.

10. The method of claim 1, wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 0.1 mg/m^2 to about 20 mg/m^2 of mitoxantrone.

11. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 1 mg/m^2 to about 175 mg/m^2 of paclitaxel.

12. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 1 mg/m^2 to about 100 mg/m^2 of docetaxel.

13. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100

mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 0.01 to about 200 mg of leuprolide over a period of about 3 days to about 12 months.

14. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 20 mg of goserelin over a period of about 28 days to about 3 months.

15. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 0.01 mg to about 20 mg of triptorelin over a period of about 1 month.

16. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 0.1 μg/day to about 500 μg/day of seocalcitol.

17. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 1 mg/day to about 300 mg/day of bicalcutamide.

18. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 1 mg/day to about 2000 mg/day flutamide.

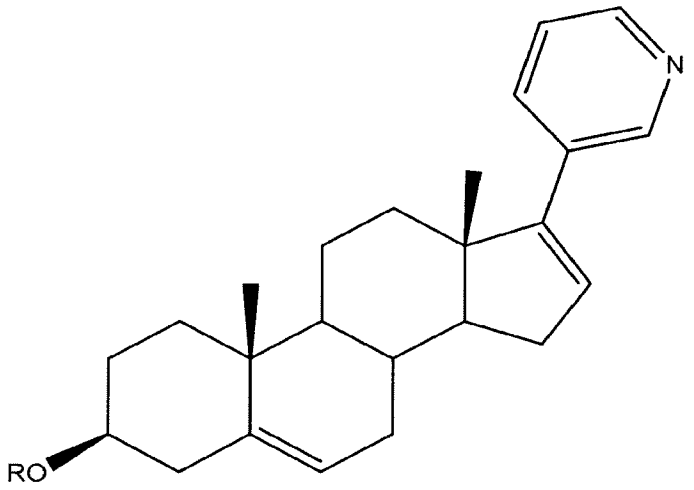
19. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg/day to about 2000 mg/day of abiraterone acetate and the therapeutically effective amount of the at least one

additional therapeutic agent comprises about 10 mg/day to about 250 mg/day of hydrocortisone.

20. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg/day to about 2000 mg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 10 mg/day to about 250 mg/day prednisone.

21. The method of claim 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg/day to about 2000 mg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 0.5 mg/day to about 25 mg/day dexamethasone.

22. A method for treating a patient having a refractory prostate or breast cancer who is currently receiving at least one treatment for cancer, the method comprising administering a therapeutically effective amount of at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor in addition to the at least one treatment the patient is currently receiving, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises a compound of the formula (I) or an analog, a derivative, a metabolite or pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

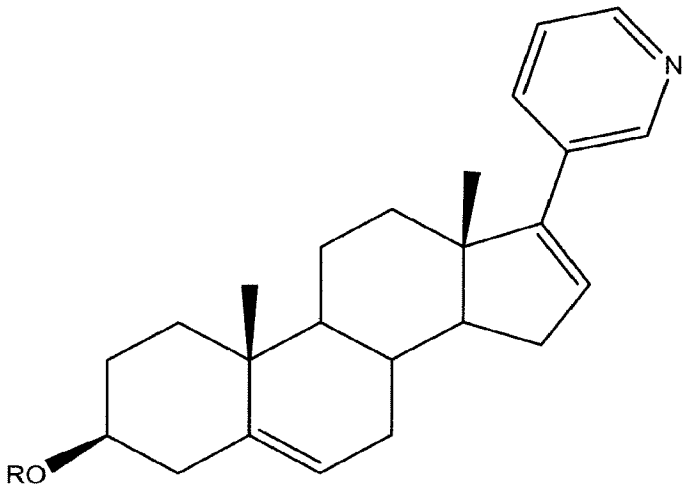
23. The method of claim 22, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises abiraterone acetate or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof.

24. The method of claim 23, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises the mesylate salt of abiraterone acetate.

25. The method of claim 22, wherein the therapeutically effective amount of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg/day to about 2000 mg/day.

26. The method of claim 22, wherein the treatment for cancer comprises the administration of an anti-cancer agent, chemotherapy, radiation or surgery.

27. A pharmaceutical composition for the treatment of a cancer in a mammal comprising a therapeutically effective amount of at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor; and at least one additional therapeutic agent; wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises a compound of the formula (I) or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

28. The composition of claim 27, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises abiraterone acetate or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof.

29. The composition of claim 28, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises the mesylate salt of abiraterone acetate.

30. The composition of claim 27, wherein the therapeutically effective amount of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg to about 500 mg.

31. The composition of claim 27, wherein the additional therapeutic agent comprises mitoxantrone, paclitaxel, docetaxel, leuprolide, goserelin, triptorelin, seocalcitol, bicalutamide, flutamide, hydrocortisone, prednisone or dexamethasone.

32. A pharmaceutical composition for the treatment of a cancer in a mammal comprising a therapeutically effective amount of abiraterone acetate; and a therapeutically effective amount of a steroid, wherein the composition is suitable for oral administration.

33. The composition of claim 32 wherein the composition is a solid dosage form.

34. The composition of claim 32, wherein the composition comprises about 50 mg to about 500 mg of abiraterone acetate, and about 0.25 mg to about 3.5 mg of the steroid.

35. The composition of claim 32, wherein the steroid comprises hydrocortisone, prednisone, or dexamethasone.

36. The composition of claim 32, wherein the composition is in the form of a pill, tablet or capsule.

ABSTRACT

Methods and compositions for treating cancer are described herein. More particularly, the methods for treating cancer comprise administering a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate (*i.e.*, 3β-acetoxy-17-(3-pyridyl) androsta-5, 16-diene), in combination with at least one additional therapeutic agent such as an anti-cancer agent or a steroid. Furthermore, disclosed are compositions comprising a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, and at least one additional therapeutic agent, such as an anti-cancer agent or a steroid.

DECLARATION FOR NON-PROVISIONAL PATENT APPLICATION*

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below at 201 et seq. beneath my name.

I believe I am the original, first and sole inventor if only one name is listed at 201 below, or an original, first and joint inventor if plural names are listed at 201 et seq. below, of the subject matter which is claimed and for which a patent is sought on the invention entitled

METHODS AND COMPOSITIONS FOR TREATING CANCER

and for which a patent application:

☒ is attached hereto and includes amendment(s) filed on (if applicable)

☒ was filed in the United States on August 24, 2007 as Application No. 11/844,440 with amendment(s) filed on (if applicable)

☐ was filed as PCT international Application No. on and was amended under PCT Article 19 on (if applicable)

I hereby authorize and request the attorneys at Jones Day to insert herein parentheses (Application No. _____ filed _____) the filing date and application number of said application when known.

I hereby state that I have reviewed and understand the contents of the above identified application, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

EARLIEST FOREIGN APPLICATION(S), IF ANY, FILED PRIOR TO THE FILING DATE OF THE APPLICATION				
APPLICATION NUMBER	COUNTRY	DATE OF FILING (day, month, year)	PRIORITY CLAIMED	
			YES ☐	NO ☐
			YES ☐	NO ☐

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below.

PROVISIONAL APPLICATION NUMBER	FILING DATE
60/921,506	August 25, 2006

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information known to me which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

NON-PROVISIONAL APPLICATION SERIAL NO.	FILING DATE	STATUS		
		PATENTED	PENDING	ABANDONED

* For use only when the application is assigned to a company, partnership or other organization.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

201	FULL NAME OF INVENTOR	LAST NAME: Auerbach	FIRST NAME: Alan	MIDDLE NAME: H.	
	RESIDENCE & CITIZENSHIP	CITY: Hermosa Beach	STATE OR FOREIGN COUNTRY: CA	COUNTRY OF CITIZENSHIP: USA	
	POST OFFICE ADDRESS	STREET: Cougar Biotechnology, Inc. 10990 Wilshire Blvd., Suite 1200	CITY: Los Angeles	STATE OR COUNTRY: CA	ZIP CODE: 90024
		SIGNATURE OF INVENTOR 201: [signature]		DATE: [illegible]	
202	FULL NAME OF INVENTOR	LAST NAME: Belldegrun	FIRST NAME: Arie	MIDDLE NAME: S.	
	RESIDENCE & CITIZENSHIP	CITY: Los Angeles	STATE OR FOREIGN COUNTRY: CA	COUNTRY OF CITIZENSHIP: USA	
	POST OFFICE ADDRESS	STREET: Cougar Biotechnology, Inc. 10990 Wilshire Blvd., Suite 1200	CITY: Los Angeles	STATE OR COUNTRY: CA	ZIP CODE: 90024
		SIGNATURE OF INVENTOR 202: [signature]		DATE: 9/11/07	
203	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	STREET	CITY	STATE OR COUNTRY	ZIP CODE
		SIGNATURE OF INVENTOR 203		DATE	
204	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	STREET	CITY	STATE OR COUNTRY	ZIP CODE
		SIGNATURE OF INVENTOR 204		DATE	
205	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	STREET	CITY	STATE OR COUNTRY	ZIP CODE
		SIGNATURE OF INVENTOR 205		DATE	

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 13/034,340

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	330
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	540
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	220
TOTAL CLAIMS (37 CFR 1.16(i))	36 minus 20 =	* 16			OR	x 52 =	832
INDEPENDENT CLAIMS (37 CFR 1.16(h))	4 minus 3 =	* 1				x 220 =	220
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $270 ($135 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						0.00
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	2142

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
13/034,340	02/24/2011	1614	2142	CGR5001USCNT1	36	4

CONFIRMATION NO. 1597

27777
PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

FILING RECEIPT

Date Mailed: 03/09/2011

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Applicant(s)

Alan H. Auerbach, Hermosa Beach, CA;
Arie S. Belldegrum, Los Angeles, CA;

Power of Attorney: The patent practitioners associated with Customer Number 27777

Domestic Priority data as claimed by applicant

This application is a CON of 11/844,440 08/24/2007
which claims benefit of 60/921,506 08/25/2006

Foreign Applications (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.)

If Required, Foreign Filing License Granted: 03/07/2011

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 13/034,340**

Projected Publication Date: 06/16/2011

Non-Publication Request: No

Early Publication Request: No

Title

Methods and Compositions for Treating Cancer

Preliminary Class

514

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4158).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as

set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1

CONFIRMATION NO. 1597

POA ACCEPTANCE LETTER

27777
PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

OC00000046407510

Date Mailed: 03/09/2011

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 02/24/2011.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

/jchery/

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1

CONFIRMATION NO. 1597

27777
PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

PUBLICATION NOTICE

Title: Methods and Compositions for Treating Cancer

Publication No.US-2011-0144016-A1
Publication Date:06/16/2011

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Office of Public Records. The Office of Public Records can be reached by telephone at (703) 308-9726 or (800) 972-6382, by facsimile at (703) 305-8759, by mail addressed to the United States Patent and Trademark Office, Office of Public Records, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently http://pair.uspto.gov/. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 11/25/2011

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	
ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
11/25/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jnjuspatent@corus.jnj.com
lhowd@its.jnj.com
gsanche@its.jnj.com

Office Action Summary	Application No.	Applicant(s)	
	13/034,340	AUERBACH ET AL.	
	Examiner	Art Unit	
	SAN-MING HUI	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-36* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☐ Claim(s) _____ is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☒ Claim(s) *1-36* are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-26, drawn to a method of treating cancer, classified in class 514, subclass 182.

II. Claims 27-36, drawn to a composition, classified in class 424, subclass 401+.

The inventions are distinct, each from the other because of the following reasons:

Inventions II and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the composition can be used in a materially different method such as pharmacokinetic study.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and/or examination burden if restriction were not required because at least the following reason(s) apply:

The search fields for the two identified patentably distinct inventions are diverse and not necessarily overlapped. Searching for all of the inventions encompassed by the claims would impose undue burden to the examiner.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Because the above restriction/election requirement is complex, a telephone call to applicant's agent to request an oral election was not made. See M.P.E.P. Sec. 812.01.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP

§ 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAN-MING HUI whose telephone number is (571)272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1628

/San-ming Hui/
Primary Examiner, Art Unit 1628

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011								
	1	÷								
	2	÷								
	3	÷								
	4	÷								
	5	÷								
	6	÷								
	7	÷								
	8	÷								
	9	÷								
	10	÷								
	11	÷								
	12	÷								
	13	÷								
	14	÷								
	15	÷								
	16	÷								
	17	÷								
	18	÷								
	19	÷								
	20	÷								
	21	÷								
	22	÷								
	23	÷								
	24	÷								
	25	÷								
	26	÷								
	27	÷								
	28	÷								
	29	÷								
	30	÷								
	31	÷								
	32	÷								
	33	÷								
	34	÷								
	35	÷								
	36	÷								

I hereby certify that this correspondence is being transmitted via The Office Electronic Filing System (EFS) in accordance with 37 CFR 1.6(a)(4).

Date of Electronic (EFS) Transmission: December 21, 2011

Signature: /Laurie A. Phillips/ Name: Laurie A. Phillips

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Applicant(s):	Alan H. Auerbach	Conf. No.:	1597
Application No.:	13/034,340	Group Art:	1628
Filing Date:	February 24, 2011	Examiner:	San Ming R. Hui
Title:	Methods and Compositions for Treating Cancer		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO RESTRICTION REQUIREMENT

Dear Sir:

The Office has issued a two-way restriction requirement relating to the present invention. Applicants hereby elect the invention of Group I, represented by newly presented claims 37 *et seq*. This election is made without traverse.

Listing of Claims:

1-36. (Canceled).

37. (New) A method for the treatment of a prostate cancer in a human comprising administering to said human a therapeutically effective amount of abiraterone acetate or a pharmaceutically acceptable salt thereof and a therapeutically effective amount of prednisone.

38. (New) The method of claim 37, wherein the therapeutically effective amount of the abiraterone acetate or pharmaceutically acceptable salt thereof is from about 50 mg/day to about 2000 mg/day.

39. (New) The method of claim 38, wherein the therapeutically effective amount of the abiraterone acetate or pharmaceutically acceptable salt thereof is from about 500 mg/day to about 1500 mg/day.

40. (New) The method of claim 39, wherein the therapeutically effective amount of the abiraterone acetate or pharmaceutically acceptable salt thereof is about 1000 mg/day.

41. (New) The method of claim 37, wherein the therapeutically effective amount of the abiraterone acetate or a pharmaceutically acceptable salt thereof is administered in at

least one dosage form comprising about 250 mg of abiraterone acetate or a pharmaceutically acceptable salt thereof.

42. (New) The method of claim 37, wherein the therapeutically effective amount of the prednisone is from about 0.01 mg/day to about 500 mg/day.

43. (New) The method of claim 42, wherein the therapeutically effective amount of the prednisone is from about 10 mg/day to about 250 mg/day.

44. (New) The method of claim 44, wherein the therapeutically effective amount of the prednisone is about 10 mg/day.

45. (New) The method of claim 37, wherein the therapeutically effective amount of the prednisone is administered in at least one dosage form comprising about 5 mg of prednisone.

46. (New) The method of claim 37, comprising administering to said human about 500 mg/day to about 1500 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 0.01 mg/day to about 500 mg/day of prednisone.

47. (New) The method of claim 46, comprising administering to said human about 1000 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 10 mg/day of prednisone.

48. (New) The method of claim 37, wherein said prostate cancer is refractory prostate cancer.

49. (New) The method of claim 48, wherein the refractory prostate cancer is not responding to at least one anti-cancer agent.

50. (New) The method of claim 49, wherein the at least one anti-cancer agent comprises a hormonal ablation agent, an anti-androgen agent, or an anti-neoplastic agent.

51. (New) The method of claim 50, wherein the hormonal ablation agent comprises deslorelin, leuprolide, goserelin, or triptorelin.

52. (New) The method of claim 50, wherein the anti-androgen agent comprises bicalutamide, flutamide, or nilutamide.

53. (New) The method of claim 50, wherein the anti-neoplastic agent comprises docetaxel.

54. (New) The method of claim 48, comprising administering to said human about 500 mg/day to about 1500 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 0.01 mg/day to about 500 mg/day of prednisone.

55. (New) The method of claim 54, comprising administering to said human about 1000 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 10 mg/day of prednisone.

56. (New) The method of claim 53, comprising administering to said human about 1000 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 10 mg/day of prednisone.

Applicants respectfully request that a timely Notice of Allowance be issued in the present application. Should the office require anything further, it is invited to contact applicants' representative at the telephone number below.

Respectfully submitted,

JOHNSON & JOHNSON
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-3957
Dated: December 21, 2011
Customer No.: 27777

By: /Andrea Jo Kamage /
Andrea Jo Kamage
Reg. No. 43,703

Electronic Acknowledgement Receipt

EFS ID:	11673171
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Andrea J. Kamage/Laurie Phillips
Filer Authorized By:	Andrea J. Kamage
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	21-DEC-2011
Filing Date:	24-FEB-2011
Time Stamp:	11:00:17
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Response to Election / Restriction Filed	CGR5001USCNT1ResponsetoRR.pdf	192109 16f7b75ef95c864b023c28abc01a2af57a98cd60	no	6

Warnings:	
Information:	

Total Files Size (in bytes):	192109

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
13/034,340	02/24/2011	

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY ☐ RATE ($)	SMALL ENTITY FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	12/21/2011	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 20	Minus	** 20	= 0	X $ =		OR	X $60=	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $ =		OR	X $250=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/STEFANIE BRYCE/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 02/03/2012

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
02/03/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jnjuspatent@corus.jnj.com
lhowd@its.jnj.com
gsanche@its.jnj.com

Office Action Summary	Application No.	Applicant(s)	
	13/034,340	AUERBACH ET AL.	
	Examiner	Art Unit	
	SAN-MING HUI	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) 37-56 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) 37-56 is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is a continuation of US serial 11/844440, filed 8/24/2007, which claims benefit of 60/921,506, filed 8/25/2006.

Election/Restrictions

Applicant's election without traverse of the invention of Group I in the reply filed on 12/21/2011 is acknowledged. Applicant's amendments filed 12/21/2011 have been entered.

Claims 37-56 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Donnell et al., British Journal of Cancer, 2004;90:2317-2325 in view of Tannock et al., J. Clin. Oncol., 1996;14:1756-1764. All of the references are of record in the parent application.

O'Donnell et al. teaches abiraterone acetate is known to be an inhibitor of 17α-hydroxylase/C17,20-lyase , which can be used to suppress testosterone level in prostate cancer patients (see the abstract for example). O'Donnell et al. teaches 800mg of abiraterone acetate as useful in suppressing the serum testosterone level (See the abstract for example). O'Donnell et al. also teaches that cocomitant glucocorticoid

therapy may be needed for continuous use of abiraterone acetate (See the abstract and page 2323, col.2 for example).

O'Donnell et al. does not expressly teach the use of prednisone in the method of treating prostate cancer. O'Donnell et al. does not expressly teach the use of the herein claimed dosage and regimen for prednisone and abiraterone acetate.

Tannock et al. teaches 10mg of prednisone in combination with other anit-cancer drug as effective in treating refractory hormonal-resistance prostate cancer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ both prednisone and abiraterone acetate, in the dosage herein claimed, together in a method of treating prostate cancer, including refractory prostate cancer.

One of ordinary skill in the art would have been motivated to employ both prednisone and abiraterone acetate, in the dosage herein claimed, together in a method of treating prostate cancer, including refractory prostate cancer. Since abiraterone acetate provide a new mechanism of action in treating prostate cancer and prednisone is known to be useful in treating refractory prostate cancer, concomitant employment of both compounds into a single method useful for the very same purpose, treting prostate cancer, would be considered *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069 (CCPA 1980)). Treating refractory prostate cancer with abiraterone acetate would be reasonably expected to be effective since abiraterone provides a new mechanism of action against prostate cancer. O'donnell et al. provides an additional motivation to

concomitantly employ prednisone since employing replacement glucocorticoid such as prednisone would ensure the safety and effectiveness of abiraterone acetate.

Furthermore, the optimization of result effect parameters (e.g., dosage range, dosing regimens) is obvious as being within the skill of the artisan. The optimization of known effective amounts of known active agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980). It is also noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 37-56 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9, 19, 21, 24, 29-32 of copending Application No. 12/898,149 (‘149). Although the conflicting claims are not identical, they are not patentably distinct from each other because ‘149 teaches the method of treating prostate cancer and refractory prostate cancer by employing the herein claimed agents, i.e., abiraterone acetate and prednisone. ‘149 does not expressly teach the herein claimed dosage. It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the herein claimed dosage of the actives in the method of treating prostate cancer. The optimization of

result effect parameters (e.g., dosage range, dosing regimens) is obvious as being within the skill of the artisan. The optimization of known effective amounts of known active agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980). It is also noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAN-MING HUI whose telephone number is (571)272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1628

/San-ming Hui/
Primary Examiner, Art Unit 1628

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

BIB DATA SHEET

CONFIRMATION NO. 1597

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
13/034,340	02/24/2011	514	1628	CGR5001USCNT1

APPLICANTS

Alan H. Auerbach, Hermosa Beach, CA;
Arie S. Belldegrum, Los Angeles, CA;

**** CONTINUING DATA ***************************

This application is a CON of 11/844,440 08/24/2007 ABN
which claims benefit of 60/921,506 08/25/2006

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ****

03/07/2011

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☐ No Verified and Acknowledged /SAN-MING R HUI/ Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		CA	0	36	4

ADDRESS

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003
UNITED STATES

TITLE

Methods and Compositions for Treating Cancer

FILING FEE RECEIVED		
2142	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012							
	1	÷								
	2	÷								
	3	÷								
	4	÷								
	5	÷								
	6	÷								
	7	÷								
	8	÷								
	9	÷								
	10	÷								
	11	÷								
	12	÷								
	13	÷								
	14	÷								
	15	÷								
	16	÷								
	17	÷								
	18	÷								
	19	÷								
	20	÷								
	21	÷								
	22	÷								
	23	÷								
	24	÷								
	25	÷								
	26	÷								
	27	÷								
	28	÷								
	29	÷								
	30	÷								
	31	÷								
	32	÷								
	33	÷								
	34	÷								
	35	÷								
	36	÷								

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012							
	37		✓							
	38		✓							
	39		✓							
	40		✓							
	41		✓							
	42		✓							
	43		✓							
	44		✓							
	45		✓							
	46		✓							
	47		✓							
	48		✓							
	49		✓							
	50		✓							
	51		✓							
	52		✓							
	53		✓							
	54		✓							
	55		✓							
	56		✓							

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1628

SEARCHED			
Class	**Subclass**	**Date**	**Examiner**
514	170, 182	1/27/11	SH

SEARCH NOTES		
Search Notes	**Date**	**Examiner**
EAST search and inventor search in PALM	1/27/11	SH

INTERFERENCE SEARCH			
Class	**Subclass**	**Date**	**Examiner**

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S29	1676	abiraterone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S30	3	prdnisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S31	26698	prednisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S32	122459	prostate	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S33	1390	S29 and S32	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S34	86	S29 same S32	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S35	914	514/170.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S36	2040	514/182.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S37	430033	cancer	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S38	1654	S29 and S37	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S39	807	S29 same S37	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S40	0	"9320097".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S41	2	"9509178".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47
S42	0	"9509178".pn. and S37	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/01/27 21:47

EAST Search History (Interference)

<This search history is empty>

1/27/2012 9:57:55 PM
C:\Users\shui\Documents\EAST\Workspaces\13-034340.wsp

I hereby certify that this correspondence is being transmitted via The Office Electronic Filing System (EFS) in accordance with 37 CFR 1.6(a)(4).

Date of Electronic (EFS) Transmission: July 3, 2012

Signature: /Laurie A. Phillips/ Name: Laurie A. Phillips

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Applicant(s):	Alan H. Auerbach	Conf. No.:	1597
Application No.:	13/034,340	Group Art:	1628
Filing Date:	February 24, 2011	Examiner:	San Ming R. Hui
Title:	Methods and Compositions for Treating Cancer		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE

Dear Sir:

In response to the Office Action mailed February 3, 2012, Applicants submit the following amendments and remarks.

Remarks/Arguments begin on page 2 of this paper.

Remarks

Rejections Under 35 U.S.C. § 103

Claims 37-56 are rejected under 35 USC §103(a) as allegedly being unpatentable over O'Donell et al. (British Journal of Cancer (2004)), in view of Tannock et al. (Journal of Clinical Oncology (1996)). Applicant respectfully traverses this rejection.

The invention is directed to a method for treating prostate cancer by administering both abiraterone acetate and prednisone to a patient. The Office alleges this invention is obvious by a combination of O'Donnell, which discloses administration of certain doses of abiraterone acetate to castrated prostate cancer patients, and Tannock, which discloses administration of prednisone in combination with a chemotherapy agent to prostate cancer patients.

Applicant believes that the Office has failed to establish a case of obviousness. At the very most, the cited art may suggest that a combination of abiraterone acetate and prednisone would be obvious to try; along with a myriad of other combinations of two cancer drugs. Nothing in the art teaches or suggests that abiraterone acetate in combination with prednisone would be a particularly useful combination for cancer treatment.

Even if one of ordinary skill would have been motivated to combine both modes of treatment, the claimed invention produces unexpected results. Applicants enclose herewith Sartor, *Nature Reviews Clinical Oncology*, 8:515-516 (2011) ("Sartor"). Sartor reports on the results of a clinical study on patients with prostate cancer who were treated with the claimed invention. According to Sartor, "Abiraterone plus prednisone prolongs overall survival relative to prednisone alone. . ." Sartor, abstract. Additionally, "reported pain was markedly reduced in the abiraterone plus prednisone arm. Second, preliminary reports indicate that circulating tumors cells (CTCs)—a novel biomarker indicative of poor prognosis —were reduced in the experimental arm and that a combination of levels

of lactate dehydrogenase (LDH) and CTCs at baseline and changes in these levels after treatment may predict survival, independently of therapy, in patients with an elevated baseline CTC count." Thus, the claimed invention produces the unexpected results of increased survival, reduced pain, and lower levels of a biomarker connected with survival.

The claimed invention has experienced an impressive commercial success. Applicant attaches herewith the label for abiraterone acetate, sold under the tradename ZYTIGA. According to the label, "ZYTIGA in combination with prednisone is indicated for the treatment of patients with metastatic castration-resistant prostate cancer who have received prior chemotherapy containing docetaxel." Thus, the ZYTIGA label directs patients to practice the claimed invention.

ZYTIGA was approved for sale in the U.S. in April 2011. Within the first year of release, worldwide sales were over $400 million. Sales for the truncated 2011 year totaled $200 million worldwide. Sales for just the first quarter of 2012 were also $200 million. Thus, not only did the claimed invention enjoy immediate commercial success, this commercial success grew over the first year of commercial availability.

The claimed invention displays unexpected results over the prior at, and shows commercial success. Thus, the present claims are non-obvious over the cited art. Accordingly, Applicant requests reconsideration and withdrawal of the rejection under 35 USC §103(a).

Double Patenting Rejection

Claims 37-56 are rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 9, 19, 21, 24, 29-32 of copending U.S. Patent Application No. 12/898,149 (the '149 application). The '149 application has been a abandoned. Thus, this rejection is now moot.

III. CONCLUSION

Early consideration and prompt allowance of the claims are respectfully requested. Should the office require anything further, it is invited to contact applicants' representative at the telephone number below.

Respectfully submitted,

JOHNSON & JOHNSON
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-3957
Dated: July 3, 2012
Customer No.: 27777

By: /Andrea Jo Kamage/
Andrea Jo Kamage
Reg. No. 43,703

Electronic Patent Application Fee Transmittal

Application Number:	13034340
Filing Date:	24-Feb-2011
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Andrea J. Kamage/Laurie Phillips
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 2 months with $0 paid	1252	1	560	560

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**560**

Electronic Acknowledgement Receipt

EFS ID:	13174927
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Andrea J. Kamage/Laurie Phillips
Filer Authorized By:	Andrea J. Kamage
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	03-JUL-2012
Filing Date:	24-FEB-2011
Time Stamp:	18:04:40
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$560
RAM confirmation Number	6502
Deposit Account	100750
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Amendment/Req. Reconsideration-After Non-Final Reject	2011_Sartor.pdf	126916 4afe12b1ef1406cfeaaa70b11fa5bd95241a0470	no	2
Warnings:					
Information:					
2	Amendment/Req. Reconsideration-After Non-Final Reject	CGR5001USCNT1_AMD_3July2012.pdf	191641 d5c121da4e9f67ab40a7c8e70c1739242ad4c92c	no	4
Warnings:					
Information:					
3	Amendment/Req. Reconsideration-After Non-Final Reject	ZYTIGAlabell.pdf	137513 148488f2d7ec8e6709e2eb17fea37313cd570d64	no	22
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	30267 099c82fcb5ece3426cbf35b2051ad19988682bf8	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	486337		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 09/11/2012

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	
ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
09/11/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jnjuspatent@corus.jnj.com
lhowd@its.jnj.com
gsanche@its.jnj.com

Office Action Summary	Application No.	Applicant(s)	
	13/034,340	AUERBACH ET AL.	
	Examiner	Art Unit	
	SAN-MING HUI	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2012*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *37-56* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *37-56* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed 7/3/2012 has been entered.

Claims 37-56 are pending.

The provisional double patenting rejection is withdrawn in view of the conflicting patent application being abandoned.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Donnell et al., British Journal of Cancer, 2004;90:2317-2325 in view of Tannock et al., J. Clin. Oncol., 1996;14:1756-1764. All of the references are of record in the parent application.

O'Donnell et al. teaches abiraterone acetate is known to be an inhibitor of 17α-hydroxylase/C17,20-lyase , which can be used to suppress testosterone level in prostate cancer patients (see the abstract for example). O'Donnell et al. teaches 800mg of abiraterone acetate as useful in suppressing the serum testosterone level (See the abstract for example). O'Donnell et al. also teaches that cocomitant glucocorticoid therapy may be needed for continuous use of abiraterone acetate (See the abstract and page 2323, col.2 for example).

O'Donnell et al. does not expressly teach the use of prednisone in the method of treating prostate cancer. O'Donnell et al. does not expressly teach the use of the herein claimed dosage and regimen for prednisone and abiraterone acetate.

Tannock et al. teaches 10mg of prednisone in combination with other anit-cancer drug as effective in treating refractory hormonal-resistance prostate cancer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ both prednisone and abiraterone acetate, in the dosage herein claimed, together in a method of treating prostate cancer, including refractory prostate cancer.

One of ordinary skill in the art would have been motivated to employ both prednisone and abiraterone acetate, in the dosage herein claimed, together in a method of treating prostate cancer, including refractory prostate cancer. Since abiraterone acetate provide a new mechanism of action in treating prostate cancer and prednisone is known to be useful in treating refractory prostate cancer, concomitant employment of both compounds into a single method useful for the very same purpose, treating prostate cancer, would be considered *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069 (CCPA 1980)). Treating refractory prostate cancer with abiraterone acetate would be reasonably expected to be effective since abiraterone provides a new mechanism of action against prostate cancer. O'donnell et al. provides an additional motivation to concomitantly employ prednisone since employing replacement glucocorticoid such as prednisone would ensure the safety and effectiveness of abiraterone acetate.

Furthermore, the optimization of result effect parameters (e.g., dosage range, dosing regimens) is obvious as being within the skill of the artisan. The optimization of known effective amounts of known active agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980). It is also noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Response to Arguments

Applicant's arguments filed 7/3/2012 averring the presence of unexpected results because abiraterine plus prednisone being more effective than prednisone alone have been fully considered but they are not persuasive. The examiner notes that it is expected because abiraterone and prednisone are known to be individually effective in treating prostate cancer. At least additive effective is expected.

Applicant's arguments filed 7/3/2012 averring the presence of commercial success have been considered, but are not found persuasive. The examiner notes that applicant bears the burden to provide evidence of commercial success. Furthermore, gross sales figures do not show commercial success absent evidence as to market share, *Cable Electric Products, Inc. v. Genmark, Inc.*, 770 F.2d 1015, 226 USPQ 881 (Fed. Cir. 1985), or as to the time period during which the product was sold, or as to

what sales would normally be expected in the market, *Ex parte Standish*, 10 USPQ2d 1454 (Bd.Pat. App. & Inter. 1988). In the instant case, there is no evidence of commercial success was provided. Therefore, possessing the teachings of the cited prior art, one of ordinary skill in the art would employ the herein claimed agents into a single method of treating refractory prostate cancer.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAN-MING HUI whose telephone number is (571)272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1628

/San-ming Hui/
Primary Examiner, Art Unit 1628

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

SEARCHED			
Class	Subclass	Date	Examiner
514	170, 182	1/27/11	SH
514	170, 182	9/5/12	SH

SEARCH NOTES		
Search Notes	Date	Examiner
EAST search and inventor search in PALM	1/27/11	SH
EAST search and inventor search in PALM	9/5/12	SH

INTERFERENCE SEARCH			
Class	Subclass	Date	Examiner

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1904	abiraterone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L2	3	prdnisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L3	28935	prednisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L4	130680	prostate	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L5	1571	L1 and L4	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L6	96	L1 same L4	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L7	956	514/170.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L8	2117	514/182.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L9	454462	cancer	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L10	1879	L1 and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L11	932	L1 same L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L12	0	"9320097".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L13	2	"9509178".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31
L14	0	"9509178".pn. and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/09/05 21:31

EAST Search History (Interference)

<This search history is empty>

9/5/2012 9:31:48 PM
C:\Users\shui\Documents\EAST\Workspaces\13-034340.wsp

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012	09/05/2012						
	1	÷								
	2	÷								
	3	÷								
	4	÷								
	5	÷								
	6	÷								
	7	÷								
	8	÷								
	9	÷								
	10	÷								
	11	÷								
	12	÷								
	13	÷								
	14	÷								
	15	÷								
	16	÷								
	17	÷								
	18	÷								
	19	÷								
	20	÷								
	21	÷								
	22	÷								
	23	÷								
	24	÷								
	25	÷								
	26	÷								
	27	÷								
	28	÷								
	29	÷								
	30	÷								
	31	÷								
	32	÷								
	33	÷								
	34	÷								
	35	÷								
	36	÷								

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1628

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012	09/05/2012						
	37		✓	✓						
	38		✓	✓						
	39		✓	✓						
	40		✓	✓						
	41		✓	✓						
	42		✓	✓						
	43		✓	✓						
	44		✓	✓						
	45		✓	✓						
	46		✓	✓						
	47		✓	✓						
	48		✓	✓						
	49		✓	✓						
	50		✓	✓						
	51		✓	✓						
	52		✓	✓						
	53		✓	✓						
	54		✓	✓						
	55		✓	✓						
	56		✓	✓						

PTO/SB/30 (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL

Subsection (b) of 35 U.S.C. § 132, effective on May 29, 2000, provides for continued examination of an utility or plant application filed on or after June 8, 1995. See The American Inventors Protection Act of 1999 (AIPA).

Application Number	13/034,340
Filing Date	February 24, 2011
First Named Inventor	Alan H. Auerbach
Group Art Unit	1628
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

This is a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114 of the above-identified application.

NOTE: 37 C.F.R. § 1.114 is effective on May 29, 2000. If the above-identified application was filed prior to May 29, 2000, applicant may wish to consider filing a continued prosecution application (CPA) under 37 C.F.R. § 1.53 (d) (PTO/SB/29) instead of a RCE to be eligible for the patent term adjustment provisions of the AIPA. See *Changes to Application Examination and Provisional Application Practice*, Final Rule, 65 *Fed. Reg.* 50092 (Aug. 16, 2000); Interim Rule, 65 *Fed. Reg.* 14865 (Mar. 20, 2000), 1233 *Off. Gaz. Pat. Office* 47 (Apr. 11, 2000), which established RCE practice.

1. **Submission required under 37 C.F.R. § 1.114**
   - a. ☐ Previously submitted
     - i. ☐ Consider the amendment(s)/reply under 37 C.F.R. § 1.116 previously filed on (any unentered amendment(s) referred to above will be entered).
     - ii. ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on
     - iii. ☐ Other
   - b. ☒ Enclosed
     - i. ☒ Amendment/Reply
     - ii. ☐ Affidavit(s)/Declaration(s)
     - iii. ☐ Information Disclosure Statement (IDS)
     - iv. ☐ Other
2. **Miscellaneous**
   - a. ☐ Suspension of action on the above-identified application is requested under 37 C.F.R. § 1.103(c) for a period of months. (Period of suspension shall not exceed 3 months; Fee under 37 C.F.R. § 1.17(i) required.)
   - b. ☐ Other
3. **Fees** - The RCE fee under 37 C.F.R. § 1.17(e) is required by 37 C.F.R. § 1.114 when the RCE is filed
   - a. ☒ The Director is hereby authorized to charge the following fees, or credit any overpayments, to Deposit Account No. **10-0750**.
     - i. ☒ RCE fee is required under 37 C.F.R. § 1.17(e)
     - ii. ☐ Extension of Time (37 C.F.R. §§ 1.136 and 1.17)
     - iii. ☐ Other
   - b. ☐ Check in the amount of $_____ enclosed
   - c. ☐ Payment by credit card (Form PTO-2038 enclosed)

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Name (print/type)	Andrea Jo Kamage	Registration No.	43,703
Signature	/Andrea Jo Kamage/	Date	January 11, 2013

CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being electronically filed via EFS-Web to the Commissioner for Patents with the U.S. Patent and Trademark Office on: January 11, 2013

Name (print/type)	Laurie A. Phillips		
Signature	/Laurie A. Phillips/	Date	January 11, 2013

Electronic Patent Application Fee Transmittal

Application Number:	13034340
Filing Date:	24-Feb-2011
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Andrea J. Kamage/Laurie Phillips
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 1 month with $0 paid	1251	1	150	150

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Request for continued examination	1801	1	930	930
		Total in USD ($)		**1080**

Electronic Acknowledgement Receipt

EFS ID:	14680477
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Andrea J. Kamage/Laurie Phillips
Filer Authorized By:	Andrea J. Kamage
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	11-JAN-2013
Filing Date:	24-FEB-2011
Time Stamp:	16:21:28
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1080
RAM confirmation Number	3408
Deposit Account	100750
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Amendment Submitted/Entered with Filing of CPA/RCE	CGR5001USCNT1_Response_to_OA_Dec_2012.pdf	197238 ccb96c6241312814853ff3fd29c9199b154e1d5f	no	8
Warnings:					
Information:					
2	Request for Continued Examination (RCE)	CGR5001USCNT1_RCE.pdf	384010 2608556abba1949dda550941b28d75e93745fe60	no	1
Warnings:					
This is not a USPTO supplied RCE SB30 form.					
Information:					
3	Non Patent Literature	RyanNEJM.pdf	214749 b8f4bc85f399435ff116e4f6c6f88aa99b81e12a	no	11
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	32130 0e979cb3c871a6ec2041abb1dc26ff270f8ed9a6	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	828127		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

I hereby certify that this correspondence is being transmitted via The Office Electronic Filing System (EFS) in accordance with 37 CFR 1.6(a)(4).

Date of Electronic (EFS) Transmission: January 11, 2013

Signature: /Laurie A. Phillips/ Name: Laurie A. Phillips

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Applicant(s):	Alan H. Auerbach	Conf. No.:	1597
Application No.:	13/034,340	Group Art:	1628
Filing Date:	February 24, 2011	Examiner:	San Ming R. Hui
Title:	Methods and Compositions for Treating Cancer		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE

Dear Sir:

In response to the final Office Action mailed September 11, 2012, Applicants submit the following amendments and remarks.

A list of the Claims are reflected in the listing of claims, which begins on page 2 of this paper.

Remarks/Arguments begin on page 4 of this paper.

Listing of Claims:

1-36. (Canceled).

37. (Previously presented) A method for the treatment of a prostate cancer in a human comprising administering to said human a therapeutically effective amount of abiraterone acetate or a pharmaceutically acceptable salt thereof and a therapeutically effective amount of prednisone.

38. (Previously presented) The method of claim 37, wherein the therapeutically effective amount of the abiraterone acetate or pharmaceutically acceptable salt thereof is from about 50 mg/day to about 2000 mg/day.

39. (Previously presented) The method of claim 38, wherein the therapeutically effective amount of the abiraterone acetate or pharmaceutically acceptable salt thereof is from about 500 mg/day to about 1500 mg/day.

40. (Previously presented) The method of claim 39, wherein the therapeutically effective amount of the abiraterone acetate or pharmaceutically acceptable salt thereof is about 1000 mg/day.

41. (Previously presented) The method of claim 37, wherein the therapeutically effective amount of the abiraterone acetate or a pharmaceutically acceptable salt thereof is administered in at least one dosage form comprising about 250 mg of abiraterone acetate or a pharmaceutically acceptable salt thereof.

42. (Previously presented) The method of claim 37, wherein the therapeutically effective amount of the prednisone is from about 0.01 mg/day to about 500 mg/day.

43. (Previously presented) The method of claim 42, wherein the therapeutically effective amount of the prednisone is from about 10 mg/day to about 250 mg/day.

44. (Previously presented) The method of claim 44, wherein the therapeutically effective amount of the prednisone is about 10 mg/day.

45. (Previously presented) The method of claim 37, wherein the therapeutically effective amount of the prednisone is administered in at least one dosage form comprising about 5 mg of prednisone.

46. (Previously presented) The method of claim 37, comprising administering to said human about 500 mg/day to about 1500 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 0.01 mg/day to about 500 mg/day of prednisone.

47. (Previously presented) The method of claim 46, comprising administering to said human about 1000 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 10 mg/day of prednisone.

48. (Previously presented) The method of claim 37, wherein said prostate cancer is refractory prostate cancer.

49. (Previously presented) The method of claim 48, wherein the refractory prostate cancer is not responding to at least one anti-cancer agent.

50. (Previously presented) The method of claim 49, wherein the at least one anti-cancer agent comprises a hormonal ablation agent, an anti-androgen agent, or an anti-neoplastic agent.

51. (Previously presented) The method of claim 50, wherein the hormonal ablation agent comprises deslorelin, leuprolide, goserelin, or triptorelin.

52. (Previously presented) The method of claim 50, wherein the anti-androgen agent comprises bicalutamide, flutamide, or nilutamide.

53. (Previously presented) The method of claim 50, wherein the anti-neoplastic agent comprises docetaxel.

54. (Previously presented) The method of claim 48, comprising administering to said human about 500 mg/day to about 1500 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 0.01 mg/day to about 500 mg/day of prednisone.

55. (Previously presented) The method of claim 54, comprising administering to said human about 1000 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 10 mg/day of prednisone.

56. (Previously presented) The method of claim 53, comprising administering to said human about 1000 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 10 mg/day of prednisone.

Remarks

Claims 37-56 are pending.

Rejections Under 35 U.S.C. § 103

Claims 37-56 are rejected under 35 USC §103(a) as allegedly being unpatentable over O'Donell et al. (*British Journal of Cancer* (2004)), in view of Tannock et al. (*Journal of Clinical Oncology* (1996)). Applicants respectfully traverse this rejection.

None of the cited prior art teaches or suggests the specific combination of the present invention, namely treating prostate cancer with a combination of abiraterone and prednisone. As stated by the Office, "O'Donnell does not expressly teach the use of prednisone in the method of treating prostate cancer. O'Donell does not expressly teach the use of the herein claimed dosage and regimen for prednisone and abiraterone acetate." Office Action, page 3. Further, according to the Office, "Tannock teaches 10mg of prednisone in combination with other anti-cancer drug as effective in treating refractory hormonal-resistance prostate cancer." Office Action, page 3. Neither of these references teach or suggest combining prednisone and abiraterone to treat prostate cancer.

Even assuming, *arguendo*, that the cited references establish a prima facie case of obviousness, the present invention has shown unexpected results. Applicants submit herewith Ryan et al., *New Engl. J. Med.*, 2012, 368:138-148 ("Ryan"), which shows some of the unexpected results for the present invention.

Ryan reports on a clinical trial of abiraterone acetate plus prednisone for treating prostate cancer. Ryan states that the "median radiographic progression-free survival was 16.5 months with abiraterone-prednisone and 8.3 months with prednisone alone. . . treatment with abiraterone plus prednisone, as compared with placebo plus prednisone, results in a 57% reduction in the risk of radiographic progression or death. . . There was a 25% decrease in the risk of death in the abiraterone-prednisone group, indicating a strong trend toward improved survival with abiraterone-prednisone. . . Radiographic progression-free survival was positvely correlated with overall survival." In contrast, Tannock teaches that "[t]here was no significant difference in overall survival [between

prednisone alone and prednisone plus mitoxantrone]." One of ordinary skill would have expected, from the prior art, no differences in survival. However, Ryan shows the unexpected survival benefit of abiraterone in combination with prednisone.

Ryan further teaches that "Abiraterone-prednisone showed superiority over prednisone alone with respect to time to initiation of cytotoxic chemotherapy, opiate use for cancer-related pain, prostate-specific antigen progression, and decline in performance status." The present invention delayed initiation of cytotoxic chemotherapy by over 8 months, delayed prostate-specific antigen progression over 5 months, and delayed time to increase in pain over 8 months as compared with prednisone alone. *See* Table 1 of Ryan. None of these unexpected effects could have been predicted from the prior art.

Additionally, in Ryan, over 62% of patients showed a decline of greater than or equal to 50% in prostate specific antigen level. In contrast, only 33% of patients treated with the combination regimen in Tannock showed a decline of greater than or equal to 50% in prostate specific antigen level. This higher percentage could not have been predicted from the prior art.

Thus, none of the cited art, either alone or in combination, teaches or suggests the methods of the present invention. The present inventions shows several surprising unexpected results over the prior art. Accordingly, Applicant requests reconsideration and withdrawal of the rejection under 35 USC §103(a).

III. CONCLUSION

Early consideration and prompt allowance of the claims are respectfully requested. Should the office require anything further, it is invited to contact applicants' representative at the telephone number below.

Applicants respectfully request that a timely Notice of Allowance be issued in the present application. Should the office require anything further, it is invited to contact applicants' representative at the telephone number below.

Respectfully submitted,

JOHNSON & JOHNSON
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-3957
Dated: January 11, 2013
Customer No.: 27777

By: /Andrea Jo Kamage /
Andrea Jo Kamage
Reg. No. 43,703

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
13/034,340	02/24/2011	

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY ☐ RATE ($)	SMALL ENTITY ☐ FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT 01/11/2013	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 20	Minus	** 36	= 0	X $ =		OR	X $62=	0
Independent (37 CFR 1.16(h))	* 1	Minus	***4	= 0	X $ =		OR	X $250=	0
☐ Application Size Fee (37 CFR 1.16(s))									
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

AMENDMENT	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))									
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/PAUL STANBACK/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 03/04/2013

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	
ART UNIT	PAPER NUMBER
1629	

NOTIFICATION DATE	DELIVERY MODE
03/04/2013	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jnjuspatent@corus.jnj.com
lhowd@its.jnj.com
gsanche@its.jnj.com

Office Action Summary	Application No.	Applicant(s)	
	13/034,340	AUERBACH ET AL.	
	Examiner	Art Unit	
	SAN-MING HUI	1629	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2013*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *37-56* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *37-56* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/11/2013 has been entered.

Claims 37-56 are pending.

The outstanding rejection under 35 USC 103(a) is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Donnell et al., British Journal of Cancer, 2004;90:2317-2325 in view of Tannock et al., J. Clin. Oncol., 1996;14:1756-1764. All of the references are of record in the parent application.

O'Donnell et al. teaches abiraterone acetate is known to be an inhibitor of 17α-hydroxylase/C17,20-lyase , which can be used to suppress testosterone level in

prostate cancer patients (see the abstract for example). O'Donnell et al. teaches 800mg of abiraterone acetate as useful in suppressing the serum testosterone level (See the abstract for example). O'Donnell et al. also teaches that cocomitant glucocorticoid therapy may be needed for continuous use of abiraterone acetate (See the abstract and page 2323, col.2 for example).

O'Donnell et al. does not expressly teach the use of prednisone in the method of treating prostate cancer. O'Donnell et al. does not expressly teach the use of the herein claimed dosage and regimen for prednisone and abiraterone acetate.

Tannock et al. teaches 10mg of prednisone in combination with other anit-cancer drug as effective in treating refractory hormonal-resistance prostate cancer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ both prednisone and abiraterone acetate, in the dosage herein claimed, together in a method of treating prostate cancer, including refractory prostate cancer.

One of ordinary skill in the art would have been motivated to employ both prednisone and abiraterone acetate, in the dosage herein claimed, together in a method of treating prostate cancer, including refractory prostate cancer. Since abiraterone acetate provide a new mechanism of action in treating prostate cancer and prednisone is known to be useful in treating refractory prostate cancer, concomitant employment of both compounds into a single method useful for the very same purpose, treating prostate cancer, would be considered *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069 (CCPA 1980)). Treating refractory prostate cancer with abiraterone

acetate would be reasonably expected to be effective since abiraterone provides a new mechanism of action against prostate cancer. O'donnell et al. provides an additional motivation to concomitantly employ prednisone since employing replacement glucocorticoid such as prednisone would ensure the safety and effectiveness of abiraterone acetate.

Furthermore, the optimization of result effect parameters (e.g., dosage range, dosing regimens) is obvious as being within the skill of the artisan. The optimization of known effective amounts of known active agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980). It is also noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Response to Arguments

Applicant's arguments filed 1/11/2013 averring the presence of unexpected results because abiraterine plus prednisone being more effective than prednisone alone, by citing Ryan et al., have been fully considered but they are not persuasive. The examiner notes that the superior results of using abiraterone and prednisone together is

expected because abiraterone and prednisone are known to be individually effective in treating prostate cancer. At least additive effective is expected.

This is an RCE of instant application. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAN-MING HUI whose telephone number is (571)272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Melenie McCormick can be reached on (571) 272-8037. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1629

/San-ming Hui/
Primary Examiner, Art Unit 1629

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
514	170, 182	1/27/11	SH
514	170, 182	9/5/12	SH
514	170, 182	2/25/13	SH

SEARCH NOTES		
Search Notes	Date	Examiner
EAST search and inventor search in PALM	1/27/11	SH
EAST search and inventor search in PALM	9/5/12	SH
EAST search and inventor search in PALM	2/25/13	SH

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012	09/05/2012	02/25/2013					
	1	÷								
	2	÷								
	3	÷								
	4	÷								
	5	÷								
	6	÷								
	7	÷								
	8	÷								
	9	÷								
	10	÷								
	11	÷								
	12	÷								
	13	÷								
	14	÷								
	15	÷								
	16	÷								
	17	÷								
	18	÷								
	19	÷								
	20	÷								
	21	÷								
	22	÷								
	23	÷								
	24	÷								
	25	÷								
	26	÷								
	27	÷								
	28	÷								
	29	÷								
	30	÷								
	31	÷								
	32	÷								
	33	÷								
	34	÷								
	35	÷								
	36	÷								

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1628

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012	09/05/2012	02/25/2013					
	37		✓	✓	✓					
	38		✓	✓	✓					
	39		✓	✓	✓					
	40		✓	✓	✓					
	41		✓	✓	✓					
	42		✓	✓	✓					
	43		✓	✓	✓					
	44		✓	✓	✓					
	45		✓	✓	✓					
	46		✓	✓	✓					
	47		✓	✓	✓					
	48		✓	✓	✓					
	49		✓	✓	✓					
	50		✓	✓	✓					
	51		✓	✓	✓					
	52		✓	✓	✓					
	53		✓	✓	✓					
	54		✓	✓	✓					
	55		✓	✓	✓					
	56		✓	✓	✓					

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2077	abiraterone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L2	3	prdnisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L3	30596	prednisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L4	137011	prostate	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L5	1716	L1 and L4	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L6	108	L1 same L4	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L7	991	514/170.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L8	2210	514/182.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L9	473008	cancer	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L10	2049	L1 and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L11	1024	L1 same L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L12	0	"9320097".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L13	2	"9509178".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44
L14	0	"9509178".pn. and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/02/25 14:44

EAST Search History (Interference)

<This search history is empty>

2/25/2013 2:46:27 PM
C:\Users\shui\Documents\EAST\Workspaces\13-034340.wsp

I hereby certify that this correspondence is being transmitted via The Office Electronic Filing System (EFS) in accordance with 37 CFR 1.6(a)(4).

Date of Electronic (EFS) Transmission: June 4, 2013

Signature: /Laurie A. Phillips/ Name: Laurie A. Phillips

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Applicant(s):	Alan H. Auerbach	Conf. No.:	1597
Application No.:	13/034,340	Group Art:	1628
Filing Date:	February 24, 2011	Examiner:	San Ming R. Hui
Title:	Methods and Compositions for Treating Cancer		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE

Dear Sir:

In response to the final Office Action mailed March 4, 2013, Applicant submits the following amendments and remarks.

A list of the Claims are reflected in the listing of claims, which begins on page 2 of this paper.

Remarks/Arguments begin on page 4 of this paper.

Listing of Claims:

1-36. (Canceled).

37. (Previously presented) A method for the treatment of a prostate cancer in a human comprising administering to said human a therapeutically effective amount of abiraterone acetate or a pharmaceutically acceptable salt thereof and a therapeutically effective amount of prednisone.

38. (Previously presented) The method of claim 37, wherein the therapeutically effective amount of the abiraterone acetate or pharmaceutically acceptable salt thereof is from about 50 mg/day to about 2000 mg/day.

39. (Previously presented) The method of claim 38, wherein the therapeutically effective amount of the abiraterone acetate or pharmaceutically acceptable salt thereof is from about 500 mg/day to about 1500 mg/day.

40. (Previously presented) The method of claim 39, wherein the therapeutically effective amount of the abiraterone acetate or pharmaceutically acceptable salt thereof is about 1000 mg/day.

41. (Previously presented) The method of claim 37, wherein the therapeutically effective amount of the abiraterone acetate or a pharmaceutically acceptable salt thereof is administered in at least one dosage form comprising about 250 mg of abiraterone acetate or a pharmaceutically acceptable salt thereof.

42. (Previously presented) The method of claim 37, wherein the therapeutically effective amount of the prednisone is from about 0.01 mg/day to about 500 mg/day.

43. (Previously presented) The method of claim 42, wherein the therapeutically effective amount of the prednisone is from about 10 mg/day to about 250 mg/day.

44. (Previously presented) The method of claim 44, wherein the therapeutically effective amount of the prednisone is about 10 mg/day.

45. (Previously presented) The method of claim 37, wherein the therapeutically effective amount of the prednisone is administered in at least one dosage form comprising about 5 mg of prednisone.

46. (Previously presented) The method of claim 37, comprising administering to said human about 500 mg/day to about 1500 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 0.01 mg/day to about 500 mg/day of prednisone.

47. (Previously presented) The method of claim 46, comprising administering to said human about 1000 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 10 mg/day of prednisone.

48. (Previously presented) The method of claim 37, wherein said prostate cancer is refractory prostate cancer.

49. (Previously presented) The method of claim 48, wherein the refractory prostate cancer is not responding to at least one anti-cancer agent.

50. (Previously presented) The method of claim 49, wherein the at least one anti-cancer agent comprises a hormonal ablation agent, an anti-androgen agent, or an anti-neoplastic agent.

51. (Previously presented) The method of claim 50, wherein the hormonal ablation agent comprises deslorelin, leuprolide, goserelin, or triptorelin.

52. (Previously presented) The method of claim 50, wherein the anti-androgen agent comprises bicalutamide, flutamide, or nilutamide.

53. (Previously presented) The method of claim 50, wherein the anti-neoplastic agent comprises docetaxel.

54. (Previously presented) The method of claim 48, comprising administering to said human about 500 mg/day to about 1500 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 0.01 mg/day to about 500 mg/day of prednisone.

55. (Previously presented) The method of claim 54, comprising administering to said human about 1000 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 10 mg/day of prednisone.

56. (Previously presented) The method of claim 53, comprising administering to said human about 1000 mg/day of abiraterone acetate or a pharmaceutically acceptable salt thereof and about 10 mg/day of prednisone.

Remarks

Claims 37-56 are pending.

Rejections Under 35 U.S.C. § 103

The rejection of claims 37-56 under 35 USC §103(a) as allegedly being unpatentable over O'Donell *et al.* (*British Journal of Cancer 90*:2317-2325 (2004)) ("O'Donell"), in view of Tannock et al. (*Journal of Clinical Oncology 14*:1756-1764 (1996)) (Tannock") was maintained. Applicant respectfully traverses this rejection.

In Applicant's previous reply, submitted January 11, 2013 (the "January Reply"), Applicant submitted the Ryan article. Ryan showed, *inter alia*, that the "median radiographic progression-free survival was 16.5 months with abiraterone-prednisone and 8.3 months with prednisone alone . . . Radiographic progression-free survival was positively correlated with overall survival." According to the Office, "the superior results of using abiraterone and prednisone together is expected because abiraterone and prednisone are known to be individually effective in treating prostate cancer. At least additive effective [sic] is expected." However, the Office failed to provide any reasoning to support the expectation of at least an additive effect. In fact, the Office's own cited art is in opposition to the Office's statement that at least an additive effect is expected.

Based on Tannock, the art cited by the Office, one of ordinary skill in the art would not expect at least an additive effect for overall survival of abiraterone and acetate and progesterone. Tannock teaches that "[t]here was no significant difference in overall survival [between prednisone alone and prednisone plus the anticancer agent mitoxantrone.]" One of ordinary skill in the art, reading Tannock, would expect there to be no difference in survival between one cancer agent alone, and that same cancer agent in combination with prednisone. Thus, the present invention possesses unexpected results and is non-obvious over the cited art.

Further, the present invention has displayed commercial success. Applicant submits herewith the currently United States Food & Drug Administration approved label

for ZYTIGA™ (the "ZYTIGA label"). The ZYTIGA label indicates that "[abiraterone acetate] is a CYP17 inhibitor indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer." Taking ZYTIGA in accordance with the approved label represents a commercial embodiment of the presently claimed invention.

Applicant also submits herewith a news release from the U.S. Food and Drug Administration dated December 10, 2012 and titled "FDA expands Zytiga's use for late-stage prostate cancer." As can be seen from this 2012 news release, ZYTIGA was initially approved in April 2011 for use in patients whose prostate cancer progressed after treatment with docetaxel, a chemotherapy drug. ZYTIGA was further approved in December 2012 for use in prostate cancer patients prior to receiving chemotherapy.

Applicant also submits two further news releases from the U.S. Food and Drug Administration, one dated June 17, 2010, announcing approval of Jevtana for use in prostate cancer; and the other dated August 31, 2012, announcing the approval of Xtandi for use in patients whose prostate cancer progressed after treatment with docetaxel.

Applicant also submits herewith "Pharmaceuticals Commericial Overview", a slideshow presented by Joaquin Duato on May 23, 2013 and currently available at http://files.shareholder.com/downloads/JNJ/2514173625x0x666408/bb2972ea-2099-4ab4-b2a3-afc39e710594/Pharmaceutical_Commercial_Overview_JNJ2013.pdf (the "2013 slideshow"). According to the 2013 slideshow, at slide 11, ZYTIGA is the most successful oral oncology launch in history.

The 2013 slideshow, at slide 12, further shows the July 2012 to April 2013 ZYTIGA market share of chemo refractory prostate cancer patients, i.e., patients who have previously received chemotherapy treatment and the December 2012 to April 2013 market share of chemo naïve prostate cancer patients, i.e., patients who have not previously received chemotherapy treatment. As can be seen from the figure on the left of slide 12, ZYTIGA had almost 70% market share in July of 2012 for chemo refractory prostate cancer patients, just slightly over a year after ZYTIGA's initial approval, and despite the fact that a JEVTANA had been approved two years earlier. Despite another product, XTANDI, being introduced in August of 2012, by April of 2013, ZYTIGA was

still the market leader as of April 2013 with 57% market share in chemo refractory prostate cancer patients.

As can be seen from the figure on the right of slide 12, shortly after its approval for chemo-naïve patients in December 2012, ZYTIGA had a market share of 15%. As of April 2013, ZYTIGA's market share was 20%, higher than two other available therapies, docetaxel and XTANDI, and approaching the market share of bicalutamide, a drug first approved in 2001 for prostate cancer.

Thus, not only is ZYTIGA the most successful oral oncology launch in history, two years after its initial approval it is still the market leader for chemo refractory patients despite an earlier-introduced therapy and a later-introduced therapy. ZYTIGA also holds a strong market share in the chemo naïve prostate cancer population, despite the presence of other marketed products. This commercial success demonstrates the non-obviousness of the presently claimed invention.

Even assuming, *arguendo*, the cited art suggests the claimed combination, the present invention has shown surprising results, and commercial success. Thus, the claims are non-obvious over the cited art. Accordingly, Applicant requests reconsideration and withdrawal of the rejection under 35 USC §103(a).

III. CONCLUSION

Early consideration and prompt allowance of the claims are respectfully requested. Should the office require anything further, it is invited to contact Applicant's representative at the telephone number below.

Applicant respectfully requests that a timely Notice of Allowance be issued in the present application. Should the office require anything further, it is invited to contact Applicant's representative at the telephone number below.

Respectfully submitted,

JOHNSON & JOHNSON
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-3957
Dated: June 4, 2013
Customer No.: 27777

By: /Andrea Jo Kamage/
Andrea Jo Kamage
Reg. No. 43,703

I hereby certify that this correspondence is being transmitted via The Office Electronic Filing System (EFS) in accordance with 37 CFR 1.6(a)(4).

Date of Electronic (EFS) Transmission: June 4, 2013

Signature: /Laurie A. Phillips/ Name: Laurie A. Phillips

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Applicant(s):	Alan H. Auerbach	Conf. No.:	1597
Application No.:	13/034,340	Group Art:	1628
Filing Date:	February 24, 2011	Examiner:	San Ming R. Hui
Title:	Methods and Compositions for Treating Cancer		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

NOTICE OF APPEAL

Applicant hereby appeals to the Board of Patent Appeals and Interferences from the decision of the Examiner dated March 4, 2013 finally rejecting Claims 37-56 of the above-identified application.

The item(s) checked below are appropriate:

1. ☐ An extension of time to respond to the final rejection was granted on for month(s).
2. ☐ A Petition For Extension Of Time under 37 CFR 1.136 is attached hereto in triplicate.
3. ☒ A timely response to the final rejection has been filed.
4. ☒ Fee $500.00: for filing of Notice of Appeal
   ☐ Not required (fee paid in prior appeal)
   ☒ Charge to Deposit Account No. 10-0750/AJK/CGR5001.
   ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment in connection herewith to Deposit Account No. 10-0750/AJK/CGR5001.

Respectfully submitted,

JOHNSON & JOHNSON
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-3957
Dated: June 4, 2013
Customer No.: 27777

By: /Andrea Jo Kamage/
Andrea Jo Kamage
Reg. No. 43,703

U.S. Food and Drug Administration
Protecting and Promoting Your Health

News & Events

FDA NEWS RELEASE

For Immediate Release: Aug. 31, 2012
Media Inquiries: Erica Jefferson, 301-796-4988, erica.jefferson@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves new treatment for a type of late stage prostate cancer

The U.S. Food and Drug Administration today approved Xtandi (enzalutamide) to treat men with late-stage (metastatic) castration-resistant prostate cancer that has spread or recurred, even with medical or surgica therapy to minimize testosterone.

Approved for prostate cancer patients previously treated with docetaxel, another anti-cancer treatment, Xtandi was reviewed under the FDA's priority review program. The program provides for an expedited six-month review for drugs that may offer major advances in treatment or that provide a treatment when no adequate therapy exists. Xtandi received FDA approval three months ahead of the product's prescription drug user fee goal date of Nov. 22, 2012.

"The need for additional treatment options for advanced prostate cancer continues to be important for patients," said Richard Pazdur, M.D., director of the Office of Hematology and Oncology Products in FDA's Center for Drug Evaluation and Research. "Xtandi is the latest treatment for this disease to demonstrate its ability to extend a patient's life."

Prostate cancer forms in a gland in the male reproductive system found below the bladder and in front of the rectum. The male sex hormone testosterone stimulates the prostate tumors to grow. According to the National Cancer Institute, an estimated 241,740 men will be diagnosed with prostate cancer and 28,170 wil die from the disease in 2012.

The safety and effectiveness of Xtandi was evaluated in a study of 1,199 patients with metastatic castration-resistant prostate cancer who had received prior treatment with docetaxel. The study was designed to measure overall survival (the length of time before death) in men receiving Xtandi compared with men receiving a placebo (sugar pill). The median overall survival for patients receiving Xtandi was 18.4 months, compared with 13.6 months for the patients who received placebo.

The most common side effects observed in study participants taking Xtandi were weakness or fatigue, bacl pain, diarrhea, joint pain, hot flush, tissue swelling, musculoskeletal pain, headache, upper respiratory infections, dizziness, spinal cord compression and cauda equina syndrome, muscular weakness, difficulty sleeping, lower respiratory infections, blood in urine, tingling sensation, anxiety, and high blood pressure.

Seizures occurred in approximately 1 percent of those receiving Xtandi. Patients in the study who had a seizure stopped Xtandi therapy. The clinical study excluded patients with a history of seizure, an underlying brain injury with loss of consciousness, a temporary decrease in blood to the brain within the past 12 months, a stroke, brain metastases, an abnormal connection of the arteries and veins in the brain, or patients taking medications that may lower the seizure threshold. The safety of Xtandi is unknown in patients with these conditions.

Xtandi will be co-marketed by Astellas Pharma U.S., Inc. of Northbrook, IL and Medivation, Inc. of San Francisco, CA.

For more information:

FDA: Office of Hematology and Oncology Products[1]

FDA: Approved Drugs: Questions and Answers[2]

FDA: Drug Innovation[3]

FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

#

Read our Blog: FDA Voice[4]

Visit the FDA on Facebook[5], Flickr[6], YouTube[7] and Twitter[8][9]

RSS Feed for FDA News Releases[10]

Page Last Updated: 08/31/2012
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)
Email FDA

Links on this page:

1. /AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm091745.htm
2. /Drugs/ResourcesForYou/Consumers/ucm054420.htm
3. http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/default.htm
4. https://blogs.fda.gov/fdavoice/
5. http://www.facebook.com/FDA
6. http://www.flickr.com/photos/fdaphotos/
7. http://www.youtube.com/user/USFoodandDrugAdmin?blend=23&ob=5
8. http://twitter.com/us_fda
9. http://www.fda.gov/AboutFDA/AboutThisWebsite/WebsitePolicies/Disclaimers/default.htm
10. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/PressReleases/rss.xml

News & Events

FDA NEWS RELEASE

For Immediate Release: June 17, 2010
Media Inquiries: Erica Jefferson, 301-796-4988, erica.jefferson@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA Approves New Treatment for Advanced Prostate Cancer

The U.S. Food and Drug Administration today approved Jevtana (cabazitaxel), a chemotherapy drug used in combination with the steroid prednisone to treat men with prostate cancer. Jevtana is the first treatment for advanced, hormone-refractory, prostate cancer that has worsened during or after treatment with docetaxel, a commonly used drug for advanced prostate cancer.

In prostate cancer, the male sex hormone testosterone can cause prostate tumors to grow. Drugs, surgery or other hormones are used to reduce testosterone production or to block it. Some men have hormone refractory prostate cancer, meaning the prostate cancer cells continue to grow, despite testosterone suppression. Different treatments are needed for men with this type of cancer.

Jevtana was reviewed under the FDA's priority review program, which provides for an expedited six-month review for drugs that may offer major advances in treatment, or provide a treatment when no adequate therapy exists. Jevtana received approval ahead of the product's Sept. 30, 2010, goal date.

"Patients have few therapeutic options in this disease setting," said Richard Pazdur, M.D., director of the Office of Oncology Drug Products, part of the FDA's Center for Drug Evaluation and Research. "FDA was able to review and approve the application for Jevtana in 11 weeks, expediting the availability of this drug to men with prostate cancer."

Jevtana's safety and effectiveness was established in a single, 755-patient study. All study participants had previously received docetaxel. The study was designed to measure overall survival (the length of time before death) in men who received Jevtana in combination with prednisone compared with those who received the chemotherapy drug, mitoxantrone, in combination with prednisone. The median overall survival for patients receiving the Jevtana regimen was 15.1 months compared with 12.7 months for those who received the mitoxantrone regimen.

Side effects in those treated with Jevtana included decrease in infection-fighting white blood cells (neutropenia), anemia, decrease in the number of white blood cells (leukopenia), low level of platelets in the blood (thrombocytopenia), diarrhea, fatigue, nausea, vomiting, constipation, weakness (asthenia), and renal failure.

Prostate cancer, which usually occurs in older men, is the second most common cancer among men in the United States, behind skin cancer. In 2006, the most recent year for which numbers were available, 203,415 men developed prostate cancer and 28,372 men died from the disease, according to the Centers for Disease Control and Prevention.

Jevtana is marketed by Bridgewater, N.J.-based Sanofi-Aventis.

For more information:

- FDA: Office of Oncology Drug Products[1]
- CDC: Informed Decision Making About Prostate Cancer[2]
- NCI: Prostate Cancer[3]

#

RSS Feed for FDA News Releases[4] [what is RSS?[5]]

Page Last Updated: 04/23/2013
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)
Email FDA

Links on this page:

1. http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm091745.htm
2. http://www.cdc.gov/cancer/prostate/informed_decision_making.htm
3. http://www.cancer.gov/cancertopics/types/prostate
4. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/PressReleases/rss.xml
5. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/ucm144575.htm

News & Events

FDA NEWS RELEASE

For Immediate Release: Dec. 10, 2012
Media Inquiries: Stephanie Yao, 301-796-0394, stephanie.yao@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA expands Zytiga's use for late-stage prostate cancer
Drug can now be used before treatment with chemotherapy

The U.S. Food and Drug Administration today expanded the approved use of Zytiga (abiraterone acetate) to treat men with late-stage (metastatic) castration-resistant prostate cancer prior to receiving chemotherapy.

The FDA initially approved Zytiga in April 2011 for use in patients whose prostate cancer progressed after treatment with docetaxel, a chemotherapy drug. Zytiga is a pill that decreases the production of male sex hormone testosterone.

In prostate cancer, testosterone stimulates prostate tumors to grow. Drugs or surgery are used to reduce testosterone production or to block testosterone's effects. Some men have castration-resistant prostate cancer, meaning the prostate cancer cells continue to grow even with low levels of testosterone.

"Today's approval demonstrates the benefit of further evaluating a drug in an earlier disease setting and provides patients and health care providers the option of using Zytiga earlier in the course of treatment," said Richard Pazdur, M.D., director of the Office of Oncology Drug Products in the FDA's Center for Drug Evaluation and Research.

The FDA reviewed Zytiga's application for this new indication under the agency's priority review program. The program provides for an expedited six-month review for drugs that may offer major advances in treatment or provide a treatment when no adequate therapy exists.

Zytiga's safety and effectiveness for its expanded use were established in a clinical study of 1,088 men with late-stage, castration-resistant prostate cancer who had not previously received chemotherapy. Participants received either Zytiga or a placebo (sugar pill) in combination with prednisone.

The study was designed to measure the length of time a patient lived before death (overall survival) and the length of time a patient lived without further tumor growth as assessed by imaging studies (radiographi progression-free survival, or rPFS).

Patients who received Zytiga had a median overall survival of 35.3 months compared with 30.1 months for those receiving the placebo. Study results also showed Zytiga improved rPFS. The median rPFS was 8.3 months in the placebo group and had not yet been reached for patients treated with Zytiga at the time of analysis.

The most common side effects reported in those receiving Zytiga include fatigue, joint swelling or discomfort, swelling caused by fluid retention, hot flush, diarrhea, vomiting, cough, high blood pressure, shortness of breath, urinary tract infection, and bruising.

The most common laboratory abnormalities included low red blood cell count; high levels of the enzyme alkaline phosphatase, which can be a sign of other serious medical problems; high levels of fatty acids, sugar, and liver enzymes in the blood; and low levels of lymphocytes, phosphorous and potassium in the blood.

Zytiga is marketed by Horsham, Pa.-based Janssen Biotech Inc.

For more information:

FDA approves Zytiga for late-stage prostate cancer (April 2011)[1]

FDA: Office of Hematology and Oncology Products[2]

FDA: Approved Drugs: Questions and Answers[3]

NCI: Prostate Cancer[4]

This press release was updated on Dec. 10, 2012 at 2:30 p.m. to correct the date when Zytiga was

originally approved to April 2011.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

#

Read our Blog: FDA Voice[5]

Visit the FDA on Facebook[6], Flickr[7], YouTube[8] and Twitter[9][10]

RSS Feed for FDA News Releases[11]

Page Last Updated: 12/10/2012
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)
Email FDA

Links on this page:

1. /NewsEvents/Newsroom/PressAnnouncements/ucm253055.htm
2. /AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm091745.htm
3. /Drugs/ResourcesForYou/Consumers/ucm054420.htm
4. http://www.cancer.gov/cancertopics/types/prostate
5. https://blogs.fda.gov/fdavoice/
6. http://www.facebook.com/FDA
7. http://www.flickr.com/photos/fdaphotos/
8. http://www.youtube.com/user/USFoodandDrugAdmin?blend=23&ob=5
9. http://twitter.com/us_fda
10. http://www.fda.gov/AboutFDA/AboutThisWebsite/WebsitePolicies/Disclaimers/default.htm
11. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/PressReleases/rss.xml

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ZYTIGA safely and effectively. See full prescribing information for ZYTIGA.

ZYTIGA®

(abiraterone acetate) Tablets

For Oral Administration

Initial U.S. Approval – 2011

RECENT MAJOR CHANGES

Indications and usage (1)	12/2012
Contraindications, Pregnancy (4.1)	12/2012
Warnings and Precautions, Mineralocorticoid excess (5.1)	12/2012
Warnings and Precautions, Adrenocortical Insufficiency (5.2)	12/2012
Warnings and Precautions, Hepatotoxicity (5.3)	12/2012

INDICATIONS AND USAGE

ZYTIGA is a CYP17 inhibitor indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer. (1)

DOSAGE AND ADMINISTRATION

Recommended dose: ZYTIGA 1,000 mg (four 250 mg tablets) administered orally once daily in combination with prednisone 5 mg administered orally twice daily. ZYTIGA must be taken on an empty stomach. No food should be consumed for at least two hours before the dose of ZYTIGA is taken and for at least one hour after the dose of ZYTIGA is taken. The tablets should be swallowed whole with water. Do not crush or chew tablets. (2.1)

- For patients with baseline moderate hepatic impairment (Child-Pugh Class B), reduce the ZYTIGA starting dose to 250 mg once daily. (2.2)
- For patients who develop hepatotoxicity during treatment, hold ZYTIGA until recovery. Retreatment may be initiated at a reduced dose. ZYTIGA should be discontinued if patients develop severe hepatotoxicity. (2.2)

DOSAGE FORMS AND STRENGTHS

Tablet 250 mg (3)

CONTRAINDICATIONS

- ZYTIGA is contraindicated in women who are or may become pregnant. (4.1, 8.1)

WARNINGS AND PRECAUTIONS

- Mineralocorticoid excess: Use ZYTIGA with caution in patients with a history of cardiovascular disease. The safety of ZYTIGA in patients with LVEF < 50% or NYHA Class III or IV heart failure in Study 1 or LVEF < 50 % or NYHA Class II to IV heart failure in Study 2 was not established. Control hypertension and correct hypokalemia before treatment. Monitor blood pressure, serum potassium and symptoms of fluid retention at least monthly. (5.1)
- Adrenocortical insufficiency: Monitor for symptoms and signs of adrenocortical insufficiency. Increased dosage of corticosteroids may be indicated before, during and after stressful situations. (5.2)
- Hepatotoxicity: Increases in liver enzymes have led to drug interruption, dose modification and/or discontinuation. Monitor liver function and modify, interrupt, or discontinue ZYTIGA dosing as recommended. (5.3)
- Food effect: ZYTIGA must be taken on an empty stomach. Exposure (area under the curve) of abiraterone increases up to 10 fold when abiraterone acetate is taken with meals. (5.4)

ADVERSE REACTIONS

The most common adverse reactions (≥ 10%) are fatigue, joint swelling or discomfort, edema, hot flush, diarrhea, vomiting, cough, hypertension, dyspnea, urinary tract infection and contusion.

The most common laboratory abnormalities (> 20%) are anemia, elevated alkaline phosphatase, hypertriglyceridemia, lymphopenia, hypercholesterolemia, hyperglycemia, elevated AST, hypophosphatemia, elevated ALT and hypokalemia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Biotech, Inc. at 1-800-526-7736 (1-800-JANSSEN) or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

ZYTIGA is an inhibitor of the hepatic drug-metabolizing enzyme CYP2D6. Avoid co-administration of ZYTIGA with CYP2D6 substrates that have a narrow therapeutic index. If an alternative treatment cannot be used, exercise caution and consider a dose reduction of the concomitant CYP2D6 substrate. (7)

USE IN SPECIFIC POPULATIONS

- Do not use ZYTIGA in patients with baseline severe hepatic impairment (Child-Pugh Class C). (8.6)

See 17 for Patient Counseling Information and FDA-approved patient labeling.

Revised: [12/2012]

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ZYTIGA is a CYP17 inhibitor indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dose of ZYTIGA is 1,000 mg (four 250 mg tablets) administered orally once daily in combination with prednisone 5 mg administered orally twice daily. ZYTIGA must be taken on an empty stomach. No food should be consumed for at least two hours before the dose of ZYTIGA is taken and for at least one hour after the dose of ZYTIGA is taken *[see Clinical Pharmacology (12.3)]*. The tablets should be swallowed whole with water. Do not crush or chew tablets.

2.2 Dose Modification Guidelines

Hepatic Impairment

In patients with baseline moderate hepatic impairment (Child-Pugh Class B), reduce the recommended dose of ZYTIGA to 250 mg once daily. A once daily dose of 250 mg in patients with moderate hepatic impairment is predicted to result in an area under the concentration curve (AUC) similar to the AUC seen in patients with normal hepatic function receiving 1,000 mg once daily. However, there are no clinical data at the dose of 250 mg once daily in patients with moderate hepatic impairment and caution is advised. In patients with moderate hepatic impairment monitor ALT, AST, and bilirubin prior to the start of treatment, every week for the first month, every two weeks for the following two months of treatment and monthly thereafter. If elevations in ALT and/or AST greater than 5X upper limit of normal (ULN) or total bilirubin greater than 3X ULN occur in patients with baseline moderate hepatic impairment, discontinue ZYTIGA and do not re-treat patients with ZYTIGA *[see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)]*.

Avoid ZYTIGA in patients with baseline severe hepatic impairment (Child-Pugh Class C), as ZYTIGA has not been studied in this population, and no dose adjustment can be predicted.

Hepatotoxicity

For patients who develop hepatotoxicity during treatment with ZYTIGA (ALT and/or AST greater than 5X ULN or total bilirubin greater than 3X ULN), interrupt treatment with ZYTIGA *[see Warnings and Precautions (5.3)]*. Treatment may be restarted at a reduced dose of 750 mg once daily following return of liver function tests to the patient's baseline or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN. For patients who resume treatment, monitor serum transaminases and bilirubin at a minimum of every two weeks for three months and monthly thereafter.

If hepatotoxicity recurs at the dose of 750 mg once daily, re-treatment may be restarted at a reduced dose of 500 mg once daily following return of liver function tests to the patient's baseline or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN.

If hepatotoxicity recurs at the reduced dose of 500 mg once daily, discontinue treatment with ZYTIGA. The safety of ZYTIGA re-treatment of patients who develop AST or ALT greater than or equal to 20X ULN and/or bilirubin greater than or equal to 10X ULN is unknown.

3 DOSAGE FORMS AND STRENGTHS

ZYTIGA (abiraterone acetate) 250 mg tablets are white to off-white, oval-shaped tablets debossed with AA250 on one side.

4 CONTRAINDICATIONS

4.1 Pregnancy

ZYTIGA can cause fetal harm when administered to a pregnant woman. ZYTIGA is not indicated for use in women. ZYTIGA is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for pregnancy loss *[see Use in Specific Populations (8.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypertension, Hypokalemia and Fluid Retention Due to Mineralocorticoid Excess

ZYTIGA may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition *[see Clinical Pharmacology (12.1)]*. In the two randomized clinical trials, grade 3 to 4 hypertension occurred in 2% of patients, grade 3 to 4 hypokalemia in 4% of patients, and grade 3 to 4 edema in 1% of patients treated with ZYTIGA *[see Adverse Reactions (6)]*.

Co-administration of a corticosteroid suppresses adrenocorticotropic hormone (ACTH) drive, resulting in a reduction in the incidence and severity of these adverse reactions. Use caution when treating patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia or fluid retention, e.g., those with heart failure, recent myocardial infarction or ventricular arrhythmia. Use ZYTIGA with caution in patients with a history of cardiovascular disease. The safety of ZYTIGA in patients with left ventricular ejection fraction < 50% or New York Heart Association (NYHA) Class III or IV heart failure (in Study 1) or NYHA Class II to IV heart failure (in Study 2) was not established because these patients were excluded from these randomized clinical trials *[see Clinical Studies (14)]*. Monitor patients for hypertension, hypokalemia, and fluid retention at least once a month. Control hypertension and correct hypokalemia before and during treatment with ZYTIGA.

5.2 Adrenocortical Insufficiency

Adrenal insufficiency occurred in the two randomized clinical studies in 0.5% of patients taking ZYTIGA and in 0.2% of patients taking placebo. Adrenocortical insufficiency was reported in patients receiving ZYTIGA in combination with prednisone, following interruption of daily steroids and/or with concurrent infection or stress. Use caution and monitor for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress. Symptoms and signs of adrenocortical insufficiency may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with ZYTIGA. If clinically indicated, perform appropriate tests to confirm the diagnosis of adrenocortical insufficiency. Increased dosage of corticosteroids may be indicated before, during and after stressful situations *[see Warnings and Precautions (5.1)]*.

5.3 Hepatotoxicity

In the two randomized clinical trials, grade 3 or 4 ALT or AST increases (at least 5X ULN) were reported in 4% of patients who received ZYTIGA, typically during the first 3 months after starting treatment. Patients whose baseline ALT or AST were elevated were more likely to experience liver test elevation than those beginning with normal values. Treatment discontinuation due to liver enzyme increases occurred in 1% of patients taking ZYTIGA. No deaths clearly related to ZYTIGA were reported due to hepatotoxicity events.

Measure serum transaminases (ALT and AST) and bilirubin levels prior to starting treatment with ZYTIGA, every two weeks for the first three months of treatment and monthly thereafter. In patients with baseline moderate hepatic impairment receiving a reduced ZYTIGA dose of 250 mg, measure ALT, AST, and bilirubin prior to the start of treatment, every week for the first month, every two weeks for the following two months of treatment and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient's baseline should prompt more frequent monitoring. If at any time AST or ALT rise above five times the ULN, or the bilirubin rises above three times the ULN, interrupt ZYTIGA treatment and closely monitor liver function.

Re-treatment with ZYTIGA at a reduced dose level may take place only after return of liver function tests to the patient's baseline or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN *[see Dosage and Administration (2.2)]*.

The safety of ZYTIGA re-treatment of patients who develop AST or ALT greater than or equal to 20X ULN and/or bilirubin greater than or equal to 10X ULN is unknown.

5.4 Increased ZYTIGA Exposures with Food

ZYTIGA must be taken on an empty stomach. No food should be consumed for at least two hours before the dose of ZYTIGA is taken and for at least one hour after the dose of ZYTIGA is taken. Abiraterone C_{max} and $AUC_{0-\infty}$ (exposure) were increased up to 17- and 10-fold higher, respectively, when a single dose of abiraterone acetate was administered with a meal compared to a fasted state. The safety of these increased exposures when multiple doses of abiraterone acetate are taken with food has not been assessed *[see Dosage and Administration (2.1) and Clinical Pharmacology (12.3)]*.

6 ADVERSE REACTIONS

The following are discussed in more detail in other sections of the labeling:

- Hypertension, Hypokalemia, and Fluid Retention due to Mineralocorticoid Excess *[see Warnings and Precautions (5.1)]*.
- Adrenocortical Insufficiency *[see Warnings and Precautions (5.2)]*.
- Hepatotoxicity *[see Warnings and Precautions (5.3)]*.
- Increased ZYTIGA Exposures with Food *[see Warnings and Precautions (5.4)]*.

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Two randomized placebo-controlled, multicenter clinical trials enrolled patients who had metastatic castration-resistant prostate cancer who were using a gonadotropin-releasing hormone (GnRH) agonist or were previously treated with orchiectomy. In both Study 1 and Study 2 ZYTIGA was administered at a dose of 1,000 mg daily in combination with prednisone 5 mg twice daily in the active treatment arms. Placebo plus prednisone 5 mg twice daily was given to control patients.

The most common adverse drug reactions (≥10%) reported in the two randomized clinical trials that occurred more commonly (>2%) in the abiraterone acetate arm were fatigue, joint swelling or discomfort, edema, hot flush, diarrhea, vomiting, cough, hypertension, dyspnea, urinary tract infection and contusion.

The most common laboratory abnormalities (>20%) reported in the two randomized clinical trials that occurred more commonly (≥2%) in the abiraterone acetate arm were anemia, elevated alkaline phosphatase, hypertriglyceridemia, lymphopenia, hypercholesterolemia, hyperglycemia, elevated AST, hypophosphatemia, elevated ALT and hypokalemia.

Study 1: Metastatic CRPC Following Chemotherapy

Study 1 enrolled 1195 patients with metastatic CRPC who had received prior docetaxel chemotherapy. Patients were not eligible if AST and/or ALT ≥ 2.5X ULN in the absence of liver metastases. Patients with liver metastases were excluded if AST and/or ALT > 5X ULN.

Table 1 shows adverse reactions on the ZYTIGA arm in Study 1 that occurred with a ≥2% absolute increase in frequency compared to placebo or were events of special interest. The median duration of treatment with ZYTIGA was 8 months.

Table 1: Adverse Reactions due to ZYTIGA in Study 1

	ZYTIGA with Prednisone (N=791)		Placebo with Prednisone (N=394)	
System/Organ Class	All Grades[1]	Grade 3-4	All Grades	Grade 3-4
Adverse reaction	%	%	%	%
Musculoskeletal and connective tissue disorders				
Joint swelling/ discomfort[2]	29.5	4.2	23.4	4.1
Muscle discomfort[3]	26.2	3.0	23.1	2.3
General disorders				
Edema[4]	26.7	1.9	18.3	0.8
Vascular disorders				
Hot flush	19.0	0.3	16.8	0.3
Hypertension	8.5	1.3	6.9	0.3
Gastrointestinal disorders				
Diarrhea	17.6	0.6	13.5	1.3
Dyspepsia	6.1	0	3.3	0
Infections and infestations				
Urinary tract infection	11.5	2.1	7.1	0.5
Upper respiratory tract infection	5.4	0	2.5	0
Respiratory, thoracic and mediastinal disorders				
Cough	10.6	0	7.6	0
Renal and urinary disorders				
Urinary frequency	7.2	0.3	5.1	0.3
Nocturia	6.2	0	4.1	0
Injury, poisoning and procedural complications				
Fractures[5]	5.9	1.4	2.3	0
Cardiac disorders				
Arrhythmia[6]	7.2	1.1	4.6	1.0
Chest pain or chest discomfort[7]	3.8	0.5	2.8	0
Cardiac failure[8]	2.3	1.9	1.0	0.3

[1]Adverse events graded according to CTCAE version 3.0
[2]Includes terms Arthritis, Arthralgia, Joint swelling, and Joint stiffness
[3]Includes terms Muscle spasms, Musculoskeletal pain, Myalgia, Musculoskeletal discomfort, and Musculoskeletal stiffness
[4]Includes terms Edema, Edema peripheral, Pitting edema, and Generalized edema
[5]Includes all fractures with the exception of pathological fracture
[6]Includes terms Arrhythmia, Tachycardia, Atrial fibrillation, Supraventricular tachycardia, Atrial tachycardia, Ventricular tachycardia, Atrial flutter, Bradycardia, Atrioventricular block complete, Conduction disorder, and Bradyarrhythmia
[7]Includes terms Angina pectoris, Chest pain, and Angina unstable. Myocardial infarction or ischemia occurred more commonly in the placebo arm than in the ZYTIGA arm (1.3% vs. 1.1% respectively).
[8]Includes terms Cardiac failure, Cardiac failure congestive, Left ventricular dysfunction, Cardiogenic shock, Cardiomegaly, Cardiomyopathy, and Ejection fraction decreased

ZYTIGA® (abiraterone acetate) Tablets

Table 2 shows laboratory abnormalities of interest from Study 1. Grade 3-4 low serum phosphorus (7%) and low potassium (5%) occurred at a greater than or equal to 5% rate in the ZYTIGA arm.

Table 2: Laboratory Abnormalities of Interest in Study 1

	Abiraterone (N=791)		Placebo (N=394)	
Laboratory Abnormality	All Grades (%)	Grade 3-4 (%)	All Grades (%)	Grade 3-4 (%)
Hypertriglyceridemia	62.5	0.4	53.0	0
High AST	30.6	2.1	36.3	1.5
Hypokalemia	28.3	5.3	19.8	1.0
Hypophosphatemia	23.8	7.2	15.7	5.8
High ALT	11.1	1.4	10.4	0.8
High Total Bilirubin	6.6	0.1	4.6	0

Study 2: Metastatic CRPC Prior to Chemotherapy

Study 2 enrolled 1088 patients with metastatic CRPC who had not received prior cytotoxic chemotherapy. Patients were ineligible if AST and/or ALT ≥ 2.5X ULN and patients were excluded if they had liver metastases.

Table 3 shows adverse reactions on the ZYTIGA arm in Study 2 that occurred with a ≥ 2% absolute increase in frequency compared to placebo. The median duration of treatment with ZYTIGA was 13.8 months.

Table 3: Adverse Reactions in ≥5% of Patients on the ZYTIGA Arm in Study 2

	ZYTIGA with Prednisone (N=542)		Placebo with Prednisone (N=540)	
System/Organ Class	All Grades[1]	Grade 3-4	All Grades	Grade 3-4
Adverse reaction	%	%	%	%
General disorders				
Fatigue	39.1	2.2	34.3	1.7
Edema[2]	25.1	0.4	20.7	1.1
Pyrexia	8.7	0.6	5.9	0.2
Musculoskeletal and connective tissue disorders				
Joint swelling/ discomfort[3]	30.3	2.0	25.2	2.0
Groin pain	6.6	0.4	4.1	0.7
Gastrointestinal disorders				
Constipation	23.1	0.4	19.1	0.6
Diarrhea	21.6	0.9	17.8	0.9
Dyspepsia	11.1	0.0	5.0	0.2
Vascular disorders				
Hot flush	22.3	0.2	18.1	0.0
Hypertension	21.6	3.9	13.1	3.0
Respiratory, thoracic and mediastinal disorders				
Cough	17.3	0.0	13.5	0.2
Dyspnea	11.8	2.4	9.6	0.9
Psychiatric disorders				
Insomnia	13.5	0.2	11.3	0.0
Injury, poisoning and procedural complications				
Contusion	13.3	0.0	9.1	0.0
Falls	5.9	0.0	3.3	0.0
Infections and infestations				
Upper respiratory tract infection	12.7	0.0	8.0	0.0
Nasopharyngitis	10.7	0.0	8.1	0.0
Renal and urinary disorders				
Hematuria	10.3	1.3	5.6	0.6
Skin and subcutaneous tissue disorders				
Rash	8.1	0.0	3.7	0.0

[1]Adverse events graded according to CTCAE version 3.0
[2]Includes terms Edema peripheral, Pitting edema, and Generalized edema
[3]Includes terms Arthritis, Arthralgia, Joint swelling, and Joint stiffness

Table 4 shows laboratory abnormalities that occurred in greater than 15% of patients, and more frequently (>5%) in the ZYTIGA arm compared to placebo in Study 2. Grade 3-4 lymphopenia (9%), hyperglycemia (7%) and high alanine aminotransferase (6%) occurred at a greater than 5% rate in the ZYTIGA arm.

Table 4: Laboratory Abnormalities in > 15% of Patients in the ZYTIGA Arm of Study 2

Laboratory Abnormality	Abiraterone (N = 542)		Placebo (N = 540)	
	Grade 1-4 %	Grade 3-4 %	Grade 1-4 %	Grade 3-4 %
Hematology				
Lymphopenia	38.2	8.7	31.7	7.4
Chemistry				
Hyperglycemia[1]	56.6	6.5	50.9	5.2
High ALT	41.9	6.1	29.1	0.7
High AST	37.3	3.1	28.7	1.1
Hypernatremia	32.8	0.4	25.0	0.2
Hypokalemia	17.2	2.8	10.2	1.7

[1]Based on non-fasting blood draws

Cardiovascular Adverse Reactions:
In the combined data for studies 1 and 2, cardiac failure occurred more commonly in patients treated with ZYTIGA compared to patients on the placebo arm (2.1% versus 0.7%). Grade 3-4 cardiac failure occurred in 1.6% of patients taking ZYTIGA and led to 5 treatment discontinuations and 2 deaths. Grade 3-4 cardiac failure occurred in 0.2% of patients taking placebo. There were no treatment discontinuations and one death due to cardiac failure in the placebo group.

In Study 1 and 2, the majority of arrhythmias were grade 1 or 2. There was one death associated with arrhythmia and one patient with sudden death in the ZYTIGA arms and no deaths in the placebo arms. There were 7 (0.5%) deaths due to cardiorespiratory arrest in the ZYTIGA arms and 3 (0.3%) deaths in the placebo arms. Myocardial ischemia or myocardial infarction led to death in 3 patients in the placebo arms and 2 deaths in the ZYTIGA arms.

7 DRUG INTERACTIONS

7.1 Effects of Abiraterone on Drug Metabolizing Enzymes

ZYTIGA is an inhibitor of the hepatic drug-metabolizing enzyme CYP2D6. In a CYP2D6 drug-drug interaction trial, the C_{max} and AUC of dextromethorphan (CYP2D6 substrate) were increased 2.8- and 2.9-fold, respectively, when dextromethorphan was given with abiraterone acetate 1,000 mg daily and prednisone 5 mg twice daily. Avoid co-administration of abiraterone acetate with substrates of CYP2D6 with a narrow therapeutic index (e.g., thioridazine). If alternative treatments cannot be used, exercise caution and consider a dose reduction of the concomitant CYP2D6 substrate drug *[see Clinical Pharmacology (12.3)]*.

In vitro, ZYTIGA inhibits CYP2C8. There are no clinical data on the use of ZYTIGA with drugs that are substrates of CYP2C8. However, patients should be monitored closely for signs of toxicity related to the CYP2C8 substrate if used concomitantly with abiraterone acetate.

7.2 Drugs that Inhibit or Induce CYP3A4 Enzymes

Based on *in vitro* data, ZYTIGA is a substrate of CYP3A4. The effects of strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, nefazodone, saquinavir, telithromycin, ritonavir, indinavir, nelfinavir, voriconazole) or inducers (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, phenobarbital) on the pharmacokinetics of abiraterone have not been evaluated, *in vivo*. Avoid or use with caution, strong inhibitors and inducers of CYP3A4 during ZYTIGA treatment *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category X *[see Contraindications (4.1)]*.
ZYTIGA can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. While there are no adequate and well-controlled studies with ZYTIGA in pregnant women and ZYTIGA is not indicated for use in women, it is important to know that maternal use of a CYP17 inhibitor could affect development of the fetus. Abiraterone acetate caused developmental toxicity in pregnant rats at exposures that were lower than in patients receiving the recommended dose. ZYTIGA is contraindicated in women who are or may become pregnant while receiving the drug. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for pregnancy loss. Advise females of reproductive potential to avoid becoming pregnant during treatment with ZYTIGA.

In an embryo-fetal developmental toxicity study in rats, abiraterone acetate caused developmental toxicity when administered at oral doses of 10, 30 or 100 mg/kg/day throughout the period of organogenesis (gestational days 6-17). Findings included embryo-fetal lethality (increased post implantation loss and resorptions and decreased number of live fetuses), fetal developmental delay (skeletal effects) and urogenital effects (bilateral ureter dilation) at doses ≥10 mg/kg/day, decreased fetal ano-genital distance at ≥30 mg/kg/day, and decreased fetal body weight at 100 mg/kg/day. Doses ≥10 mg/kg/day caused maternal toxicity. The doses tested in rats resulted in systemic exposures (AUC) approximately 0.03, 0.1 and 0.3 times, respectively, the AUC in patients.

ZYTIGA® (abiraterone acetate) Tablets

8.3 Nursing Mothers

ZYTIGA is not indicated for use in women. It is not known if abiraterone acetate is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from ZYTIGA, a decision should be made to either discontinue nursing, or discontinue the drug taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness of ZYTIGA in pediatric patients have not been established.

8.5 Geriatric Use

Of the total number of patients receiving ZYTIGA in phase 3 trials, 73% of patients were 65 years and over and 30% were 75 years and over. No overall differences in safety or effectiveness were observed between these elderly patients and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Patients with Hepatic Impairment

The pharmacokinetics of abiraterone were examined in subjects with baseline mild (n = 8) or moderate (n = 8) hepatic impairment (Child-Pugh Class A and B, respectively) and in 8 healthy control subjects with normal hepatic function. The systemic exposure (AUC) of abiraterone after a single oral 1,000 mg dose of ZYTIGA increased by approximately 1.1-fold and 3.6-fold in subjects with mild and moderate baseline hepatic impairment, respectively compared to subjects with normal hepatic function.

No dosage adjustment is necessary for patients with baseline mild hepatic impairment. In patients with baseline moderate hepatic impairment (Child-Pugh Class B), reduce the recommended dose of ZYTIGA to 250 mg once daily. If elevations in ALT or AST >5X ULN or total bilirubin >3X ULN occur in patients with baseline moderate hepatic impairment, discontinue ZYTIGA treatment *[see Dosage and Administration (2.1) and Clinical Pharmacology (12.3)]*.

The safety of ZYTIGA in patients with baseline severe hepatic impairment has not been studied. These patients should not receive ZYTIGA.

For patients who develop hepatotoxicity during treatment, interruption of treatment and dosage adjustment may be required *[see Dosage and Administration (2.2), Warnings and Precautions (5.3), and Clinical Pharmacology (12.3)]*.

8.7 Patients with Renal Impairment

In a dedicated renal impairment trial, the mean PK parameters were comparable between healthy subjects with normal renal function (N=8) and those with end stage renal disease (ESRD) on hemodialysis (N=8) after a single oral 1,000 mg dose of ZYTIGA. No dosage adjustment is necessary for patients with renal impairment *[see Dosage and Administration (2.1) and Clinical Pharmacology (12.3)]*.

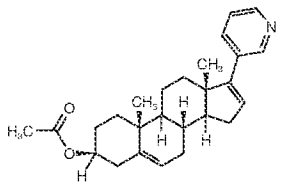
10 OVERDOSAGE

There have been no reports of overdose of ZYTIGA during clinical studies.

There is no specific antidote. In the event of an overdose, stop ZYTIGA, undertake general supportive measures, including monitoring for arrhythmias and cardiac failure and assess liver function.

11 DESCRIPTION

Abiraterone acetate, the active ingredient of ZYTIGA is the acetyl ester of abiraterone. Abiraterone is an inhibitor of CYP17 (17α-hydroxylase/C17,20-lyase). Each ZYTIGA tablet contains 250 mg of abiraterone acetate. Abiraterone acetate is designated chemically as (3β)-17-(3-pyridinyl)androsta-5,16-dien-3-yl acetate and its structure is:



Abiraterone acetate is a white to off-white, non-hygroscopic, crystalline powder. Its molecular formula is $C_{26}H_{33}NO_2$ and it has a molecular weight of 391.55. Abiraterone acetate is a lipophilic compound with an octanol-water partition coefficient of 5.12 (Log P) and is practically insoluble in water. The pKa of the aromatic nitrogen is 5.19.

Inactive ingredients in the tablets are colloidal silicon dioxide, croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone, and sodium lauryl sulfate.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Abiraterone acetate (ZYTIGA) is converted *in vivo* to abiraterone, an androgen biosynthesis inhibitor, that inhibits 17 α-hydroxylase/C17,20-lyase (CYP17). This enzyme is expressed in testicular, adrenal, and prostatic tumor tissues and is required for androgen biosynthesis.

CYP17 catalyzes two sequential reactions: 1) the conversion of pregnenolone and progesterone to their 17α-hydroxy derivatives by 17α-hydroxylase activity and 2) the subsequent formation of dehydroepiandrosterone (DHEA) and androstenedione, respectively, by C17, 20 lyase activity. DHEA and androstenedione are androgens and are precursors of testosterone. Inhibition of CYP17 by abiraterone can also result in increased mineralocorticoid production by the adrenals *[see Warnings and Precautions (5.1)]*.

Androgen sensitive prostatic carcinoma responds to treatment that decreases androgen levels. Androgen deprivation therapies, such as treatment with GnRH agonists or orchiectomy, decrease androgen production in the testes but do not affect androgen production by the adrenals or in the tumor.

ZYTIGA decreased serum testosterone and other androgens in patients in the placebo-controlled phase 3 clinical trial. It is not necessary to monitor the effect of ZYTIGA on serum testosterone levels.

Changes in serum prostate specific antigen (PSA) levels may be observed but have not been shown to correlate with clinical benefit in individual patients.

12.3 Pharmacokinetics

Following administration of abiraterone acetate, the pharmacokinetics of abiraterone and abiraterone acetate have been studied in healthy subjects and in patients with metastatic castration-resistant prostate cancer (CRPC). *In vivo*, abiraterone acetate is converted to abiraterone. In clinical studies, abiraterone acetate plasma concentrations were below detectable levels (< 0.2 ng/mL) in > 99% of the analyzed samples.

Absorption

Following oral administration of abiraterone acetate to patients with metastatic CRPC, the median time to reach maximum plasma abiraterone concentrations is 2 hours. Abiraterone accumulation is observed at steady-state, with a 2-fold higher exposure (steady-state AUC) compared to a single 1,000 mg dose of abiraterone acetate.

At the dose of 1,000 mg daily in patients with metastatic CRPC, steady-state values (mean ± SD) of C_{max} were 226 ± 178 ng/mL and of AUC were 1173 ± 690 ng.hr/mL. No major deviation from dose proportionality was observed in the dose range of 250 mg to 1,000 mg.

Systemic exposure of abiraterone is increased when abiraterone acetate is administered with food. Abiraterone C_{max} and $AUC_{0-\infty}$ were approximately 7- and 5-fold higher, respectively, when abiraterone acetate was administered with a low-fat meal (7% fat, 300 calories) and approximately 17- and 10-fold higher, respectively, when abiraterone acetate was administered with a high-fat (57% fat, 825 calories) meal. Given the normal variation in the content and composition of meals, taking ZYTIGA with meals has the potential to result in increased and highly variable exposures. Therefore, no food should be consumed for at least two hours before the dose of ZYTIGA is taken and for at least one hour after the dose of ZYTIGA is taken. The tablets should be swallowed whole with water *[see Dosage and Administration (2.1)]*.

Distribution and Protein Binding

Abiraterone is highly bound (>99%) to the human plasma proteins, albumin and alpha-1 acid glycoprotein. The apparent steady-state volume of distribution (mean ± SD) is 19,669 ± 13,358 L. *In vitro* studies show that at clinically relevant concentrations, abiraterone acetate and abiraterone are not substrates of P-glycoprotein (P-gp) and that abiraterone acetate is an inhibitor of P-gp. No studies have been conducted with other transporter proteins.

Metabolism

Following oral administration of ^{14}C-abiraterone acetate as capsules, abiraterone acetate is hydrolyzed to abiraterone (active metabolite). The conversion is likely through esterase activity (the esterases have not been identified) and is not CYP mediated. The two main circulating metabolites of abiraterone in human plasma are abiraterone sulphate (inactive) and N-oxide abiraterone sulphate (inactive), which account for about 43% of exposure each. CYP3A4 and SULT2A1 are the enzymes involved in the formation of N-oxide abiraterone sulphate and SULT2A1 is involved in the formation of abiraterone sulphate.

Excretion

In patients with metastatic CRPC, the mean terminal half-life of abiraterone in plasma (mean ± SD) is 12 ± 5 hours. Following oral administration of ^{14}C-abiraterone acetate, approximately 88% of the radioactive dose is recovered in feces and approximately 5% in urine. The major compounds present in feces are unchanged abiraterone acetate and abiraterone (approximately 55% and 22% of the administered dose, respectively).

ZYTIGA® (abiraterone acetate) Tablets

Patients with Hepatic Impairment

The pharmacokinetics of abiraterone was examined in subjects with baseline mild (n = 8) or moderate (n = 8) hepatic impairment (Child-Pugh Class A and B, respectively) and in 8 healthy control subjects with normal hepatic function. Systemic exposure to abiraterone after a single oral 1,000 mg dose given under fasting conditions increased approximately 1.1-fold and 3.6-fold in subjects with mild and moderate baseline hepatic impairment, respectively. The mean half-life of abiraterone is prolonged to approximately 18 hours in subjects with mild hepatic impairment and to approximately 19 hours in subjects with moderate hepatic impairment. ZYTIGA has not been studied in patients with baseline severe hepatic impairment (Child-Pugh Class C) *[see Dosage and Administration (2.2) and Use in Specific Populations (8.6)]*.

Patients with Renal Impairment

The pharmacokinetics of abiraterone were examined in patients with end-stage renal disease (ESRD) on a stable hemodialysis schedule (N=8) and in matched control subjects with normal renal function (N=8). In the ESRD cohort of the trial, a single 1,000 mg ZYTIGA dose was given under fasting conditions 1 hour after dialysis, and samples for pharmacokinetic analysis were collected up to 96 hours post dose. Systemic exposure to abiraterone after a single oral 1,000 mg dose did not increase in subjects with end-stage renal disease on dialysis, compared to subjects with normal renal function *[see Use in Specific Populations (8.7)]*.

Drug Interactions

In vitro studies with human hepatic microsomes showed that abiraterone is a strong inhibitor of CYP1A2, CYP2D6 and CYP2C8, a moderate inhibitor of CYP2C9, CYP2C19 and CYP3A4/5.

In an *in vivo* drug-drug interaction trial, the C_{max} and AUC of dextromethorphan (CYP2D6 substrate) were increased 2.8- and 2.9-fold, respectively when dextromethorphan 30 mg was given with abiraterone acetate 1,000 mg daily (plus prednisone 5 mg twice daily). The AUC for dextrorphan, the active metabolite of dextromethorphan, increased approximately 1.3 fold *[see Drug Interactions (7.1)]*.

In a clinical study to determine the effects of abiraterone acetate 1,000 mg daily (plus prednisone 5 mg twice daily) on a single 100 mg dose of the CYP1A2 substrate theophylline, no increase in systemic exposure of theophylline was observed.

Abiraterone is a substrate of CYP3A4, *in vitro*. The effects of strong CYP3A4 inhibitors or inducers on the pharmacokinetics of abiraterone have not been evaluated, *in vivo*. Strong inhibitors and inducers of CYP3A4 should be avoided or used with caution *[see Drug Interactions (7.2)]*.

12.6 QT Prolongation

In a multi-center, open-label, single-arm trial, 33 patients with metastatic CRPC received ZYTIGA orally at a dose of 1,000 mg once daily at least 1 hour before or 2 hours after a meal in combination with prednisone 5 mg orally twice daily. Assessments up to Cycle 2 Day 2 showed no large changes in the QTc interval (i.e., >20 ms) from baseline. However, small increases in the QTc interval (i.e., <10 ms) due to abiraterone acetate cannot be excluded due to study design limitations.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of abiraterone acetate.

Abiraterone acetate and abiraterone did not induce mutations in the microbial mutagenesis (Ames) assay and was not clastogenic in both the *in vitro* cytogenetic assay using primary human lymphocytes and in the *in vivo* rat micronucleus assay.

ZYTIGA has the potential to impair reproductive function and fertility in humans based on findings in animals. In repeat-dose toxicity studies in male rats (13- and 26-weeks) and monkeys (39-weeks), atrophy, aspermia/hypospermia, and hyperplasia in the reproductive system were observed at ≥ 50 mg/kg/day in rats and ≥ 250 mg/kg/day in monkeys and were consistent with the antiandrogenic pharmacological activity of abiraterone *[see Nonclinical Toxicology (13.2)]*. These effects were observed in rats at systemic exposures similar to humans and in monkeys at exposures approximately 0.6 times the AUC in humans.

In fertility studies in rats, reduced organ weights of the reproductive system, sperm counts, sperm motility, altered sperm morphology and decreased fertility were observed in males dosed for 4 weeks at ≥ 30 mg/kg/day. Mating of untreated females with males that received 30 mg/kg/day abiraterone acetate resulted in a reduced number of corpora lutea, implantations and live embryos and an increased incidence of pre-implantation loss. Effects on male rats were reversible after 16 weeks from the last abiraterone acetate administration. Female rats dosed for 2 weeks until day 7 of pregnancy at ≥ 30 mg/kg/day had an increased incidence of irregular or extended estrous cycles and pre-implantation loss (300 mg/kg/day). There were no differences in mating, fertility, and litter parameters in female rats that received abiraterone acetate. Effects on female rats were reversible after 4 weeks from the last abiraterone acetate administration. The dose of 30 mg/kg/day in rats is approximately 0.3 times the recommended dose of 1000 mg/day based on body surface area.

13.2 Animal Toxicology and/or Pharmacology

In 13- and 26-week studies in rats and 13- and 39-week studies in monkeys, a reduction in circulating testosterone levels occurred with abiraterone acetate at approximately one half the human clinical exposure based on AUC. As a result, decreases in organ weights and toxicities were observed in the male and female reproductive system, adrenal glands, liver, pituitary (rats only), and male mammary glands. The changes in the reproductive organs are consistent with the antiandrogenic pharmacological activity of abiraterone acetate. A dose-dependent increase in cataracts was observed in rats at 26 weeks starting at ≥ 50 mg/kg/day (similar to the human clinical exposure based on AUC). In the 39-week monkey study, no cataracts were observed at higher doses (2 times greater than the clinical exposure based on AUC). All other toxicities associated with abiraterone acetate reversed or were partially resolved after a 4-week recovery period.

14 CLINICAL STUDIES

The efficacy and safety of ZYTIGA in patients with metastatic castration-resistant prostate cancer (CRPC) that has progressed on androgen deprivation therapy was demonstrated in two randomized, placebo-controlled, multicenter phase 3 clinical trials. Patients with prior ketoconazole treatment for prostate cancer and a history of adrenal gland or pituitary disorders were excluded from these trials.

Study 1

Patients with metastatic CRPC who had received prior docetaxel chemotherapy:
A total of 1195 patients were randomized 2:1 to receive either ZYTIGA orally at a dose of 1,000 mg once daily in combination with prednisone 5 mg orally twice daily (N=797) or placebo once daily plus prednisone 5 mg orally twice daily (N=398). Patients randomized to either arm were to continue treatment until disease progression (defined as a 25% increase in PSA over the patient's baseline/nadir together with protocol-defined radiographic progression and symptomatic or clinical progression), initiation of new treatment, unacceptable toxicity or withdrawal.

The following patient demographics and baseline disease characteristics were balanced between the treatment arms. The median age was 69 years (range 39-95) and the racial distribution was 93.3% Caucasian, 3.6% Black, 1.7% Asian, and 1.6% Other. Eighty-nine percent of patients enrolled had an ECOG performance status score of 0-1 and 45% had a Brief Pain Inventory-Short Form score of ≥ 4 (patient's reported worst pain over the previous 24 hours). Ninety percent of patients had metastases in bone and 30% had visceral involvement. Seventy percent of patients had radiographic evidence of disease progression and 30% had PSA-only progression. Seventy percent of patients had previously received one cytotoxic chemotherapy regimen and 30% received two regimens.

The protocol pre-specified interim analysis was conducted after 552 deaths and showed a statistically significant improvement in overall survival in patients treated with ZYTIGA compared to patients in the placebo arm (Table 5 and Figure 1). An updated survival analysis was conducted when 775 deaths (97% of the planned number of deaths for final analysis) were observed. Results from this analysis were consistent with those from the interim analysis (Table 5).

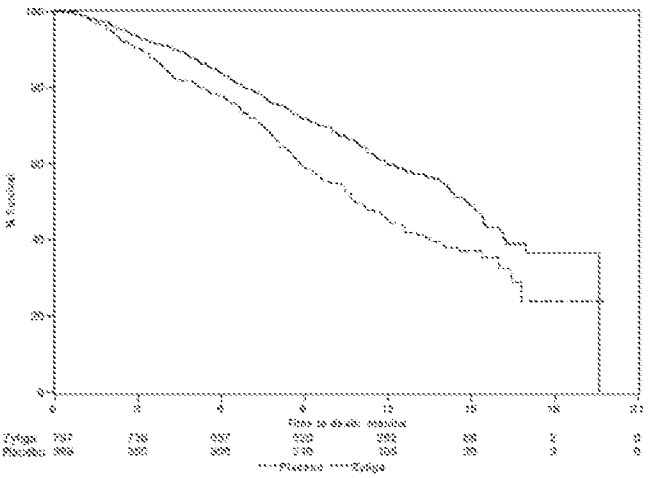
Table 5: Overall Survival of Patients Treated with Either ZYTIGA or Placebo in Combination with Prednisone in Study 1 (Intent-to-Treat Analysis)

	ZYTIGA (N=797)	Placebo (N=398)
Primary Survival Analysis		
Deaths (%)	333 (42%)	219 (55%)
Median survival (months) (95% CI)	14.8 (14.1, 15.4)	10.9 (10.2, 12.0)
p-value [a]	< 0.0001	
Hazard ratio (95% CI) [b]	0.646 (0.543, 0.768)	
Updated Survival Analysis		
Deaths (%)	501 (63%)	274 (69%)
Median survival (months) (95% CI)	15.8 (14.8, 17.0)	11.2 (10.4, 13.1)
Hazard ratio (95% CI) [b]	0.740 (0.638, 0.859)	

[a] P-value is derived from a log-rank test stratified by ECOG performance status score (0-1 vs. 2), pain score (absent vs. present), number of prior chemotherapy regimens (1 vs. 2), and type of disease progression (PSA only vs. radiographic).
[b] Hazard Ratio is derived from a stratified proportional hazards model. Hazard ratio <1 favors ZYTIGA

ZYTIGA® (abiraterone acetate) Tablets

Figure 1: Kaplan-Meier Overall Survival Curves in Study 1 (Intent-to-Treat Analysis)



Study 2

Patients with metastatic CRPC who had not received prior cytotoxic chemotherapy
In Study 2, 1088 patients were randomized 1:1 to receive either ZYTIGA at a dose of 1,000 mg once daily (N=546) or Placebo once daily (N=542). Both arms were given concomitant prednisone 5 mg twice daily. Patients continued treatment until radiographic or clinical (cytotoxic chemotherapy, radiation or surgical treatment for cancer, pain requiring chronic opioids, or ECOG performance status decline to 3 or more) disease progression, unacceptable toxicity or withdrawal. Patients with moderate or severe pain, opiate use for cancer pain, or visceral organ metastases were excluded.

Patient demographics were balanced between the treatment arms. The median age was 70 years. The racial distribution of patients treated with ZYTIGA was 95.4% Caucasian, 2.8% Black, 0.7% Asian and 1.1% Other. The ECOG performance status was 0 for 76% of patients, and 1 for 24% of patients. Co-primary efficacy endpoints were overall survival and radiographic progression-free survival (rPFS). Baseline pain assessment was 0-1 (asymptomatic) in 66% of patients and 2-3 (mildly symptomatic) in 26% of patients as defined by the Brief Pain Inventory-Short Form (worst pain over the last 24 hours).

Radiographic progression-free survival was assessed with the use of sequential imaging studies and was defined by bone scan identification of 2 or more new bone lesions with confirmation (Prostate Cancer Working Group 2 criteria) and/or modified Response Evaluation Criteria in Solid Tumors (RECIST) criteria for progression of soft tissue lesions. Analysis of rPFS utilized centrally-reviewed radiographic assessment of progression.

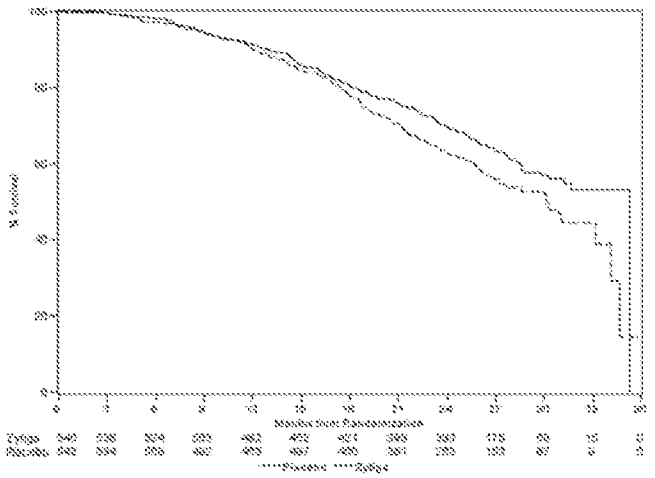
At the protocol pre-specified third interim analysis for overall survival, 37% (200 of 546) of patients treated with ZYTIGA, compared with 43% (234 of 542) of patients treated with placebo, had died. Overall survival was longer for ZYTIGA than placebo with a hazard ratio of 0.792 (95% CI: 0.655 - 0.956). The p- value was 0.0151 which did not meet the pre-specified value for statistical significance (Table 6 and Figure 2).

Table 6: Overall Survival of Patients Treated with Either ZYTIGA or Placebo in Combination with Prednisone in Study 2 (Intent-to-Treat Analysis)

Overall Survival	ZYTIGA (N=546)	Placebo (N=542)
Deaths	200 (37%)	234 (43%)
Median survival (months) (95% CI)	35.3 (31.24, 35.29)	30.1 (27.30, 34.10)
p-value[a]	0.0151	
Hazard ratio[b] (95% CI)	0.792 (0.655, 0.956)	

[a] P-value is derived from a log-rank test stratified by ECOG performance status score (0 vs. 1).
[b] Hazard Ratio is derived from a stratified proportional hazards model. Hazard ratio <1 favors ZYTIGA

Figure 2: Kaplan Meier Overall Survival Curves in Study 2 (Intent-to-Treat analysis)



At the pre-specified rPFS analysis, 150 (28%) patients treated with ZYTIGA and 251 (46%) patients treated with placebo had radiographic progression. A significant difference in rPFS between treatment groups was observed (Table 7 and Figure 3).

Table 7: Radiographic Progression-free Survival of Patients Treated with Either ZYTIGA or Placebo in Combination with Prednisone in Study 2 (Intent-to-Treat Analysis)

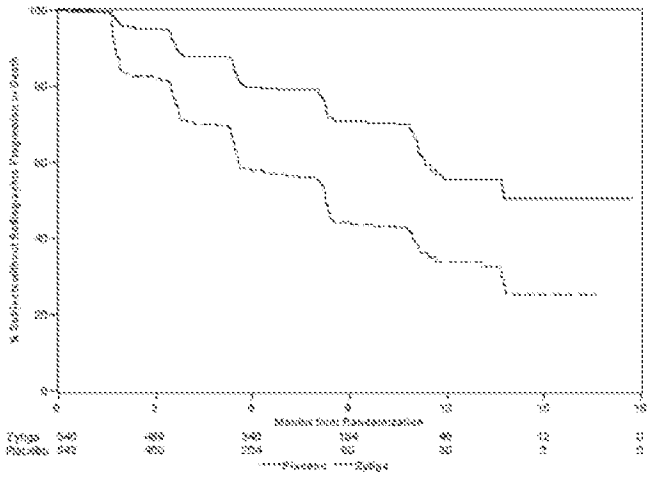
Radiographic Progression-free Survival	ZYTIGA (N=546)	Placebo (N=542)
Progression or death	150 (28%)	251 (46%)
Median rPFS (months) (95% CI)	NR (11.66, NR)	8.28 (8.12, 8.54)
p-value[a]	<0.0001	
Hazard ratio[b] (95% CI)	0.425 (0.347, 0.522)	

NR= Not reached

[a] P-value is derived from a log-rank test stratified by ECOG performance status score (0 vs. 1).

[b] Hazard Ratio is derived from a stratified proportional hazards model. Hazard ratio <1 favors ZYTIGA

Figure 3: Kaplan Meier Curves of Radiographic Progression-free Survival in Study 2 (Intent-to-Treat Analysis)



The primary efficacy analyses are supported by the following prospectively defined endpoints. The median time to initiation of cytotoxic chemotherapy was 25.2 months for patients receiving ZYTIGA and 16.8 months for patients receiving placebo (HR=0.580; 95% CI: [0.487, 0.691], p<0.0001).

ZYTIGA® (abiraterone acetate) Tablets

The median time to opiate use for prostate cancer pain was not reached for patients receiving ZYTIGA and was 23.7 months for patients receiving placebo (HR=0.686, 95% CI: [0.566, 0.833], p=0.0001). The time to opiate use result was supported by a delay in patient reported pain progression favoring the ZYTIGA arm.

16 HOW SUPPLIED/STORAGE AND HANDLING

ZYTIGA (abiraterone acetate) 250 mg tablets are white to off-white, oval tablets debossed with AA250 on one side. ZYTIGA 250 mg tablets are available in high-density polyethylene bottles of 120 tablets.

NDC Number 57894-150-12

Storage and Handling

Store at 20°C to 25°C (68°F to 77°F); excursions permitted in the range from 15°C to 30°C (59°F to 86°F) *[see USP controlled room temperature]*.

Based on its mechanism of action, ZYTIGA may harm a developing fetus. Therefore, women who are pregnant or women who may be pregnant should not handle ZYTIGA without protection, e.g., gloves *[see Use in Specific Populations (8.1)]*.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information)

- Patients should be informed that ZYTIGA and prednisone are used together and that they should not interrupt or stop either of these medications without consulting their physician.
- Patients receiving GnRH agonists should be informed that they need to maintain this treatment during the course of treatment with ZYTIGA and prednisone.
- Patients should be informed that ZYTIGA must not be taken with food and that no food should be consumed for at least two hours before the dose of ZYTIGA is taken and for at least one hour after the dose of ZYTIGA is taken. They should be informed that the tablets should be swallowed whole with water without crushing or chewing. Patients should be informed that taking ZYTIGA with food causes increased exposure and this may result in adverse reactions.
- Patients should be informed that ZYTIGA is taken once daily and prednisone is taken twice daily according to their physician's instructions.
- Patients should be informed that in the event of a missed daily dose of ZYTIGA or prednisone, they should take their normal dose the following day. If more than one daily dose is skipped, patients should be told to inform their physician.
- Patients should be apprised of the common side effects associated with ZYTIGA, including peripheral edema, hypokalemia, hypertension, elevated liver function tests, and urinary tract infection. Direct the patient to a complete list of adverse drug reactions in PATIENT INFORMATION.
- Patients should be advised that their liver function will be monitored using blood tests.
- Patients should be informed that ZYTIGA may harm a developing fetus; thus, women who are pregnant or women who may be pregnant should not handle ZYTIGA without protection, e.g., gloves. Patients should also be informed that it is not known whether abiraterone or its metabolites are present in semen and they should use a condom if having sex with a pregnant woman. The patient should use a condom and another effective method of birth control if he is having sex with a woman of child-bearing potential. These measures are required during and for one week after treatment with ZYTIGA.

Manufactured by:
Patheon Inc.
Mississauga, Canada

Manufactured for:
Janssen Biotech, Inc.
Horsham, PA 19044

Revised: December 2012

janssen

PATIENT INFORMATION
ZYTIGA® (Zye-tee-ga)
(abiraterone acetate)
Tablets

Read this Patient Information that comes with ZYTIGA before you start taking it and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What is ZYTIGA?

ZYTIGA is a prescription medicine that is used along with prednisone. ZYTIGA is used to treat men with castration-resistant prostate cancer (prostate cancer that is resistant to medical or surgical treatments that lower testosterone) that has spread to other parts of the body.

ZYTIGA is not for use in women.

It is not known if ZYTIGA is safe or effective in children.

Who should not take ZYTIGA?

Do not take ZYTIGA if you are pregnant or may become pregnant. ZYTIGA may harm your unborn baby.

Women who are pregnant or who may become pregnant should not touch ZYTIGA without protection, such as gloves.

What should I tell my healthcare provider before taking ZYTIGA?

Before you take ZYTIGA, tell your healthcare provider if you:

- have heart problems
- have liver problems
- have a history of adrenal problems
- have a history of pituitary problems
- have any other medical conditions
- plan to become pregnant. See "Who should not take ZYTIGA?"
- are breastfeeding or plan to breastfeed. It is not known if ZYTIGA passes into your breast milk. You and your healthcare provider should decide if you will take ZYTIGA or breastfeed. You should not do both. See "Who should not take ZYTIGA?"

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. ZYTIGA can interact with many other medicines.

You should not start or stop any medicine before you talk with the healthcare provider that prescribed ZYTIGA.

Know the medicines you take. Keep a list of them with you to show to your healthcare provider and pharmacist when you get a new medicine.

How should I take ZYTIGA?

- Take ZYTIGA and prednisone exactly as your healthcare provider tells you.
- Take your prescribed dose of ZYTIGA one time a day.
- Your healthcare provider may change your dose if needed.
- Do not stop taking your prescribed dose of ZYTIGA or prednisone without talking with your healthcare provider first.
- Take ZYTIGA on an empty stomach. **Do not take ZYTIGA with food.** Taking ZYTIGA with food may cause more of the medicine to be absorbed by the body than is needed and this may cause side effects.

ZYTIGA® (abiraterone acetate) Tablets

- No food should be eaten 2 hours before and 1 hour after taking ZYTIGA.
- Swallow ZYTIGA tablets whole. Do not crush or chew tablets.
- Take ZYTIGA tablets with water.
- Men who are sexually active with a pregnant woman must use a condom during and for one week after treatment with ZYTIGA. If their sexual partner may become pregnant, a condom and another form of birth control must be used during and for one week after treatment with ZYTIGA. Talk with your healthcare provider if you have questions about birth control.
- If you miss a dose of ZYTIGA or prednisone, take your prescribed dose the following day. If you miss more than 1 dose, tell your healthcare provider right away.
- Your healthcare provider will do blood tests to check for side effects.

What are the possible side effects of ZYTIGA?

ZYTIGA may cause serious side effects including:

- **High blood pressure (hypertension), low blood potassium levels (hypokalemia) and fluid retention (edema).** Tell your healthcare provider if you get any of the following symptoms:
  - o dizziness
  - o fast heartbeats
  - o feel faint or lightheaded
  - o headache
  - o confusion
  - o muscle weakness
  - o pain in your legs
  - o swelling in your legs or feet
- **Adrenal problems** may happen if you stop taking prednisone, get an infection, or are under stress.
- **Liver problems**. You may develop changes in liver function blood test. Your healthcare provider will do blood tests to check your liver before treatment with ZYTIGA and during treatment with ZYTIGA.

The most common side effects of ZYTIGA include:

- o weakness
- o joint swelling or pain
- o swelling in your legs or feet
- o hot flushes
- o diarrhea
- o vomiting
- o cough
- o high blood pressure
- o shortness of breath
- o urinary tract infection
- o bruising
- o low red blood cells (anemia) and low blood potassium levels
- o high blood sugar levels, high blood cholesterol and triglycerides
- o certain other abnormal blood tests

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of ZYTIGA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store ZYTIGA?

- Store ZYTIGA at 59°F to 86°F (15°C to 30°C).

Keep ZYTIGA and all medicines out of the reach of children.

General information about ZYTIGA.

Medicines are sometimes prescribed for purposes other than those listed in a patient information leaflet. Do not use ZYTIGA for a condition for which it was not prescribed. Do not give your ZYTIGA to other people, even if they have the same symptoms that you have. It may harm them.

This leaflet summarizes the most important information about ZYTIGA. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about ZYTIGA that is written for healthcare professionals.

For more information contact Janssen Biotech, Inc. at 1-800-526-7736 (1-800-JANSSEN) or www.Zytiga.com.

What are the ingredients of ZYTIGA?

Active ingredient: abiraterone acetate

Inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone, and sodium lauryl sulfate.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Manufactured by:
Patheon Inc.
Mississauga, Canada

Manufactured for:
Janssen Biotech, Inc.
Horsham, PA 19044

Revised: December 2012

2000005445

K08Z121174

janssen

Pharmaceuticals Commercial Overview

Joaquin Duato

Worldwide Chairman, Pharmaceuticals

janssen | PHARMACEUTICAL COMPANIES

Note on Forward-looking Statements

These presentations contain "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995. The viewer is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of the Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to, general industry conditions and competition; economic factors, such as interest rate and currency exchange rate fluctuations; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approvals; challenges to patents; significant adverse litigation or government action; impact of business combinations; financial distress and bankruptcies experienced by significant customers and suppliers; changes to governmental laws and regulations and domestic and foreign health care reforms; trends toward health care cost containment; increased scrutiny of the health care industry by government agencies; changes in behavior and spending patterns of purchasers of health care products and services; financial instability of international economies and sovereign risk; disruptions due to natural disasters; manufacturing difficulties or delays; complex global supply chains with increasing regulatory requirements; and product efficacy or safety concerns resulting in product recalls or regulatory action. A further list and description of these risks, uncertainties and other factors can be found in Exhibit 99 of Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 30, 2012. Copies of this Form 10-K, as well as subsequent filings, are available online at www.sec.gov, www.investor.jnj.com or on request from Johnson & Johnson. Neither the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statements as a result of new information or future events or developments.

Notice Regarding Non-GAAP Statements

These presentations may refer to certain non-GAAP financial measures. These non-GAAP financial measures should not be considered replacements for, and should be read together with, the most comparable GAAP financial measures. A reconciliation of these non-GAAP financial measures to the most directly comparable GAAP financial measures can be found in the Investor Relations section of the Company's website at www.investor.jnj.com.

Note: Operational sales growth excludes currency impact and is a non-GAAP financial measure.

New Molecular Entities

These presentations contain statements about new molecular entities ("NMEs") and other medicines or line extensions in various stages of development. These statements are based on the Company's current knowledge of the status of development of these NMEs, medicines and line extensions and are subject to the challenges and difficulties inherent in product development. The Company assumes no obligation to update any statements regarding these NMEs, medicines or line extensions as a result of new information or future events or developments.

In addition, in biopharmaceuticals, there are higher possibilities of encountering infringement claims by competitors with respect to patents or other intellectual property rights.

Strategic Partnerships, Collaborations and Licensing Arrangements

During the course of this morning's presentations, we will discuss a number of products and compounds developed in collaboration with strategic partners or licensed from other companies. Following is an acknowledgement of those relationships that are not otherwise referenced in today's presentations.

Immunology REMICADE® and SIMPONI® marketing partners are Schering-Plough (Ireland) Company, a subsidiary of Merck & Co., Inc. and Mitsubishi Tanabe Pharma Corporation, ASP015K-JAK Inhibitor licensed from Astellas Pharma Inc., Sirukumab developed in collaboration with GlaxoSmithKline.

Neuroscience INVEGA® SUSTENNA®/XEPLION® includes technology licensed from Alkermes, Inc., NUCYNTA® co-developed with Grunenthal GmbH, RISPERDAL® CONSTA® developed in collaboration with Alkermes, Fulranumab licensed from Amgen, Inc., Bapineuzumab is being developed through a collaboration between Janssen Alzheimer Immunotherapy and Pfizer Inc., Bace Inhibitor–Prodormal Alzheimer's disease licensed from Shionogi & Co., MGluR2 PAM developed in collaboration with Addex Therapeutics, NR2B licensed from Evotec, MGluR5 PAM developed in collaboration with Vanderbilt University, AAB-003 and AAC-001 developed in collaboration with Pfizer, ULTRAM® ER licensed from Grunenthal GmbH, TRAMACET® developed in collaboration with Grunenthal GmbH, AXERT® licensed from Almirall Prodesfarma, REMINYL® is licensed from Shire PLC., LEXAPRO® co-marketed and license agreement between Xian-Janssen and Lundbeck A/S,

Infectious Diseases & Virology INCIVO® developed in collaboration with Vertex Pharmaceuticals, Simeprevir (TMC435) developed in collaboration with Medivir AB, Darunavir/cobicistat fixed-dose combination developed in collaboration with Gilead Sciences, Inc., LEVAQUIN® licensed from Daiichi Sankyo Co., Ltd., QUINVAXEM® developed in collaboration with Novartis Vaccines and Diagnostics, HIV Vaccine developed in collaboration with Beth Israel Deaconess Medical Center and National Institutues of Health, (NIH), Rabies mAb co-promoted with Sanofi Pasteur, FlumAb partially funded by NIH.

Cardiovascular/ Metabolism INVOKANA™ licensed from Mitsubishi Tanabe Pharma Corporation, XARELTO® co-developed with Bayer HealthCare.

Oncology Ibrutinib (PCI-32765) developed in collaboration and upon approval will be co-marketed with Pharmacyclics, Inc., ZYTIGA® licensed from BTG International Ltd., VELCADE® developed in collaboration with Millennium: The Takeda Oncology Company, DACOGEN® developed in collaboration with Eisai Corporation of North America, Daratumumab licensed from Genmab A/S, YONDELIS® developed in collaboration with Pharma Mar S.A., Intetumumab licensed to and co-developed with BeiGene, Ltd., PROCRIT®/EPREX® licensed from Amgen Inc., FGFR Inhibitor is licensed from Astex Pharmaceuticals, Inc.

The Pharmaceuticals Market Is Attractive and Growing

- Global market $963B in 2012
- Compound annual growth ~4.5% to $1.2T in 2017
- Market drivers
  - Aging demographics
  - Growing middle class in emerging markets
  - Rising incidence of chronic disease
  - Significant unmet medical needs

Tremendous Opportunity to Improve the Lives of Patients

Source: IMS Market Prognosis Reports, March 2013.

janssen | Pharmaceutical Companies of Johnson & Johnson

Building on the Strong Momentum in Pharmaceuticals

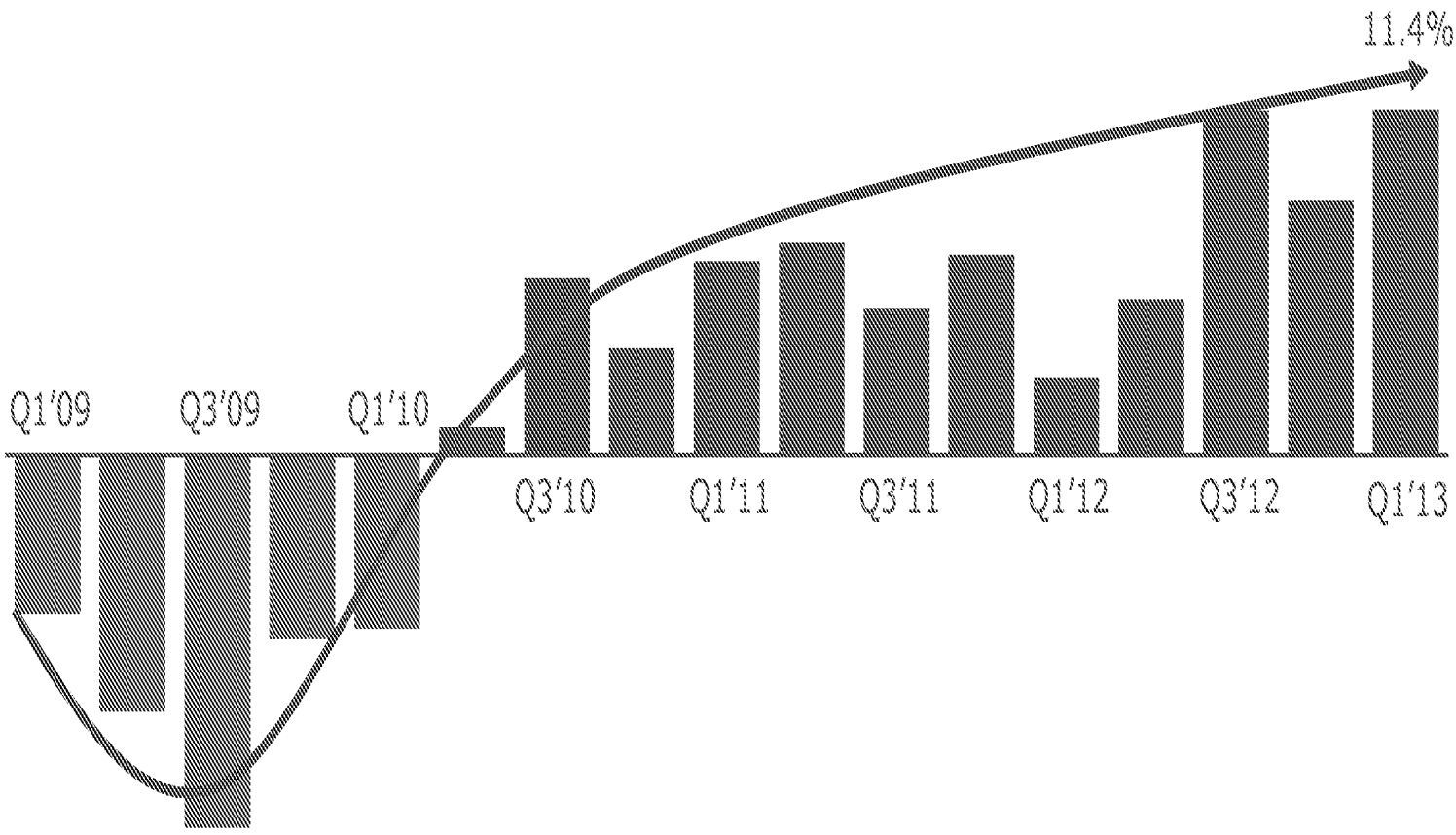
Focus on Transformational Medical Innovation

- Revitalizing our portfolio:
  11 new product launches in the last 4 years
- Combining superior science with
  best-in-class commercial capabilities
- Delivering robust growth and outpacing
  our peers in markets where we compete
- Next wave of growth:
  Potential for >10 NMEs & >25 LEs by 2017

janssen

Fastest Growing Top 10 Pharmaceutical Company[1]

WW Pharmaceuticals: Operational Sales Change vs. Prior Year Respective Quarter*



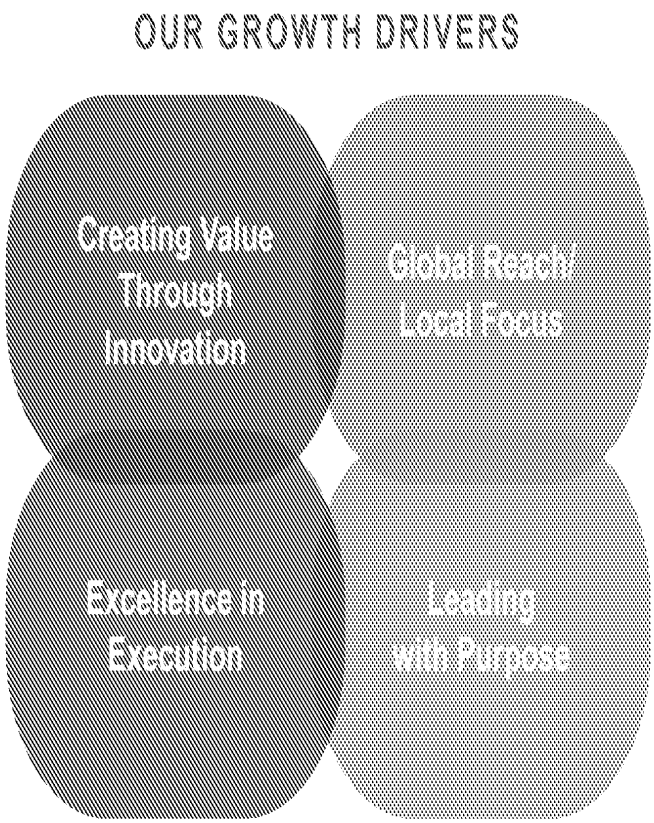
Source: 1. IMS MIDAS as of 1Q 2013 vs. prior year respective quarter (based on available data May 20, 2013).

* Q4 2009 and Q4 2010 operational sales change adjusted for the dynamics of the 53rd week in Q4 2009.

janssen | Pharmaceutical Companies of Johnson & Johnson

Johnson & Johnson

Strategic Framework



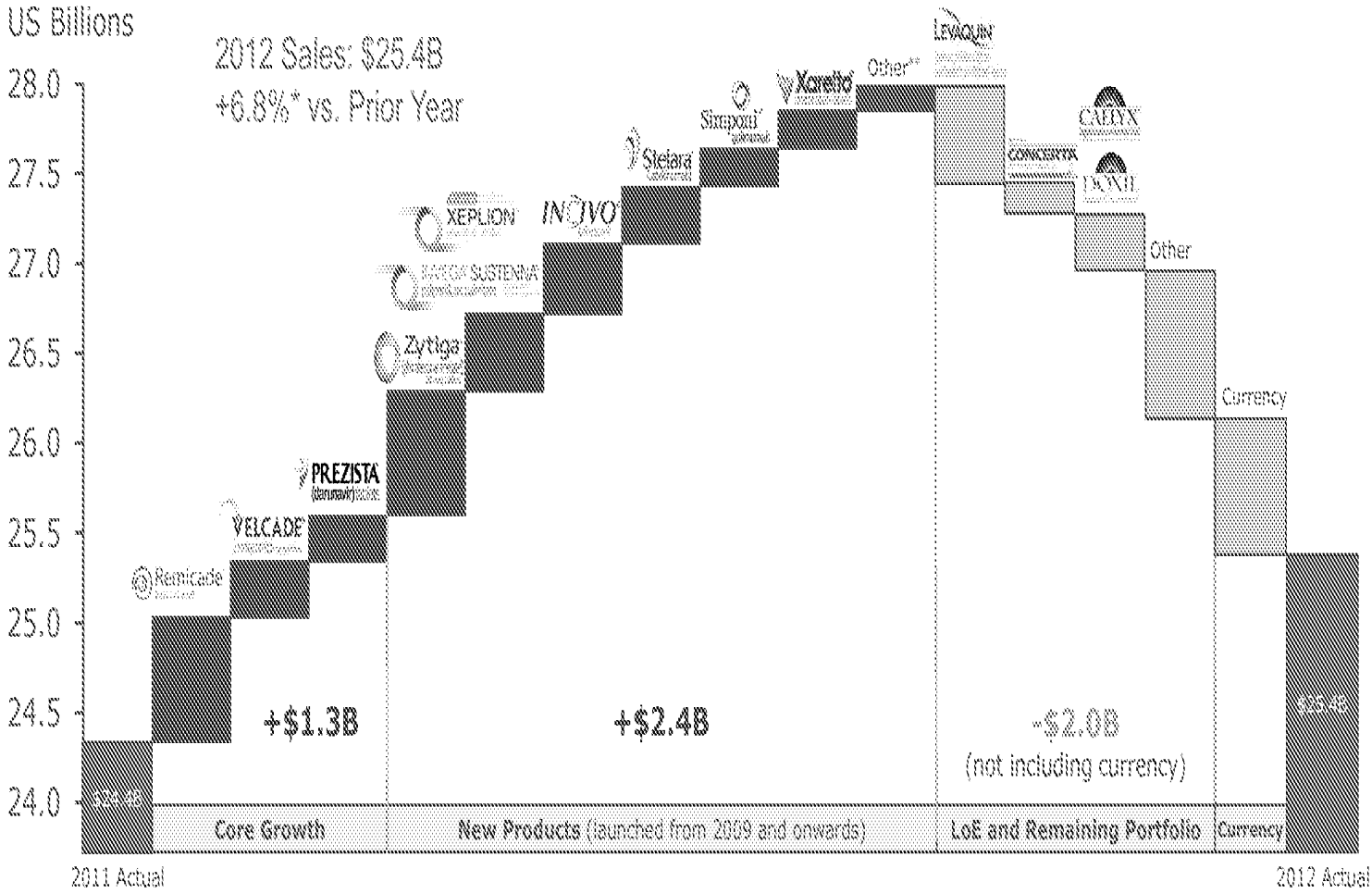
janssen | Pharmaceutical Companies of Johnson & Johnson

Johnson & Johnson

Strategic Framework

janssen | PHARMACEUTICAL COMPANIES of Johnson & Johnson

Robust Performance from Core Growth and New Products



*Operational change. **Other new products include NUCYNTA®, EDURANT®/COMPLERA®, and DACOGEN®.

janssen | Pharmaceutical Companies of Johnson & Johnson

Core Growth Products Continue to Make a Strong Contribution

VELCADE® (bortezomib) FOR INJECTION

- Backbone of Multiple Myeloma treatment
  - Reached $1.5B in 2012 (+25%)*
  - Recently approved subcutaneous formulation
  - Label expansion planned in Mantle Cell Lymphoma

Q1 2013 SALES	Q1 YoY GROWTH*
$353MM	3%

PREZISTA® (darunavir) tablets

- Leading HIV Protease Inhibitor (PI), robust growth
  - Reached $1.4B in 2012 (+21%)*, #1 PI in Europe and US
  - New fixed-dose combination being developed with Gilead's cobicistat in Phase III

Q1 2013 SALES	Q1 YoY GROWTH*
$367MM	14%

Remicade® INFLIXIMAB

- Largest Johnson & Johnson brand, continued strong growth
  - Revenues over $6B in 2012 (+13%)*
  - 16 indications: 75% share of US Intravenous (IV) Immunology market[1]

Q1 2013 SALES	Q1 YoY GROWTH
$1.6B	6%

Source: 1. IMS Health. *Operational change.

janssen | Pharmaceutical Companies of Johnson & Johnson

Immunology Portfolio Expanding on REMICADE® Legacy of Leadership

WW Market[1]		
2012	2017	CAGR
$35B	$52B	8%

Simponi® golimumab

Expanding Geographies and Indications

- Over $600MM in 2012 (+51%)*
- Additional FDA approval for moderately to severely active Ulcerative Colitis, May 2013
- Rheumatoid Arthritis IV formulation PDUFA July 2013

Q1 2013 SALES	Q1 YoY GROWTH*
$237MM	**

Remicade® INFLIXIMAB

Stelara® (ustekinumab)

Game-Changing, First-in-Class

- Crossed $1B threshold in 2012 (+42%)*
- 5-Year efficacy and safety data – 9,000 patient years of experience
- Psoriatic Arthritis Signs and Symptoms submitted 2012

Q1 2013 SALES	Q1 YoY GROWTH*
$346MM	57%

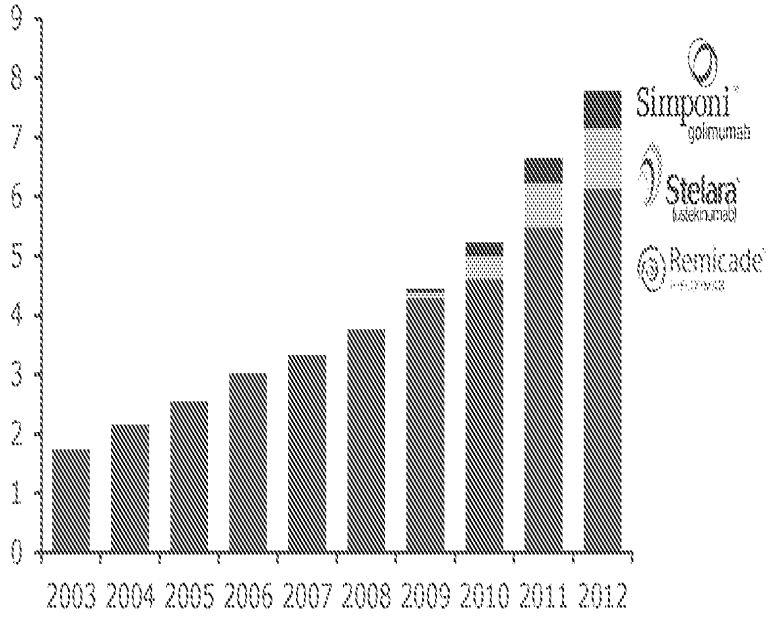
Sources: 1. EvaluatePharma, April 2013 (Immunology market includes small and large molecules for Rheumatoid Arthritis, Ankylosing Spondylitis, Lupus, Psoriatic Arthritis, Crohn's Disease, Ulcerative Colitis, and Psoriasis). * Operational change. ** Percent greater than 100%.

janssen | Pharmaceutical Companies of Johnson & Johnson

US Immunology Leader, Poised for Continued Growth

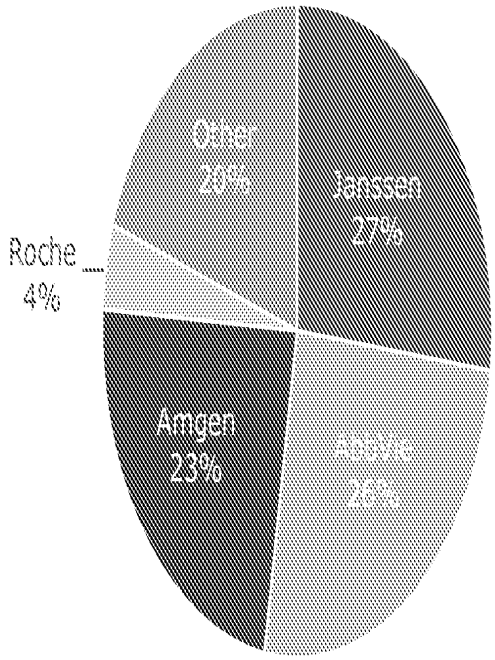
Total Immunology Products Delivered $7.9B in 2012; 19% Operational Compound Annual Growth Rate Since 2009

WW Immunology Portfolio Sales ($B)



Janssen Is #1 in US Immunology Sales and #2 Worldwide[1]

US Immunology Sales, 2012 ($17B)[1]



Source: 1. EvaluatePharma, May 2013 (Immunology market includes US small and large molecules for Rheumatoid Arthritis, Ankylosing Spondylitis, Lupus, Psoriatic Arthritis, Crohn's Disease, Ulcerative Colitis, and Psoriasis).

janssen | Pharmaceutical Companies of Johnson & Johnson

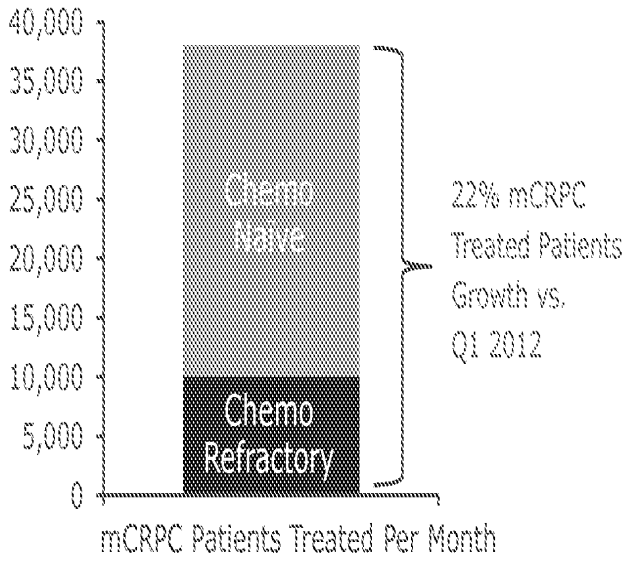
ZYTIGA®: Most Successful Oral Oncology Launch in History[1]

- Generated $961MM revenue in 2012
- Changed treatment paradigm for metastatic Castration-Resistant Prostate Cancer (mCRPC)
- Approved in 75+ countries for chemo refractory and more than 60,000 patients treated
- Approved in 40+ countries for chemo naïve (US/EU approvals December 2012)

WW Market[2]		
2012	2017	CAGR
$4.5B	$8.0B	12%

Q1 2013 SALES	Q1 YoY GROWTH
$344MM	72%

Q1 2013 US Patient Population[3]



Sources: 1. EvaluatePharma, Oncology launch view orals, May 14, 2013. 2. EvaluatePharma, April 2013 (Prostate Cancer market). 3. IMS Health and internal analysis.
* Operational change.

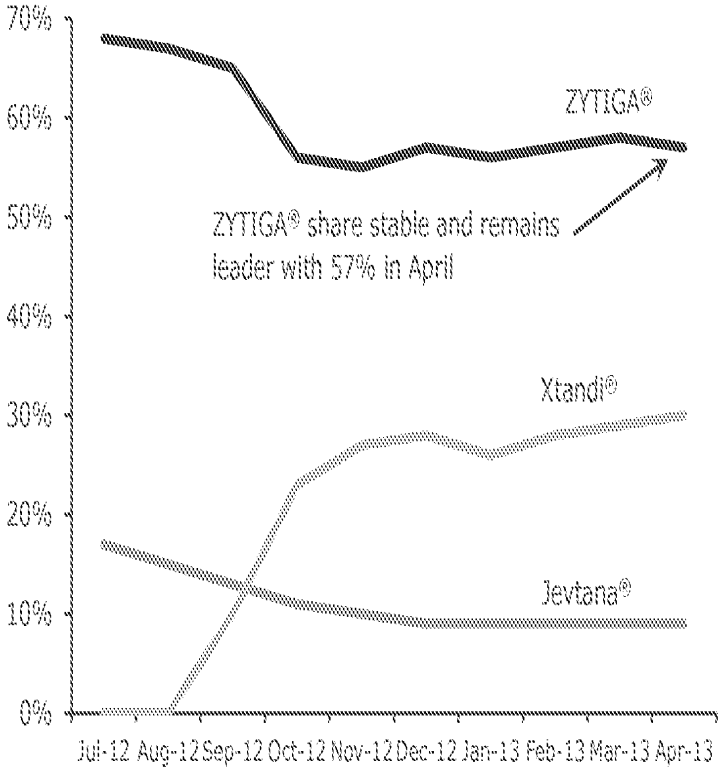
janssen | Pharmaceutical Companies of Johnson & Johnson

Overall US Patient Share Continues to Grow

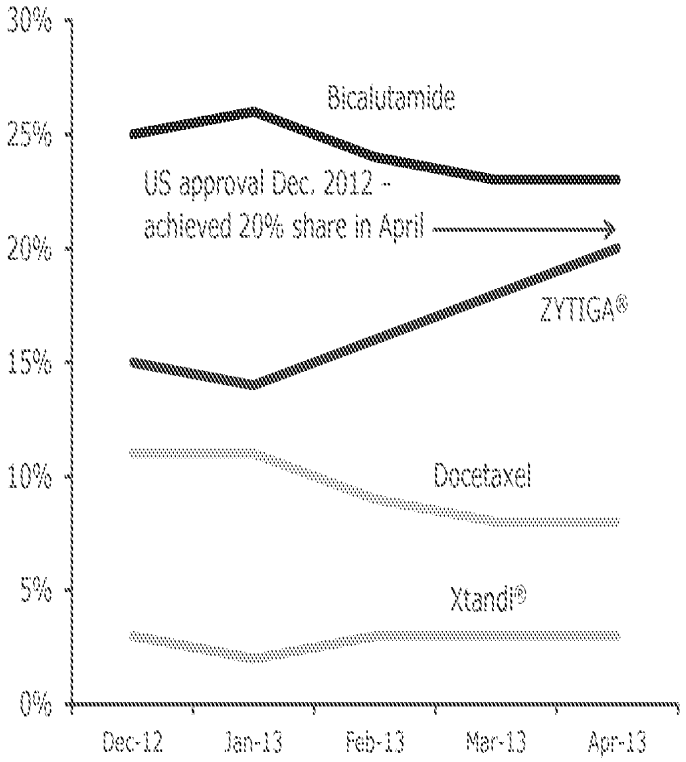
Total mCRPC Share in April Over 30%, Up ~3 Points from Q4 2012

Zytiga (abiraterone acetate) 250 mg tablets

Chemo Refractory



Chemo Naïve



Sources: ZYTIGA® – IMS DDD. Wolters Kluwer Health (WKH). Xtandi® – WKH data based on ZYTIGA® Xponent samples to IMS DDD universe (sample of claims from SPP/Pharmacy to Payer). Note: Patient share percentages are preliminary estimates based on limited data available. Patient level detailed sales data by indication only available on a 2 month lag (i.e., March data at the beginning of June).

janssen | Pharmaceutical Companies of Johnson & Johnson

INCIVO®: Maintaining Leadership Position

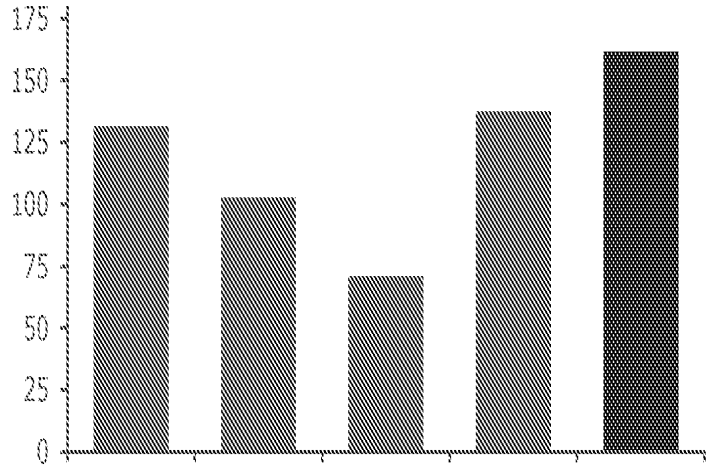
INCIVO® telaprevir

- EMA approved 2011; now launched in over 30 countries
- Maintaining strong lead vs. Victrelis® across Europe
- Received CHMP recommendation for twice-daily dosing April 2013

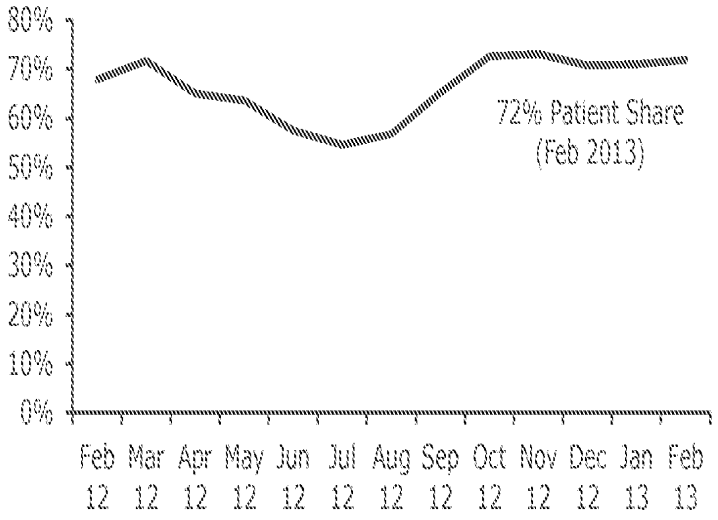
OUS Market[2]		
2012	2017	CAGR
$2.8B	$7.7B	22%

Q1 2013 SALES	Q1 YoY GROWTH*
$162MM	25%

INCIVO® Sales ($MM)



INCIVO® Patient Share (EMEA) – Direct-Acting Antivirals[1]



Sources: 1. IMS Health. 2. EvaluatePharma, April 2013 (HCV market excluding OTC products). * Operational change.

XARELTO®: Broadest Profile of Any Novel Oral Anticoagulant

Xarelto® (rivaroxaban tablets)

- Strong customer value proposition with once-a-day dosing convenience and multiple indications
- Broad market access
  - Over 90% formulary coverage for insured patients
  - 85% of Commercial and 85% of Part D have Tier 2 access and lowest branded co-pay
- Leader in the novel oral market[1]
  - Surpassed 1MM prescriptions in 2012
  - Over 1MM prescriptions already in 2013

US Market[2]		
2012	2017	CAGR
$2.2B	$5.6B	21%

Q1 2013 SALES	Q1 YoY GROWTH*
$158MM	**

6 FDA-Approved Indications

- Atrial Fibrillation (AF)
- Deep Vein Thrombosis (DVT)
- Pulmonary Embolism (PE)
- Risk of DVT/PE reoccurrence
- Prophylaxis of DVT/PE – Knee
- Prophylaxis of DVT/PE – Hip

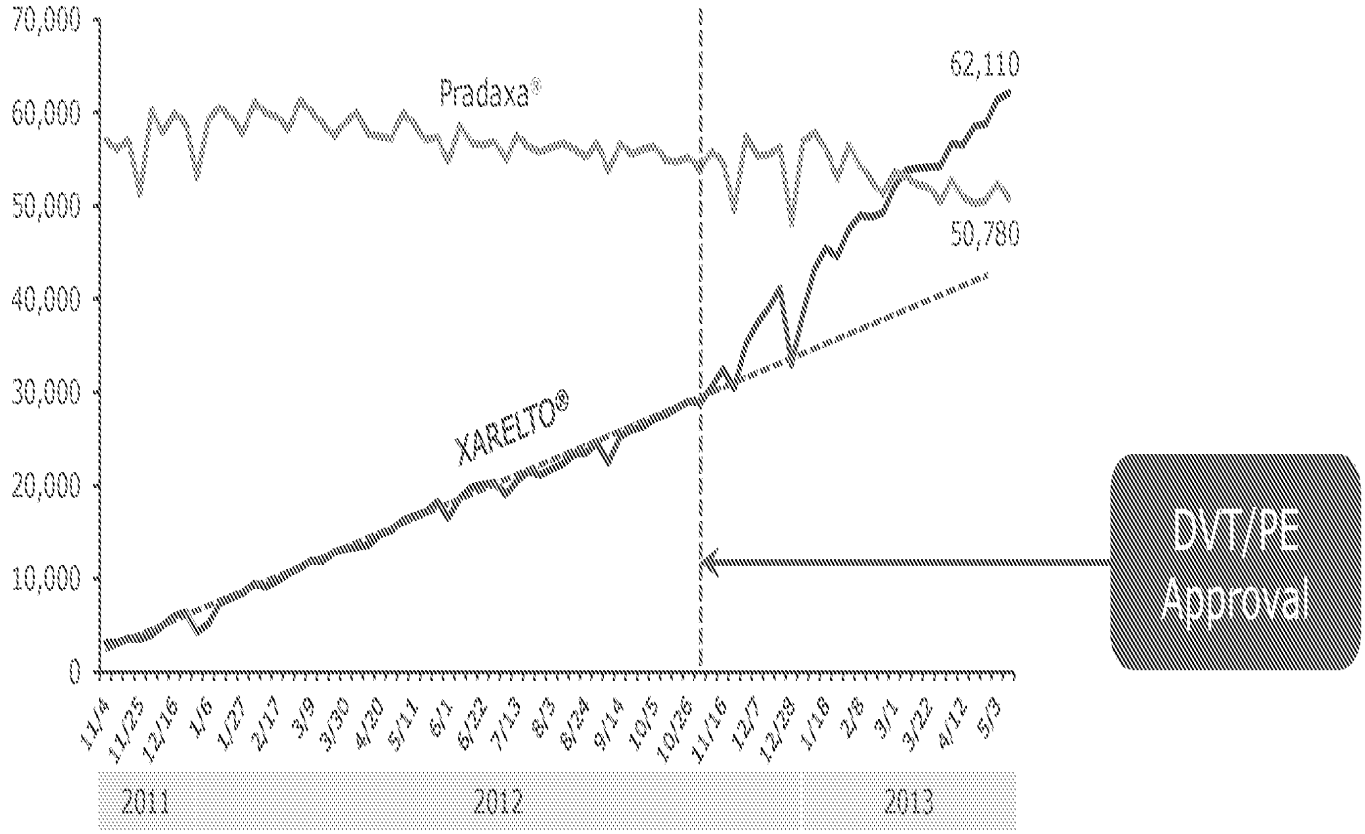
Sources: 1. IMS Health. 2. EvaluatePharma, May 2013 (oral anticoagulants).
* Operational change. ** Percent greater than 100%.

janssen | Pharmaceutical Companies of Johnson & Johnson

Novel Oral Anticoagulant Leader in the US

Xarelto® (rivaroxaban) tablets

Novel Orals – US TRx Volume

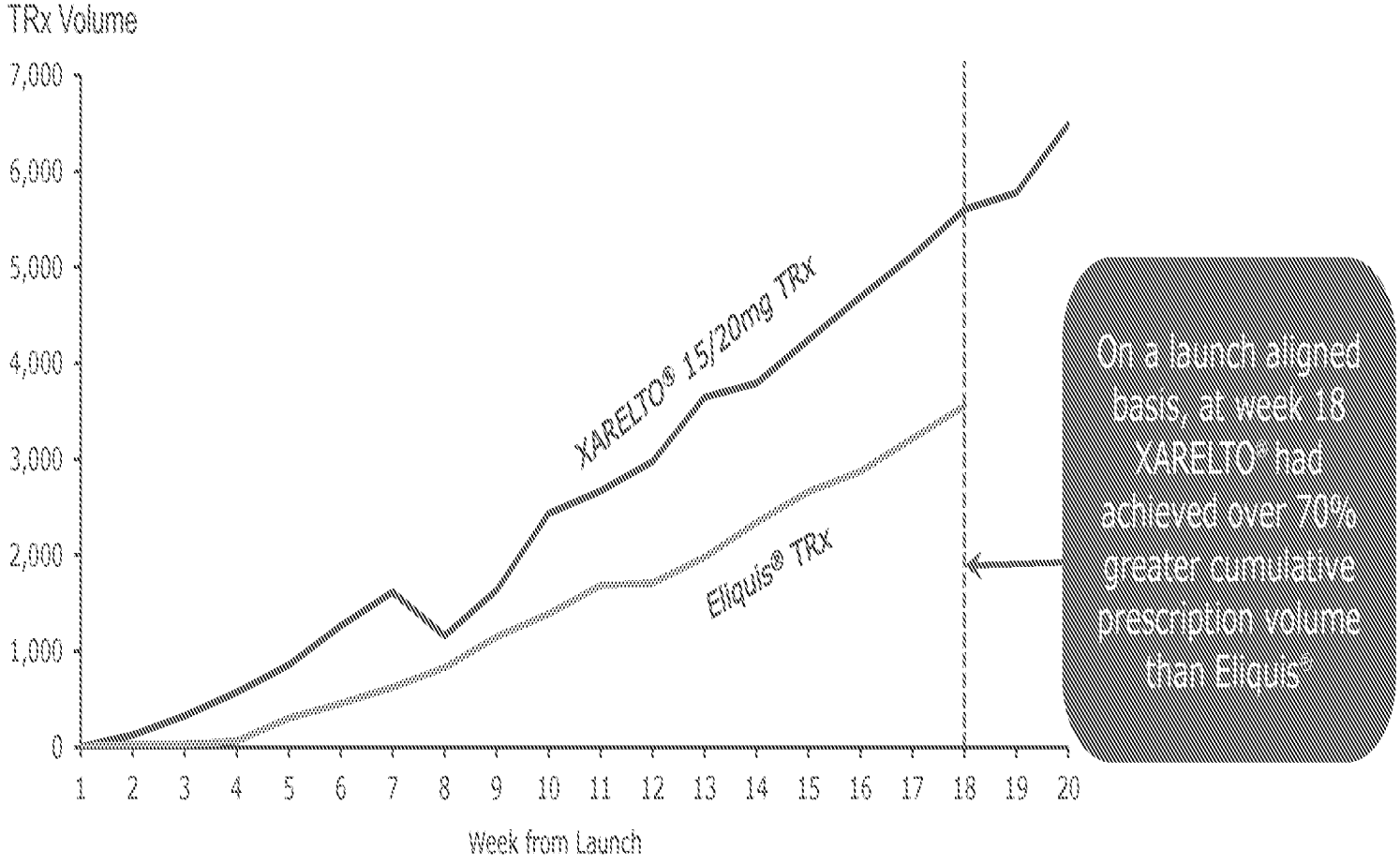


Source: IMS Health.

janssen | Pharmaceutical Companies of Johnson & Johnson

Unmatched Early Performance

Factor Xa – US Atrial Fibrillation Launch Aligned Performance



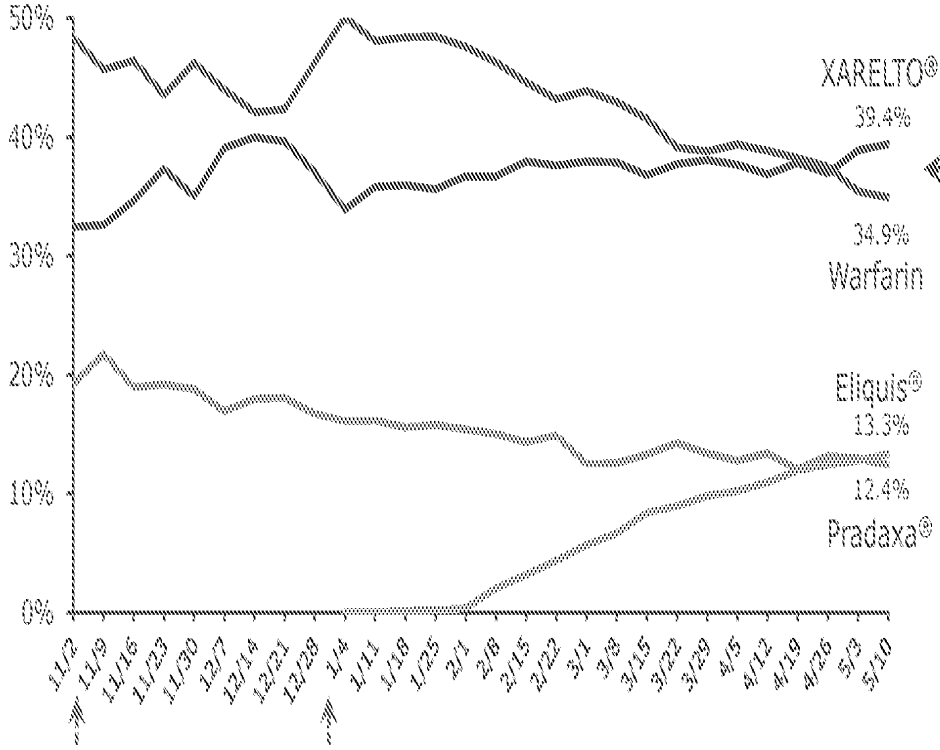
Source: IMS Health.

XARELTO® AF approval date: Nov 4, 2011. Eliquis® approval date: Dec 28, 2012.

Surpassing Warfarin Among Cardiologists

Xarelto® (rivaroxaban tablets)

US Oral Anti-Coagulant NBRx* Share in Cardiology



XARELTO® has overtaken warfarin in New-to-Brand share (NBRx)*

Source: IMS NPA Weekly, data through May 10, 2013.

* NBRx share includes new therapy starts, switch-to, and add-on prescriptions.

janssen | Pharmaceutical Companies of Johnson & Johnson

Best-in-Class Commercial Capabilities Have Unlocked the Potential of New Products

High Sales Force Effectiveness

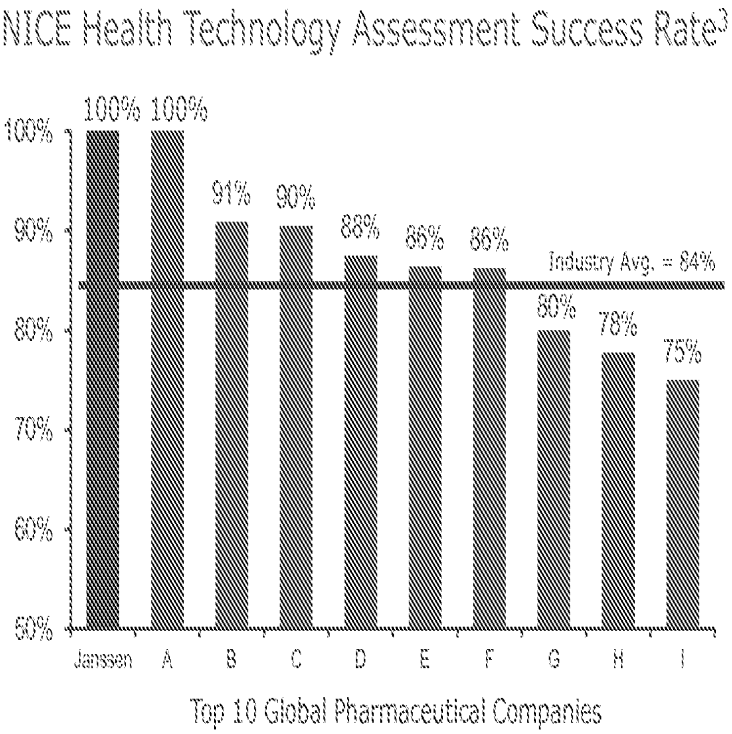
8 of 14 sales forces assessed were rated as "best-in-class" by our customers[1]

Strong Net Promoter Scores

5 of 6 key brands ranked #1 vs. competitors[2]

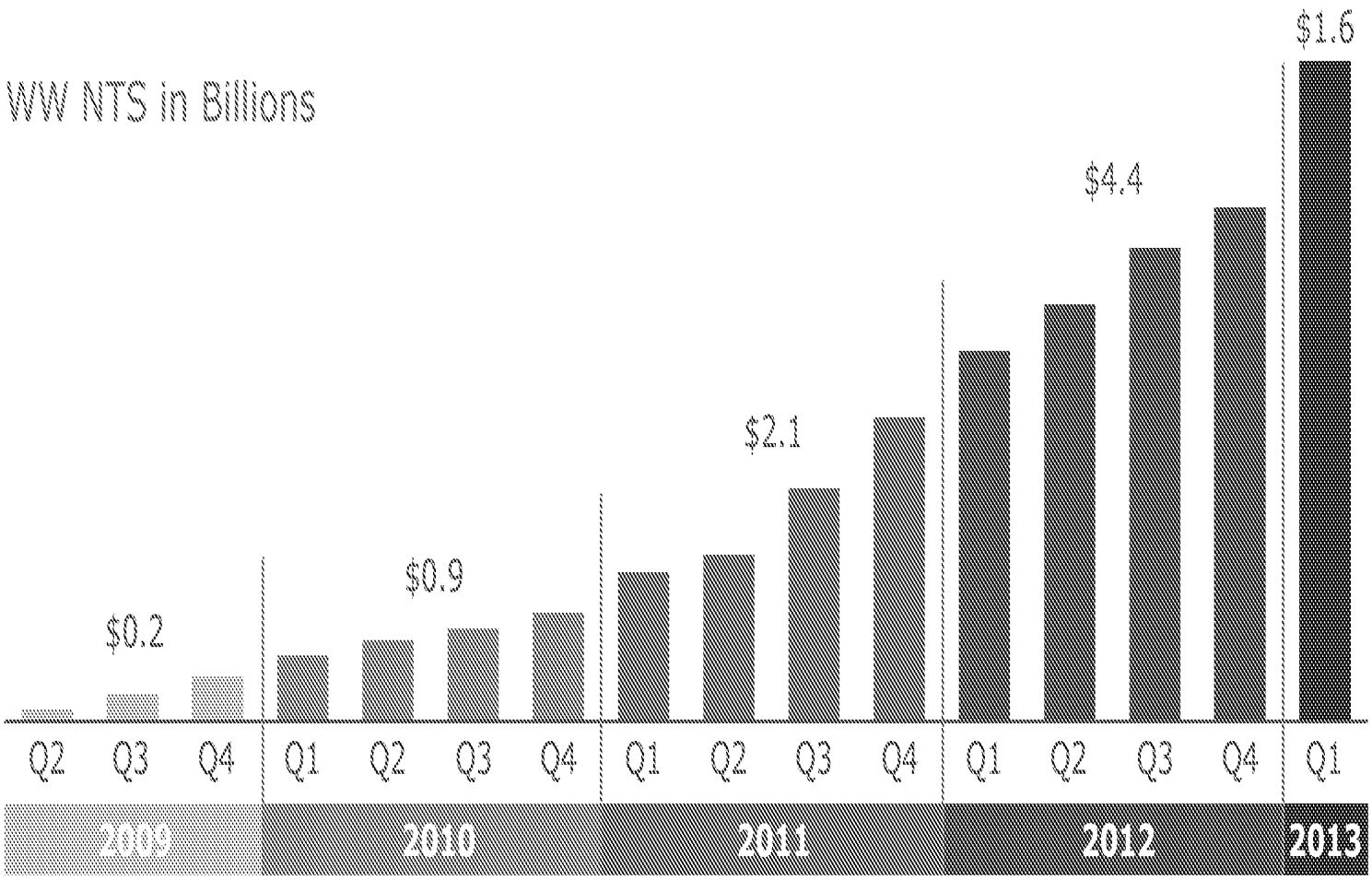
Deep Market Access Expertise

100% success rate for NICE submissions since 2000[3]



Sources: 1. Proprietary Sales Force Effectiveness and Activity Study, 2H 2012 conducted by Harris Interactive. 2. EU5 CONNECT Customer loyalty survey wave 3, Q4 2012, EU5, (VELCADE®, PREZISTA®, STELARA®, ZYTIGA®, INCIVO®, and XEPLION®). 3. Internal analysis of NICE Technology Appraisal Guidance.

New Products Contributed $4.4B in 2012

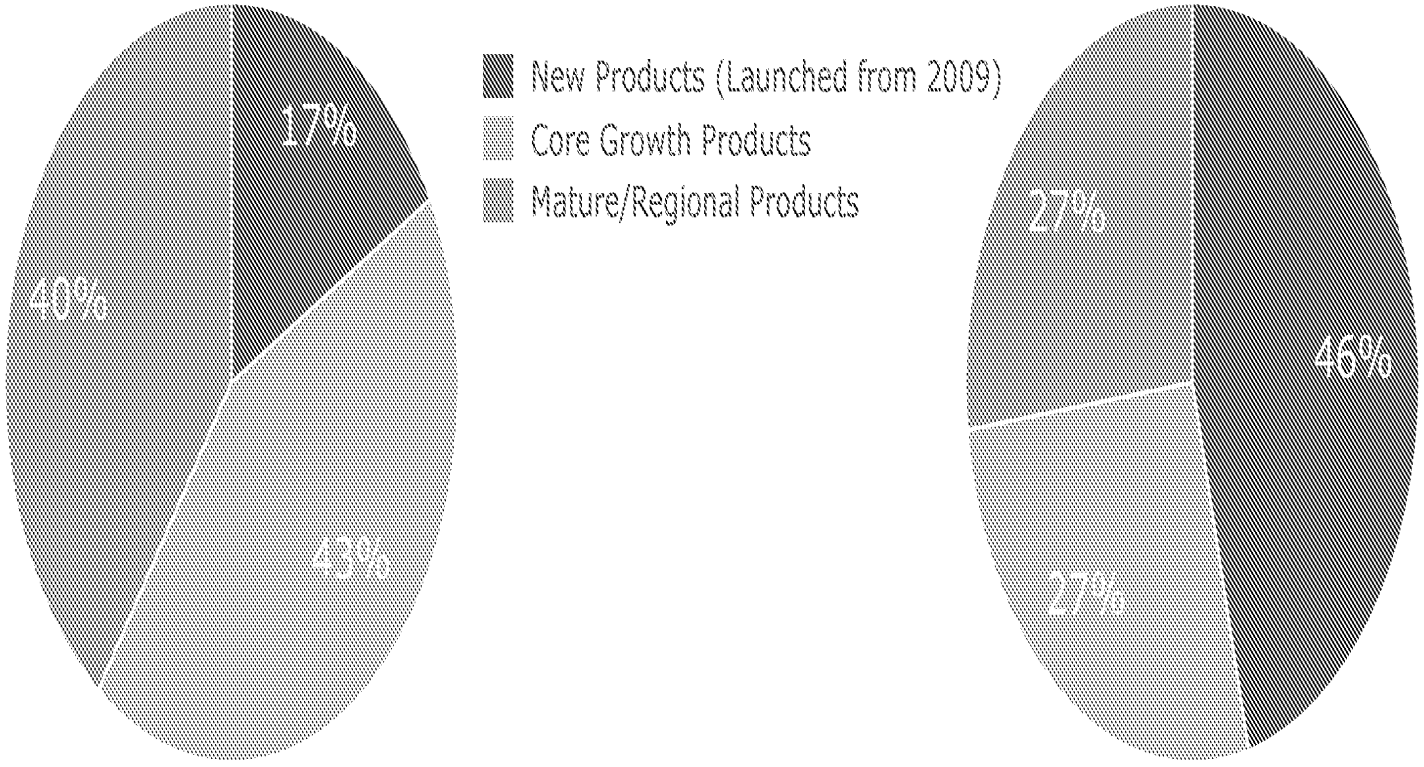


Note: New Products include ZYTIGA®, INVEGA® SUSTENNA®/XEPLION®, INCIVO®, STELARA®, SIMPONI®, XARELTO®, NUCYNTA®, EDURANT®/COMPLERA®, and DACOGEN®.

janssen | Pharmaceutical Companies of Johnson & Johnson

New Products Expected to Make Up ~46% of a Well Balanced Portfolio in 2017

Sales as % of Total Pharmaceuticals

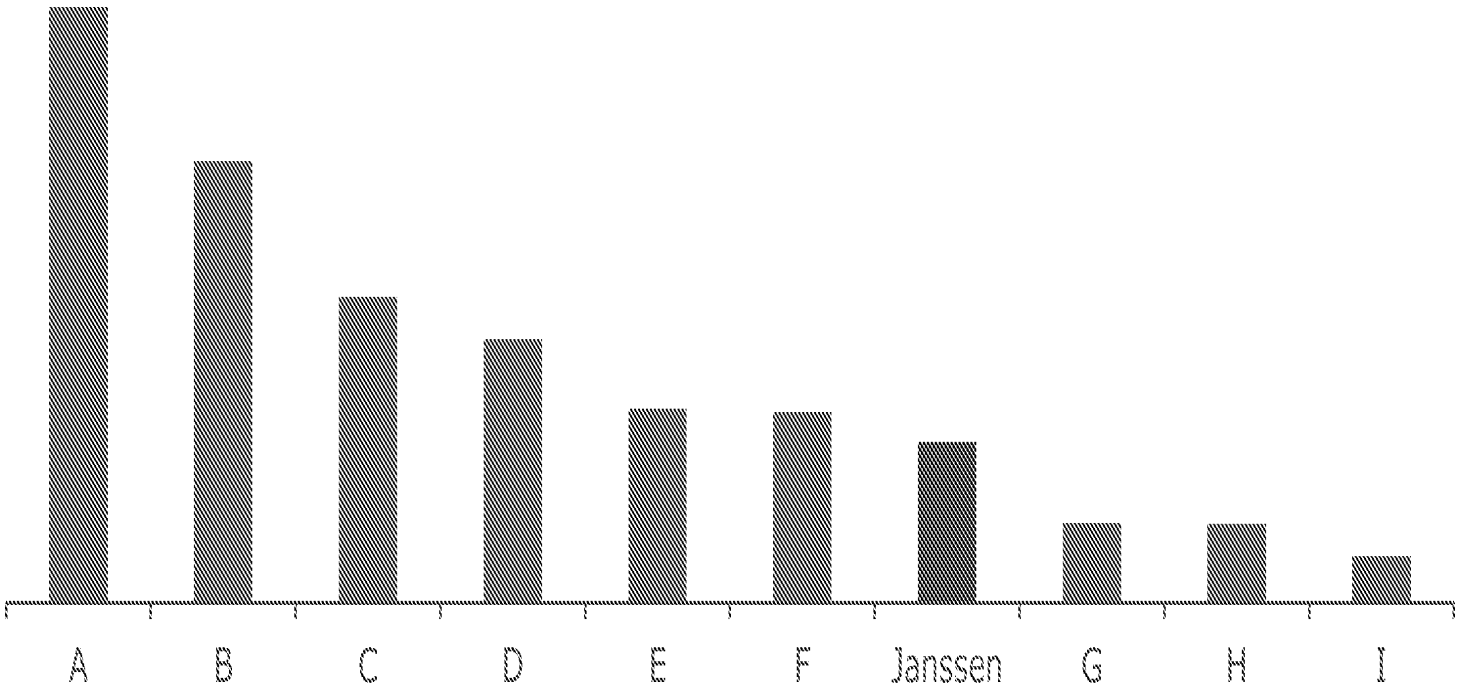


* Internal estimate.

janssen | Pharmaceutical Companies of Johnson & Johnson

Favorable Loss of Exclusivity Position from Refreshed Portfolio Helps Protect Future Revenues

Top 10 Global Pharmaceutical Companies – Potential 2013-2017 LoE Exposure



Source: IMS Health, April 2013 (included in analysis: US, Canada, Japan, Major EU markets, and S. Korea. Analysis excludes biologics).

Well Positioned for Potential Infliximab Biosimilars

- Expectations
  - Biosimilars compete like branded products rather than small molecule generics
  - Moderate impact in early years
- Infliximab patent situation
  - Potential 2015+ in Europe
  - Potential 2018+ in US

Janssen Strategies

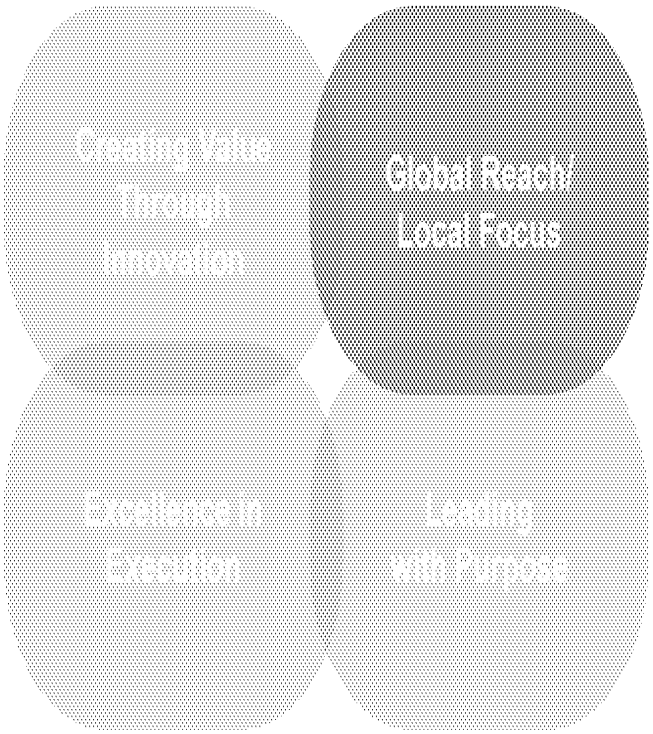
- Support policies that promote patient safety and informed stakeholder decisions
- Leverage extensive REMICADE® expertise and safety data from almost 2MM patients
- Develop innovative new therapies, both large and small molecule

Source: Internal assumptions.

Johnson & Johnson

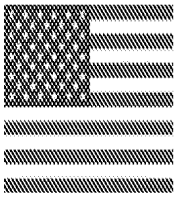
Strategic Framework

OUR GROWTH DRIVERS

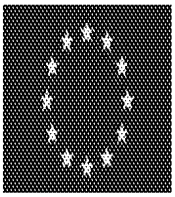


janssen | Pharmaceutical Companies of Johnson & Johnson

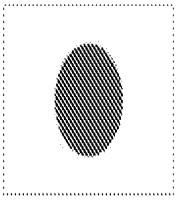
Fastest Growing Top 10 Global Pharmaceutical Company



RANK	COMPANY	GROWTH
#1	Janssen	12%
#2	Roche	7%
#3	AbbVie	5%
#4	Teva	1%
#5	Lilly	1%
Industry Average		-4%



RANK	COMPANY	GROWTH
#1	Janssen	7%
#2	AbbVie	5%
#3	Teva	4%
#4	Novartis	2%
#5	Merck	1%
Industry Average		1%



RANK	COMPANY	GROWTH
#1	Janssen	27%
#2	Teva	14%
#3	Roche	7%
#4	AZ	5%
#5	GSK	1%
Industry Average		0%

Source: IMS MIDAS as of Q4 2012 (vs. Q4 2011).

janssen | Pharmaceutical Companies of Johnson & Johnson

Johnson & Johnson Continues to Lead the Pharmaceutical Industry in US Sales

Cumulative Sales from Products Launched from 2009 to March 2013

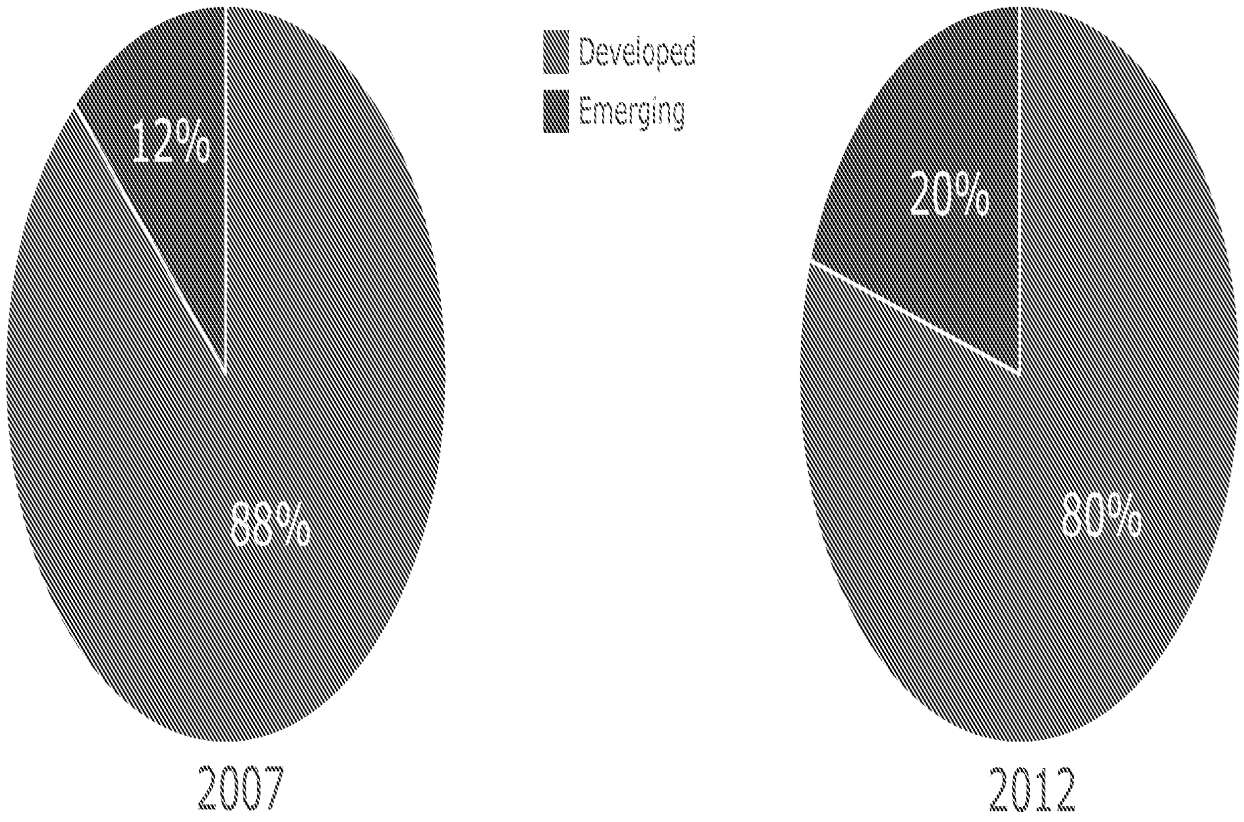
RANK	COMPANY	($MM)
1	JOHNSON & JOHNSON	$ 5,841
2	NOVARTIS	$ 3,236
3	PFIZER	$ 3,062
4	SANOFI	$ 2,947
5	TAKEDA	$ 2,760
6	BMS	$ 2,715
7	VERTEX PHARMA	$ 2,530
8	BOEHRINGER INGELHEIM	$ 2,296
9	NOVO NORDISK	$ 2,249
10	GLAXOSMITHKLINE	$ 1,937

Source: IMS National Sales Perspectives, Mar 2013, Rx only.

janssen | Pharmaceutical Companies of Johnson & Johnson

Core Growth and New Products Have Almost Doubled Footprint in Emerging Markets

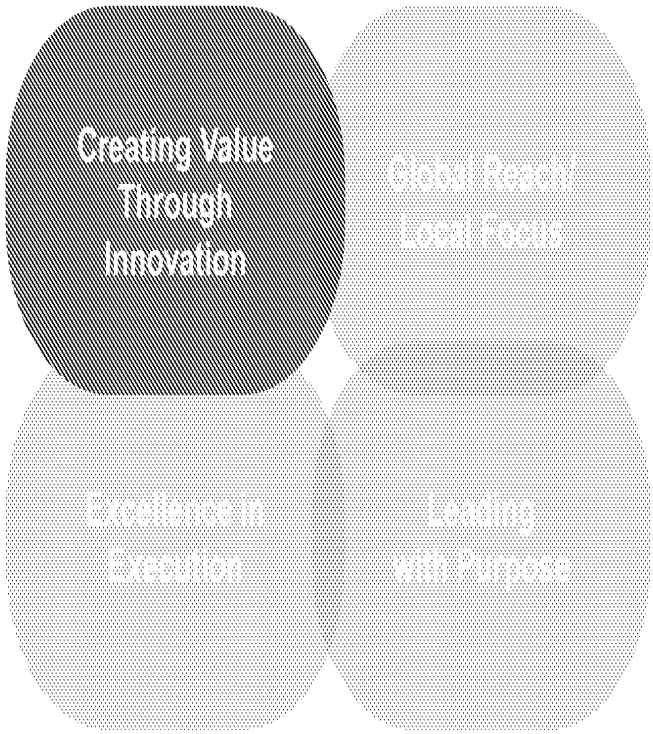
Sales as % of Total Pharmaceuticals



Johnson & Johnson

Strategic Framework

OUR GROWTH DRIVERS



janssen | PHARMACEUTICAL COMPANIES of Johnson & Johnson

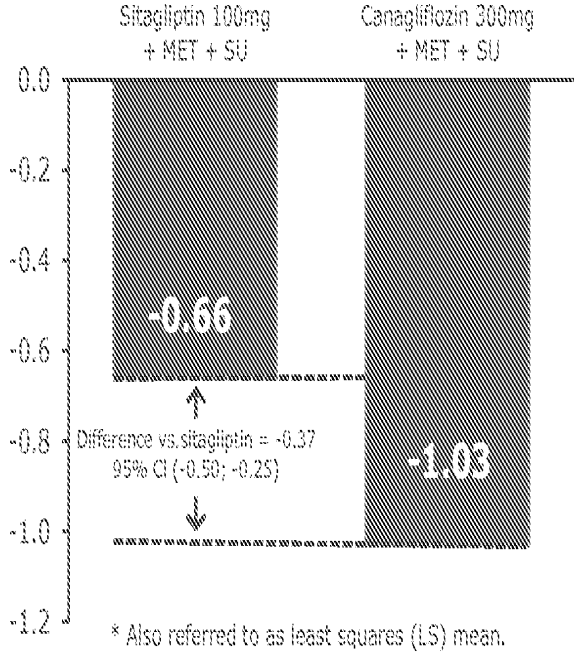
INVOKANA™: A New Approach in the Treatment of Type 2 Diabetes

Invokana™
canagliflozin tablets

WW Market[1]		
2012	2017	CAGR
$14.5B	$30.6B	16%

- First-in-class SGLT2 inhibitor launched in April in collaboration with Diabetes Care franchise
- Oral, once-daily medication that reduces HbA_{1C}, body weight, and systolic blood pressure
- Extensive clinical program
- Filed fixed-dose combination with metformin (US – December 2012, EU – March 2013)
- Superiority at 300mg dose vs. Januvia® (sitagliptin) on HbA_{1C} reduction

Adjusted Mean Change* in HbA_{1C} from Baseline to Week 52[2]



* Also referred to as least squares (LS) mean.
Abbreviation: CI=confidence interval.

Sources: 1. EvaluatePharma, April 2013 (diabetes market excluding Insulin).
2. Schernthaner G, et al. Diabetes Care. 2013 Apr 5. [Epub ahead of print].

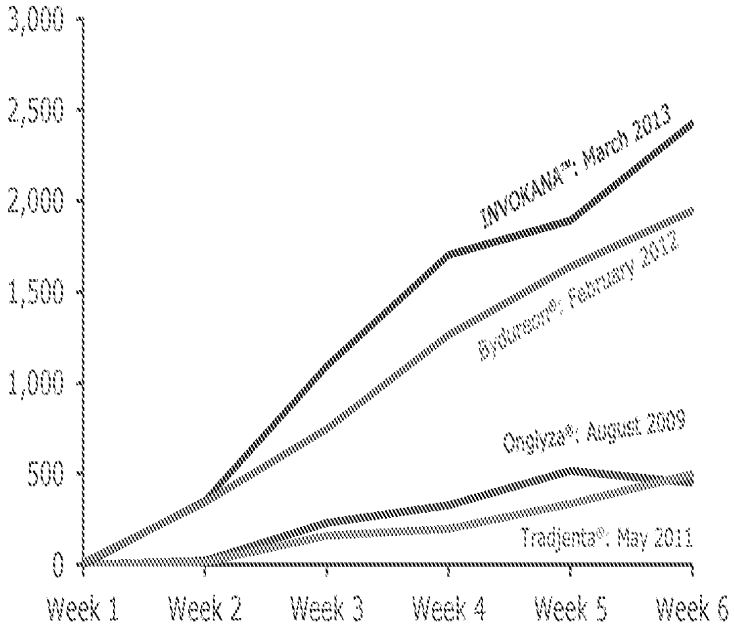
janssen | Pharmaceutical Companies of Johnson & Johnson

Strong Initial Market Reaction

Invokana™
canagliflozin tablets

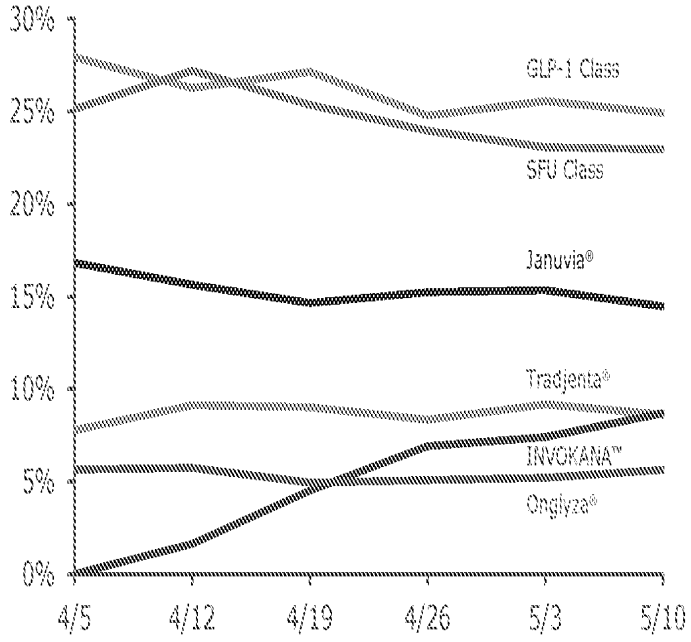
Strong Launch-Aligned Performance in the Early Weeks Following US Launch

US Launch Aligned TRx Volume



Nearly 9% NBRx Share Among US Endocrinologists in Week 6, Surpassing Onglyza® and Tradjenta®

US Total NBRx Share



Source: IMS NPA Weekly.

janssen | Pharmaceutical Companies of Johnson & Johnson

Simeprevir: Next Generation HCV Treatment with Priority FDA Review

- Filed in Japan in February, US in March and EU in April; additional filings in process
- Potential best-in-class protease inhibitor
  - Efficacy across all patient populations with shorter duration of therapy for most patients
  - Safety/tolerability comparable to peg-interferon and ribavirin alone
  - Convenient once-daily dosing
- Opportunity in IFN-free regimens
  - COSMOS Ph 2 showed IFN-free efficacy rate 93-96%[1]
  - 5 IFN-free Phase 2 trials initiated with Simeprevir

WW Market[2]		
2012	2017	CAGR
$4.9B	$10.6B	17%

Significant Unmet Need

- High burden disease – long-term health problems and death
- 150 Million infected, only 25% diagnosed[3]

Sources: 1. Lawitz, et al. CROI 2013; abstract 155 LB.
2. EvaluatePharma, April 2013 (HCV market excluding OTC products). 3. CDC, WHO.

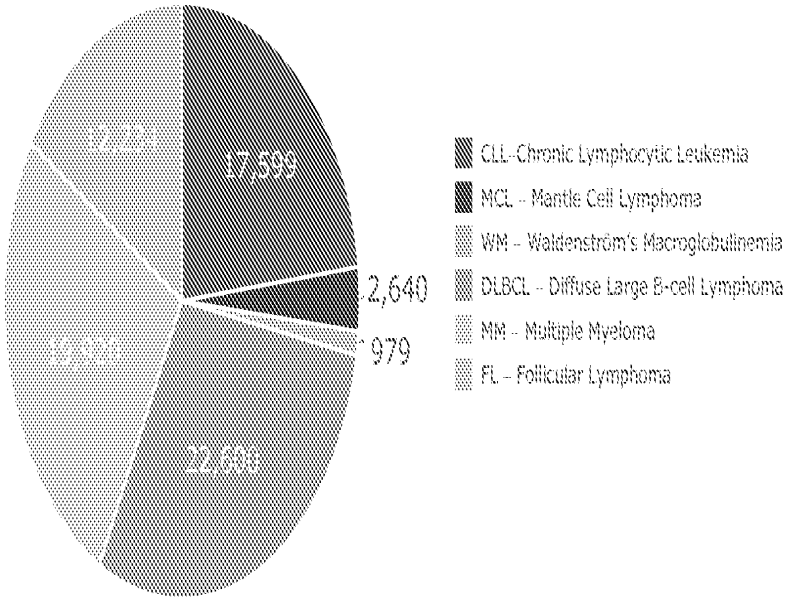
janssen | Pharmaceutical Companies of Johnson & Johnson

Ibrutinib: Granted Breakthrough Therapy Designations for Rel/Ref MCL, WM and 17p del CLL

- Highly differentiated, novel compound
  - Orally active, small molecule, targeted agent
  - Novel mechanism with compelling activity across several B-cell malignancies
  - Development in CLL, MCL, WM, DLBCL, FL, and MM
- WW license agreement with Pharmacyclics 50/50 profit and loss split
- Early Access Program announced May 2013
- MCL filing targeted before end of Q3 2013

WW Market[1]		
2012	2017	CAGR
$21.1B	$29.9B	7%

US Incidence[2]

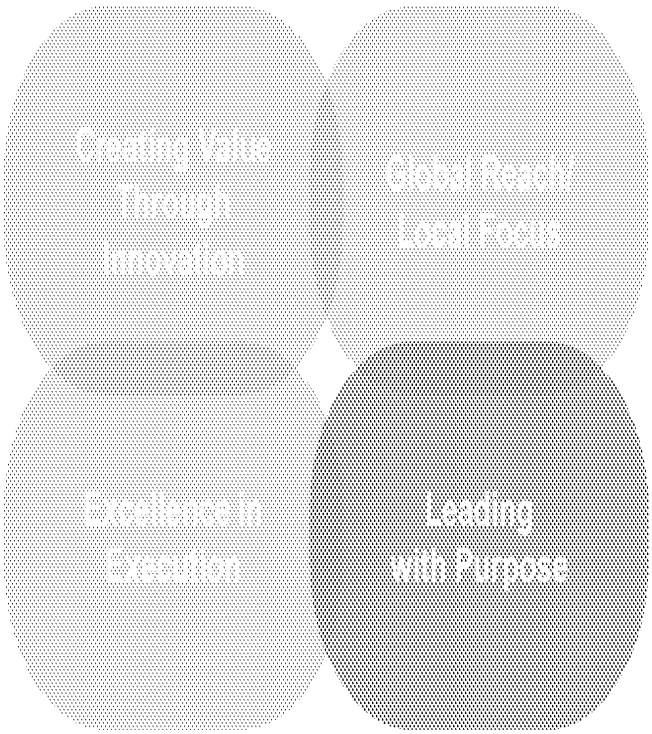


Sources: 1. EvaluatePharma, April 2013 (Hematology market). 2. Decision Resources, 2009 and SEER data.

Johnson & Johnson

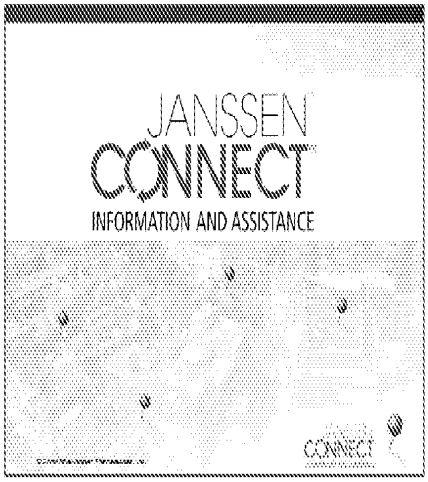
Strategic Framework

OUR GROWTH DRIVERS



janssen | PHARMACEUTICAL COMPANIES of Johnson & Johnson

Improving Patient Care Through Innovation and Integration in Schizophrenia



Helping patients access and maintain appropriate treatment

Leveraging pharmaceuticals and diagnostics capabilities to improve patient care

INVEGA SUSTENNA® paliperidone palmitate

XEPLION® paliperidone palmitate

Q1 2013 SALES	Q1 YoY GROWTH*
$284MM	76%

- Part of a $2.2B LAI antipsychotic franchise that grew 17% operationally in 2012
- Investigational new formulation requires only 4 injections per year

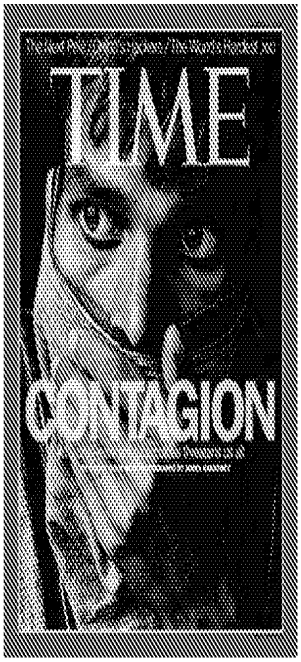
* Operational change (includes INVEGA® SUSTENNA®/XEPLION®).
LAI antipsychotic franchise includes INVEGA® SUSTENNA®/XEPLION® and RISPERDAL® CONSTA®.

janssen | Pharmaceutical Companies of Johnson & Johnson

SIRTURO™: First New Mechanism for Multi-Drug-resistant Tuberculosis (MDR-TB) in 40 Years

"MDR-TB is a time bomb"
Margaret Chan, WHO Director General, Beijing, 2009

- Affects 630,000 worldwide[1]
- 150,000 deaths each year[2]
- 2MM new cases expected 2011-2015[3]
- ~90% untreated, only 50% cure rate[1]



斯面瑞™
100mg

Innovative Models to Accelerate Patient Access and Improve Treatment Standards

- Registration efforts prioritized based on greatest need
- Appropriate use through responsible distribution and partnerships
- Equitable, tiered pricing approach

Sources: 1. WHO Global Tuberculosis Report 2012. 2. WHO 2011/2012 Tuberculosis Global Facts.
3. WHO Press Release, "Partners call for increased commitment to tackle MDR-TB," March 23 2011.

janssen | Pharmaceutical Companies of Johnson & Johnson

Company Group Chairmen

Jane Griffiths
Company Group Chairman,
Europe, Middle East & Africa

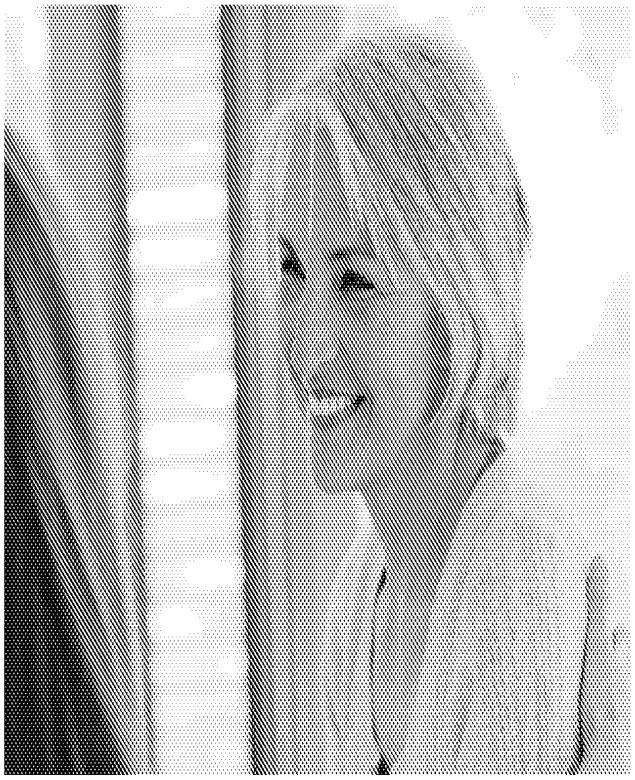
Jennifer Taubert
Company Group Chairman,
North America

Kim Taylor
Company Group Chairman,
Asia Pacific

janssen

Key Takeaways

- Making a difference through transformational medical innovation
- Transforming our business with leading science and best-in-class commercial capabilities
- Enhancing pipeline to deliver the next wave of growth



Building on the Strong Momentum in Pharmaceuticals


janssen
PHARMACEUTICAL COMPANIES
of Johnson & Johnson

Electronic Patent Application Fee Transmittal

Application Number:	13034340
Filing Date:	24-Feb-2011
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Andrea J. Kamage/Laurie Phillips
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Notice of Appeal	1401	1	800	800
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**800**

Electronic Acknowledgement Receipt

EFS ID:	15948999
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Andrea J. Kamage/Laurie Phillips
Filer Authorized By:	Andrea J. Kamage
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	04-JUN-2013
Filing Date:	24-FEB-2011
Time Stamp:	18:03:18
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$800
RAM confirmation Number	5706
Deposit Account	100750
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Amendment After Final	CGR5001USCNT1_Response_to_OA_June_2013.pdf	116303 8487a35b7f7f2ebe2257327facdadeef903e431d	no	9
Warnings:					
Information:					
2	Notice of Appeal Filed	CGR5001USCNT1_Notice_of_Appeal_June_2013.pdf	74179 d713f789b27c0940884a4b38d7f4be85e387e2c2	no	1
Warnings:					
Information:					
3	Miscellaneous Incoming Letter	Press_Announcements_FDA_approves_new_treatment_for_a_type_of_late_stage_prostate_cancer_Xtandi.pdf	113364 5d03a7faa234e138ade991ee13c93c818c56 2ddf	no	2
Warnings:					
Information:					
4	Miscellaneous Incoming Letter	Press_Announcements_FDA_Approves_New_Treatment_for_Advanced_Prostate_Cancer_Jevtana.pdf	112420 d4c1093684962c8452ccdac5817863c1297517af	no	2
Warnings:					
Information:					
5	Miscellaneous Incoming Letter	Press_Announcements_FDA_expands_Zytigas_use_for_late_stage_prostate_cancer.pdf	132426 4c05fb496c3354026ade31614d9a0c0b679caafe	no	2
Warnings:					
Information:					
6	Miscellaneous Incoming Letter	ZYTIGA_full_product_information.pdf	223379 1c1f484d8b4c97a61baa8a7b81cb389da62f91c7	no	9
Warnings:					
Information:					
7	Miscellaneous Incoming Letter	Pharmaceutical_Commercial_Overview_JNJ2013.pdf	1283733 4329919cff3db5a30d535af59b22f6f012fd465d	no	41
Warnings:					
Information:					
8	Fee Worksheet (SB06)	fee-info.pdf	30009 014857821ac9105732a8e7a473cfb18c9547e12f	no	2

Warnings:	
Information:	
Total Files Size (in bytes):	2085813

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/034,340	Filing Date 02/24/2011	☐ To be Mailed

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT **06/04/2013**

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 20	Minus	** 36	= 0	X $80 =	0
Independent (37 CFR 1.16(h))	* 1	Minus	***4	= 0	X $420 =	0
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	0

AMENDMENT

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/BRIDGET MONROE/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

27777 7590 07/03/2013

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1629	

DATE MAILED: 07/03/2013

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

TITLE OF INVENTION: Methods and Compositions for Treating Cancer

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1780	$300	$0	$2080	10/03/2013

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

27777 7590 07/03/2013
PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

TITLE OF INVENTION: Methods and Compositions for Treating Cancer

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1780	$300	$0	$2080	10/03/2013

EXAMINER	ART UNIT	CLASS-SUBCLASS
HUI, SAN MING R	1629	514-170000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29	NOTE: Absent a valid certification of Micro Entity Status (see form PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
❑ Applicant asserting small entity status. See 37 CFR 1.27	NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
❑ Applicant changing to regular undiscounted fee status.	NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 07/03/2013

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1629	

DATE MAILED: 07/03/2013

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 13/034,340	Applicant(s) AUERBACH ET AL.	
	Examiner SAN-MING HUI	Art Unit 1629	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *6/4/2013*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *37-56*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☒ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/San-ming Hui/
Primary Examiner, Art Unit 1629

DETAILED ACTION

Applicant's response filed June 4, 2013 has been entered.

Claims 37-56 are pending.

The following is an examiner's statement of reasons for allowance: The unexpected commercial success of the launch of the drug obviates the rejection under 35 USC 103(a).

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Claims 37-56 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAN-MING HUI whose telephone number is (571)272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Melenie McCormick can be reached on (571) 272-8037. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1629

/San-ming Hui/
Primary Examiner, Art Unit 1629

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

CPC		
Symbol	**Type**	**Version**

CPC Combination Sets				
Symbol	**Type**	**Set**	**Ranking**	**Version**

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	20	
/SAN-MING HUI/ Primary Examiner.Art Unit 1629	06/28/2013	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	1

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
514	170	A	6	1	K	31 / 56 (2006.01.01)						

CROSS REFERENCE(S)					
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)				
514	180				

NONE	Total Claims Allowed:
(Assistant Examiner) (Date)	20
/SAN-MING HUI/ Primary Examiner.Art Unit 1629 06/28/2013	O.G. Print Claim(s): 1 / O.G. Print Figure: 1
(Primary Examiner) (Date)	

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 20	
/SAN-MING HUI/ Primary Examiner.Art Unit 1629 (Primary Examiner)	06/28/2013 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 1

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
514	170, 182	1/27/11	SH
514	170, 182	9/5/12	SH
514	170, 182	2/25/13	SH
514	170, 182	6/28/13	SH

SEARCH NOTES		
Search Notes	Date	Examiner
EAST search and inventor search in PALM	1/27/11	SH
EAST search and inventor search in PALM	9/5/12	SH
EAST search and inventor search in PALM	2/25/13	SH
EAST search and inventor search in PALM	6/28/2013	SH

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
514	170, 182	6/28/13	SH

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2201	abiraterone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L2	3	prdnisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L3	31828	prednisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L4	141199	prostate	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L5	1830	L1 and L4	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L6	122	L1 same L4	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L7	1018	514/170.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L8	2253	514/182.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L9	484642	cancer	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L10	2170	L1 and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L11	1093	L1 same L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L12	0	"9320097".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L13	2	"9509178".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08
L14	0	"9509178".pn. and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/28 11:08

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L15	2237	514/182.ccls.	US-PGPUB; USPAT	OR	ON	2013/06/28 11:10
L16	1010	514/170.ccls.	US-PGPUB; USPAT	OR	ON	2013/06/28 11:10

6/ 28/ 2013 12:03:30 PM
C:\ Users\ shui\ Documents\ EAST\ Workspaces\ 13-034340.wsp

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1629

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012	09/05/2012	02/25/2013	06/28/2013				
	1	÷								
	2	÷								
	3	÷								
	4	÷								
	5	÷								
	6	÷								
	7	÷								
	8	÷								
	9	÷								
	10	÷								
	11	÷								
	12	÷								
	13	÷								
	14	÷								
	15	÷								
	16	÷								
	17	÷								
	18	÷								
	19	÷								
	20	÷								
	21	÷								
	22	÷								
	23	÷								
	24	÷								
	25	÷								
	26	÷								
	27	÷								
	28	÷								
	29	÷								
	30	÷								
	31	÷								
	32	÷								
	33	÷								
	34	÷								
	35	÷								
	36	÷								

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012	09/05/2012	02/25/2013	06/28/2013				
	37		✓	✓	✓	=				
	38		✓	✓	✓	=				
	39		✓	✓	✓	=				
	40		✓	✓	✓	=				
	41		✓	✓	✓	=				
	42		✓	✓	✓	=				
	43		✓	✓	✓	=				
	44		✓	✓	✓	=				
	45		✓	✓	✓	=				
	46		✓	✓	✓	=				
	47		✓	✓	✓	=				
	48		✓	✓	✓	=				
	49		✓	✓	✓	=				
	50		✓	✓	✓	=				
	51		✓	✓	✓	=				
	52		✓	✓	✓	=				
	53		✓	✓	✓	=				
	54		✓	✓	✓	=				
	55		✓	✓	✓	=				
	56		✓	✓	✓	=				

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 07/30/2013

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1629	

NOTIFICATION DATE	DELIVERY MODE
07/30/2013	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jnjuspatent@corus.jnj.com
lhowd@its.jnj.com
gsanche@its.jnj.com

Notice of Allowability	Application No. 13/034,340	Applicant(s) AUERBACH ET AL.	
	Examiner SAN-MING HUI	Art Unit 1629	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to _____.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *37-56*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☒ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/San-ming Hui/
Primary Examiner, Art Unit 1629

DETAILED ACTION

This communication is to correct the dependency of claim 44. It apparently depends from claim 43.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

The application has been amended as follows:

In claim 44, line 1, replace "claim 44" with "claim 43".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAN-MING HUI whose telephone number is (571)272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Melenie McCormick can be reached on (571) 272-8037. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1629

/San-ming Hui/
Primary Examiner, Art Unit 1629

Notice of References Cited	Application/Control No. 13/034,340	Applicant(s)/Patent Under Reexamination AUERBACH ET AL.	
	Examiner SAN-MING HUI	Art Unit 1629	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
*	U	O'Donnell et al., British Journal of Cancer, 2004;90:2317-2325
*	V	Tannock et al., J. Clin. Oncol., 1996;14:1 756-1764
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

PTO/SB/30 (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL

Subsection (b) of 35 U.S.C. § 132, effective on May 29, 2000, provides for continued examination of an utility or plant application filed on or after June 8, 1995. See The American Inventors Protection Act of 1999 (AIPA).

Application Number	13/034,340
Filing Date	February 24, 2011
First Named Inventor	Alan H. Auerbach
Group Art Unit	1629
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

This is a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114 of the above-identified application.

NOTE: 37 C.F.R. § 1.114 is effective on May 29, 2000. If the above-identified application was filed prior to May 29, 2000, applicant may wish to consider filing a continued prosecution application (CPA) under 37 C.F.R. § 1.53 (d) (PTO/SB/29) instead of a RCE to be eligible for the patent term adjustment provisions of the AIPA. See Changes to Application Examination and Provisional Application Practice, Final Rule, 65 Fed. Reg. 50092 (Aug. 16, 2000); Interim Rule, 65 Fed. Reg. 14865 (Mar. 20, 2000), 1233 Off. Gaz. Pat. Office 47 (Apr. 11, 2000), which established RCE practice.

1. **Submission required under 37 C.F.R. § 1.114**
   - a. ☐ Previously submitted
     - i. ☐ Consider the amendment(s)/reply under 37 C.F.R. § 1.116.
     - ii. ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on
     - iii. ☐ Other
   - b. ☒ Enclosed
     - i. ☐ Amendment/Reply
     - ii. ☐ Affidavit(s)/Declaration(s)
     - iii. ☒ Information Disclosure Statement (IDS)
     - iv. ☐ Other
2. **Miscellaneous**
   - a. ☐ Suspension of action on the above-identified application is requested under 37 C.F.R. § 1.103(c) for a period of months. (Period of suspension shall not exceed 3 months; Fee under 37 C.F.R. § 1.17(i) required.)
   - b. ☐ Other
3. **Fees** - The RCE fee under 37 C.F.R. § 1.17(e) is required by 37 C.F.R. § 1.114 when the RCE is filed
   - a. ☒ The Director is hereby authorized to charge the following fees, or credit any overpayments, to Deposit Account No. **10-0750**.
     - i. ☒ RCE fee is required under 37 C.F.R. § 1.17(e)
     - ii. ☐ Extension of Time (37 C.F.R. §§ 1.136 and 1.17)
     - iii. ☐ Other
   - b. ☐ Check in the amount of $_____ enclosed
   - c. ☐ Payment by credit card (Form PTO-2038 enclosed)

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Name (print/type)	Timothy E. Tracy	Registration No.	39,401
Signature	/Timothy E. Tracy/	Date	October 3, 2013

CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being electronically filed via EFS-Web to the Commissioner for Patents with the U.S. Patent and Trademark Office on: October 3, 2013

Name (print/type)	Laurie A. Russo		
Signature	/Laurie A. Russo/	Date	October 3, 2013

SUBMISSION UNDER MPEP 609.06 Page 1 of 1		
	Confirmation Number	1597
	Application Number	13/034,340
	Filing Date	February 24, 2011
	First Named Inventor	Alan H. Auerbach
	Group Art Unit	1629
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	U.S. Patent Document Number	Kind Code[2] (if known)	Pages, Columns, Lines, where relevant passages or relevant figures appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	Foreign Patent Document Office[3]	Number[4]	KindCode[5]	Pages, Columns, Lines, where relevant passages or relevant figures appear	T[6]

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Third Party Observations dated October 18, 2012 for EP Appln. No. 07837326.3	
		Third Party Observations dated March 28, 2013 for EP Appln. No. 07837326.3	
		Third Party Observations dated July 1, 2013 for EP Appln. No. 07837326.3	

Examiner Signature		Date Considered	

Electronic Patent Application Fee Transmittal

Application Number:	13034340
Filing Date:	24-Feb-2011
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Timothy E. Tracy/Laurie Russo
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
RCE - 2nd and Subsequent Request	1820	1	1700	1700
		Total in USD ($)		**1700**

Electronic Acknowledgement Receipt

EFS ID:	17031305
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Laurie Russo
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	03-OCT-2013
Filing Date:	24-FEB-2011
Time Stamp:	14:27:41
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1700
RAM confirmation Number	816
Deposit Account	100750
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Continued Examination (RCE)	CGR5001USCNT1_RCE.pdf	175163 b9a99920f5dcb72185972c83bb0e1e82f2c6a0f8	no	1
Warnings:					
This is not a USPTO supplied RCE SB30 form.					
Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	CGR5001USCNT1_IDS_CERT.pdf	109847 86024224b95868779065f0be0c9bfb62eabe6d85	no	1
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Information Disclosure Statement (IDS) Form (SB08)	CGR5001USCNT1_1449.pdf	66460 87a8a8de5593aefb807e900da4f38f70c47f05ed	no	4
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
4	Information Disclosure Statement (IDS) Form (SB08)	CGR5001USCNT1_MPEP_609_06.pdf	85899 459be19c98e6d1fc9c774772a811b63ac2fcceea	no	1
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
5	Other Reference-Patent/App/Search documents	CGR5001EPEPT_THIRD_PARTY_OBS_10_18_2012.pdf	119307 c1c3c706e51b724dd0e637dd83071f45eaa6c155	no	15
Warnings:					
Information:					
6	Other Reference-Patent/App/Search documents	CGR5001EP_Third_party_observations_07_01_13.pdf	1620199 9fbf28817928a2bac350f941bb326a5a5ab493f3	no	9
Warnings:					
Information:					
7	Other Reference-Patent/App/Search documents	CGR5001EP_Third_Party_Observations_03_28_13_Part4.pdf	1797586 90ebef34f08c38f89b2312a919dc2681743771d0	no	2
Warnings:					

Information:					
8	Other Reference-Patent/App/Search documents	CGR5001EP_Third_Party_Observations_03_28_13_Part3.pdf	15413303 48f4e4d8a30dbe2ca4f6f5c47e49c9dd3423f243	no	11
Warnings:					
Information:					
9	Other Reference-Patent/App/Search documents	CGR5001EP_Third_Party_Observations_03_28_13_Part2.pdf	16988366 fd9d05a49120cc53fc9bd9c7f9db1d14058e7071	no	11
Warnings:					
Information:					
10	Other Reference-Patent/App/Search documents	CGR5001EP_Third_Party_Observations_03_28_13_Part1.pdf	7988953 d8e91ff7fe29cc8189cad46643b04ab9d2d6bc39	no	11
Warnings:					
Information:					
11	Fee Worksheet (SB06)	fee-info.pdf	29845 a9a30ac5959fa982c57728c0480c5c44f0f51264	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	44394928	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Sheet 1 of 1

Confirmation Number	1597
Application Number	13/034,340
Filing Date	February 24, 2011
First Named Inventor	Alan H. Auerbach
Group Art Unit	1629
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☒ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement (See 37 CFR 1.97(e)(1)), or before the mailing date of a first Office Action on the merits of the above-identified application, or before the mailing date of a first Office Action after the filing of a request for continued examination under §1.114, no additional fee is required.

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☒ Identification of Prior Application in which some of the listed information was already cited and for which no copies are submitted or need to be submitted. This application relies, under 35 U.S.C. §120, on the earlier filing date of prior application serial no.: 11/844,440 filed on 08-24-07. If any of the foregoing publications are not available to the Examiner, Applicant will endeavor to supply copies at the Examiner's request.

☒ **REMINDER TO THE EXAMINER**
In view of, and pursuant to, the holdings of the Federal Circuit Court of Appeals in the cases *Dayco Products, Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 66 U.S.P.Q.2d 1801 (Fed. Cir. 2003); *McKesson Info. Sol'ns v. Bridge Med.*, 487 F.3d 897, 927 (Fed. Cir. 2007); and related cases, Applicants hereby inform the Examiner of the existence of commonly owned pending U.S. Patent Application Serial Nos. 11/844,440. This application has published and is therefore publicly available in PAIR. Moreover, the Patent Office has issued one or more Office Actions in this application. The Examiner is invited to review the prosecution of this application to determine its impact, if any, on the prosecution of the present application. In an effort not to overwhelm the Examiner with an overly large IDS, Applicants are not submitting copies of these publicly available documents. Of course, Applicants would be happy to do so at the Examiner's request.

In addition, submitted herewith are Third Party Observations that were submitted in the European Patent Office for the corresponding European Application to the captioned application.

☐ Attached are copies of search report(s) from corresponding patent application(s), which are listed on the attached Submission Under MPEP 609.06.

☐ The relevance of those listed references which are not in the English language is as follows:

☒ Copies of copyrighted material were made and delivered to the government under license from Copyright Clearance Center, Inc. No further reproduction is permitted.

☒ Any fee set forth in 37 CFR 1.17 (p) has been submitted herewith. The Commissioner is hereby authorized to charge any additional fees which may be required in connection with the filing of this communication, or credit any overpayment, to Account No. 10-0750.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Timothy E. Tracy/	Date (YYYY-MM-DD)	October 3, 2013
Name/Print	Timothy E. Tracy	Registration Number	39,401

CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being electronically filed via EFS-Web to the Commissioner for Patents with the U.S. Patent and Trademark Office on: October 3, 2013

Name (print/type)	Laurie A. Russo		
Signature	/Laurie A. Russo/	Date	October 3, 2013

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	ALAN H. AUERBACH
	Art Unit	1629
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

U.S.PATENTS						
Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					
If you wish to add additional U.S. Patent citation information please click the Add button.						

U.S.PATENT APPLICATION PUBLICATIONS						
Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					
If you wish to add additional U.S. Published Application citation information please click the Add button.						

FOREIGN PATENT DOCUMENTS								
Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] ¡	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐
If you wish to add additional Foreign Patent Document citation information please click the Add button								

NON-PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	ALAN H. AUERBACH
	Art Unit	1629
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	1	ASCO CANCER FOUNDATION, Poster Session F: Hormone Refractory, ASCO, 2005, -, -	☐
	2	BRUNO ET AL, Targeting cytochrome P450 enzymes: A new approach in anti-cancer drug development, Elsevier, 2007, pages 5047-5060, vol. 15	☐
	3	CANNELL, 100th Annual Meeting of the American Association for Cancer Research, Los Angeles, CA, USA;, http://oncology.thelancet.com, 2007, pp 471, Volume 8	☐
	4	Collins, et al. "A Systematic Review of the effectiveness of Docetaxel and Mitoxantrone for the Treatement of Metastatic Hormone-Refractory Prostate Cancer", British J. of Cancer, 95, pp 457-462 (2006)	☐
	5	COUGAR BIOTECHNOLOGY, Cougar Biotechnology Announces Initiation of Phase I/II Trial for CB7630 (Arbiraterone Acetate), Cougar Biotechnology, 12-14-2004, -, -	☐
	6	COUGAR BIOTECHNOLOGY, Cougar Biotechnology Announces Presentation of Positive CB7630 Clinical Data at AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, Cougar Biotechnology, 10-2007, -, -	☐
	7	COUGAR BIOTECHNOLOGY, Cougar Biotechnology Announces Presentation of Positive CB7630 Clinical Data at ESMO Conference, Drugs.com, 7-2007, -, -	☐
	8	COUGAR BIOTECHNOLOGY, Cougar Biotechnology announces presentation of positive phase I and phase II data at ASCO Prostate Cancer Symposium, Cougar Biotechnology, 02-23-2007, -, -	☐
	9	COUGAR BIOTECHNOLOGY, Cougar Biotechnology presents CB7630 Phase I clinical data at the 2005 Prostate Cancer Symposium, AllBusiness, 2005, -, -	☐
	10	COUGAR BIOTECHNOLOGY, Cougar Biotechnology presents positive CB7630 Clinical Data at AACR Annual Meeting Late-Breaking Clinical Trials Session, Cougar Biotechnology, 04-17-2007, -, -	☐
	11	COUGAR BIOTECHNOLOGY, Cougar Technology Announces Presentation of Positive CB7630 Clinical Data at ASCO Annual Meeting, The Free Library, 06-04-2007, -, -	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	ALAN H. AUERBACH
	Art Unit	1629
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	12	DE BONO ET AL, Inhibition of CYP450c17 by abiraterone administered once daily to castrate patients with prostate cancer resistant to LHRH analogues, anti-androgens and steriod therapy is well tolerated..., The institute of Cancer Research, 2007, -, -	☐
	13	DE COSTER, ET AL., Effects of High-Dose Ketoconazole and Dexamethason on ACTH-Stimulated Adrenal Steriodogenesis in Orchiectomized Prostatic Cancer Patients, Acta Endocrinologica (Copenh), 1987, pp 265-271, Volume 115	☐
	14	DUC ET AL, In Vitro and in vivo models for the evaluation of potent inhibitors of male rat 17 -hydroxylase/C-lyase, Pergamon, 2003, pages 537-542, vol. 84	☐
	15	ENDOCRINOLOGY, Inhibition of Androgen Synthesis in Human Testicular and Prostatic Microsomes and in Male Rats by Novel Steroidal Compounds, Endocrinology, 1999, pages 2891-2897, vol. 140 No. 6	☐
	16	FOSSA, ET AL., Weekly Docetaxel and Prednisone Versus Prednisolone Alone in Androgen-Independent Prostate Cancer: A Randomized Phase II Study, European Urology, 2007, pp 1691-1699, Volume 52	☐
	17	GERBER, ET AL., Prostate Specific Antigen for Assessing Response to Ketoconazole and Prednisone in Patients with Hormone Refractory Metastatic Prostate Cancer, The Journal of Urology, 1990, pp 1177-1179, Volume 144, Number 5	☐
	18	HAKKI ET AL, CYP17- and CYP11B-dependent steriod hydroxylases as drug development targets, Elsevier, 2006, pages 27-52, vol. 11	☐
	19	HARRIS, ET AL., Low Dose Ketoconazole with Replacement Doses of Hydrocortisone in Patients with Progressive Androgen Independent Prostate Cancer, The Journal of Urology, 2002, pp 542-545, Volume 168	☐
	20	MOREIRA ET AL, Synthesis and evaluation of novel 17-indazole androstene derivatives designed as CYP17 inhibitors, Elsevier, 2007, pages 939-948, vol. 72	☐
	21	NEWELL ET AL, The Cancer Research UK experience of pre-clinical toxicology studies to support early clinical trials with novel cancer therapies, Elsevier, 2004, pages 899-906, vol. 40	☐
	22	PETRYLAK, ET AL., Future Directions in the Treatment of Androgen-Independent Prostate Cancer, Urology, 2005, pp 8-13, Volume 65, Supplement 6A	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	ALAN H. AUERBACH
	Art Unit	1629
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	23	SCHOLZ, ET AL., Long-Term Outcome for Men with Androgen Independent Prostate Cancer Treated with Ketoconazole and Hydrocortisone, The Journal of Urology, 2005, pp 1947-1952, Volume 173	☐
	24	SMALL ET AL, The Case for Socondary Hormaonal Therapies in the Chemotherapy Age, The Journal of Urology, 2006, pages S66 - S71, vol. 176	☐
	25	WIKIPEDIA, Corticosteriod, undated, website	☐
	26		☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

Electronic Acknowledgement Receipt

EFS ID:	17033608
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Laurie Russo
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	03-OCT-2013
Filing Date:	24-FEB-2011
Time Stamp:	15:59:26
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Non Patent Literature	ASCO_Cancer_Foundation_2005.pdf	307380 f463df82c1768e3ee7797757d0850b0427d429d0	no	6

Warnings:	
Information:	

2	Non Patent Literature	BRUNO_ET_AL_2007.pdf	1231900 32ad432f48c0d9a104b9a71bd86b62c87af4205c	no	14
Warnings:					
Information:					
3	Non Patent Literature	Collins_2006.pdf	461077 abe43dcb368513da732f233a945f27bd74b64dc4	no	6
Warnings:					
Information:					
4	Non Patent Literature	COUGAR_BIOTECHNOLOGY__12_2005.pdf	111892 f977801238756cd72e93421e33c4751bf575a903	no	2
Warnings:					
Information:					
5	Non Patent Literature	COUGAR_BIOTECHNOLOGY_2_2005.pdf	312570 b73da9f296894923c630fb968547f10dc607e710	no	3
Warnings:					
Information:					
6	Non Patent Literature	COUGAR_BIOTECHNOLOGY_2_2007.pdf	247314 1196c296217cd077e3c42a9c5b788e1620a45d48	no	3
Warnings:					
Information:					
7	Non Patent Literature	COUGAR_BIOTECHNOLOGY_4_2007.pdf	219291 db89196262a05d8b48305e0a910755b18ba7a9bc	no	3
Warnings:					
Information:					
8	Non Patent Literature	COUGAR_BIOTECHNOLOGY_6_2007.pdf	344225 bc05d79e94e0d1b669fc18077689edd23c6e581c	no	3
Warnings:					
Information:					
9	Non Patent Literature	Cougar_Biotechnology_7_2007.pdf	395276 5bbf2231fc1652d17c92045bc0147d282158d8b6	no	3
Warnings:					
Information:					
10	Non Patent Literature	COUGAR_BIOTECHNOLOGY_10_2007.pdf	145874 ce2d0ff000741e6c16e91443ba35bc394431d935	no	2
Warnings:					
Information:					

11	Non Patent Literature	DE_BONO_ET_AL_2007.pdf	253053 661395f1e9555c78a0d81379ce6ac6eeb7826f7a	no	2
Warnings:					
Information:					
12	Non Patent Literature	DUC_ET_AL_2003.pdf	558530 d6d66cbd6d7f152517c0387c1bb4cc4e8433765f	no	6
Warnings:					
Information:					
13	Non Patent Literature	Fossa_et_al_2007.pdf	211005 695553ac862870bd585dfc45235d3707ce4eafe1	no	9
Warnings:					
Information:					
14	Non Patent Literature	HAKKI_ET_AL_2006.pdf	2539889 66ee73138eacf2f49776fea320c653e744ca6e98	no	26
Warnings:					
Information:					
15	Non Patent Literature	Harris_et_al_2002.pdf	53313 a16ff4a3e3a9ff45a081b48da42876f339a49baa	no	4
Warnings:					
Information:					
16	Non Patent Literature	MOREIRA_ET_AL_2007.pdf	917808 1efca2466defc6430481dc474381e871b366c6f8	no	10
Warnings:					
Information:					
17	Non Patent Literature	NEWELL_ET_AL_2004.pdf	706705 359d8ed7da166c3f79e8710db38ece18a5c67245	no	8
Warnings:					
Information:					
18	Non Patent Literature	PETRYLAK.pdf	482423 cf57dd505332573227ffb7bd2831819e78aa3f4e	no	6
Warnings:					
Information:					
19	Non Patent Literature	Scholz_et_al_2005.pdf	302464 35ce6099813bfc4bbe23a85c8046db05d93a893e	no	6
Warnings:					
Information:					

20	Non Patent Literature	SMALL_ET_AT_2006.pdf	697928 95adfa86ab19126222c8ed0ab762cd282825943d	no	6
Warnings:					
Information:					
21	Non Patent Literature	CANNELL.pdf	220527 c089ee108fd084821906f08113df0d35bd980ddb	no	2
Warnings:					
Information:					
22	Non Patent Literature	DECOSTER.pdf	460047 262259e9426672c7b67eb72af175b9f349b23a46	no	7
Warnings:					
Information:					
23	Non Patent Literature	GERBER.pdf	1586492 b0d5a5383827ecb1595f165a0d01a165a819b18e	no	3
Warnings:					
Information:					
24	Non Patent Literature	WIKI.pdf	354529 42e9974bf83d0eee6969a2f5de85b88aaf3bb1d5	no	7
Warnings:					
Information:					
			Total Files Size (in bytes):	13121512	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Electronic Acknowledgement Receipt

EFS ID:	17033778
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	Methods and Compositions for Treating Cancer
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Laurie Russo
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	03-OCT-2013
Filing Date:	24-FEB-2011
Time Stamp:	16:06:23
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Other Reference-Patent/App/Search documents	CGR5001_REFS_FROM_PAIR.pdf	1879808 351692168f177b6ceaa9a9d7e3505fe307d82c42	no	23

Warnings:	
Information:	

Total Files Size (in bytes):	1879808

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

27777 7590 10/25/2013

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1629	

DATE MAILED: 10/25/2013

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR TREATING CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1780	$300	$0	$2080	01/27/2014

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

27777 7590 10/25/2013
PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR TREATING CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1780	$300	$0	$2080	01/27/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
HUI, SAN MING R	1629	514-170000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29	NOTE: Absent a valid certification of Micro Entity Status (see form PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
❑ Applicant asserting small entity status. See 37 CFR 1.27	NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
❑ Applicant changing to regular undiscounted fee status.	NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 10/25/2013

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1629	

DATE MAILED: 10/25/2013

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notices of Allowance and Fee(s) Due mailed between October 1, 2013 and December 31, 2013

(Addendum to PTOL-85)

If the "Notice of Allowance and Fee(s) Due" has a mailing date on or after October 1, 2013 and before January 1, 2014, the following information is applicable to this application.

If the issue fee is being timely paid on or after January 1, 2014, the amount due is the issue fee and publication fee in effect January 1, 2014. On January 1, 2014, the issue fees set forth in 37 CFR 1.18 decrease significantly and the publication fee set forth in 37 CFR 1.18(d)(1) decreases to $0.

If an issue fee or publication fee has been previously paid in this application, applicant is not entitled to a refund of the difference between the amount paid and the amount in effect on January 1, 2014.

Notice of Allowability	Application No. 13/034,340	Applicant(s) AUERBACH ET AL.	
	Examiner SAN-MING HUI	Art Unit 1629	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to _____.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *37-56*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☒ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/San-ming Hui/
Primary Examiner, Art Unit 1629

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10/3/2013 has been entered.

Claims 37-56 are pending.

The following is an examiner's statement of reasons for allowance: essentially the same reason of allowance as previous communicated in the previous notice of allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAN-MING HUI whose telephone number is (571)272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Melenie McCormick can be reached on (571) 272-8037. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1629

/San-ming Hui/
Primary Examiner, Art Unit 1629

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1629

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012	09/05/2012	02/25/2013	06/28/2013	10/21/2013			
	1	÷								
	2	÷								
	3	÷								
	4	÷								
	5	÷								
	6	÷								
	7	÷								
	8	÷								
	9	÷								
	10	÷								
	11	÷								
	12	÷								
	13	÷								
	14	÷								
	15	÷								
	16	÷								
	17	÷								
	18	÷								
	19	÷								
	20	÷								
	21	÷								
	22	÷								
	23	÷								
	24	÷								
	25	÷								
	26	÷								
	27	÷								
	28	÷								
	29	÷								
	30	÷								
	31	÷								
	32	÷								
	33	÷								
	34	÷								
	35	÷								
	36	÷								

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1629

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012	09/05/2012	02/25/2013	06/28/2013	10/21/2013			
	37		✓	✓	✓	=	=			
	38		✓	✓	✓	=	=			
	39		✓	✓	✓	=	=			
	40		✓	✓	✓	=	=			
	41		✓	✓	✓	=	=			
	42		✓	✓	✓	=	=			
	43		✓	✓	✓	=	=			
	44		✓	✓	✓	=	=			
	45		✓	✓	✓	=	=			
	46		✓	✓	✓	=	=			
	47		✓	✓	✓	=	=			
	48		✓	✓	✓	=	=			
	49		✓	✓	✓	=	=			
	50		✓	✓	✓	=	=			
	51		✓	✓	✓	=	=			
	52		✓	✓	✓	=	=			
	53		✓	✓	✓	=	=			
	54		✓	✓	✓	=	=			
	55		✓	✓	✓	=	=			
	56		✓	✓	✓	=	=			

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	ALAN H. AUERBACH
	Art Unit	1629
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] ¡	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

NON-PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	ALAN H. AUERBACH
	Art Unit	1629
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	1	ASCO CANCER FOUNDATION, Poster Session F: Hormone Refractory, ASCO, 2005, -, -	☐
	2	BRUNO ET AL, Targeting cytochrome P450 enzymes: A new approach in anti-cancer drug development, Elsevier, 2007, pages 5047-5060, vol. 15	☐
	3	CANNELL, 100th Annual Meeting of the American Association for Cancer Research, Los Angeles, CA, USA;, http://oncology.thelancet.com, 2007, pp 471, Volume 8	☐
	4	Collins, et al. "A Systematic Review of the effectiveness of Docetaxel and Mitoxantrone for the Treatement of Metastatic Hormone-Refractory Prostate Cancer", British J. of Cancer, 95, pp 457-462 (2006)	☐
	5	COUGAR BIOTECHNOLOGY, Cougar Biotechnology Announces Initiation of Phase I/II Trial for CB7630 (Arbiraterone Acetate), Cougar Biotechnology, 12-14-2004, -, -	☐
	6	COUGAR BIOTECHNOLOGY, Cougar Biotechnology Announces Presentation of Positive CB7630 Clinical Data at AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, Cougar Biotechnology, 10-2007, -, -	☐
	7	COUGAR BIOTECHNOLOGY, Cougar Biotechnology Announces Presentation of Positive CB7630 Clinical Data at ESMO Conference, Drugs.com, 7-2007, -, -	☐
	8	COUGAR BIOTECHNOLOGY, Cougar Biotechnology announces presentation of positive phase I and phase II data at ASCO Prostate Cancer Symposium, Cougar Biotechnology, 02-23-2007, -, -	☐
	9	COUGAR BIOTECHNOLOGY, Cougar Biotechnology presents CB7630 Phase I clinical data at the 2005 Prostate Cancer Symposium, AllBusiness, 2005, -, -	☐
	10	COUGAR BIOTECHNOLOGY, Cougar Biotechnology presents positive CB7630 Clinical Data at AACR Annual Meeting Late-Breaking Clinical Trials Session, Cougar Biotechnology, 04-17-2007, -, -	☐
	11	COUGAR BIOTECHNOLOGY, Cougar Technology Announces Presentation of Positive CB7630 Clinical Data at ASCO Annual Meeting, The Free Library, 06-04-2007, -, -	☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	ALAN H. AUERBACH
	Art Unit	1629
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	12	DE BONO ET AL, Inhibition of CYP450c17 by abiraterone administered once daily to castrate patients with prostate cancer resistant to LHRH analogues, anti-androgens and steriod therapy is well tolerated..., The institute of Cancer Research, 2007, -, -	☐
	13	DE COSTER, ET AL., Effects of High-Dose Ketoconazole and Dexamethason on ACTH-Stimulated Adrenal Steriodogenesis in Orchiectomized Prostatic Cancer Patients, Acta Endocrinologica (Copenh), 1987, pp 265-271, Volume 115	☐
	14	DUC ET AL, In Vitro and in vivo models for the evaluation of potent inhibitors of male rat 17 -hydroxylase/C-lyase, Pergamon, 2003, pages 537-542, vol. 84	☐
	15	ENDOCRINOLOGY, Inhibition of Androgen Synthesis in Human Testicular and Prostatic Microsomes and in Male Rats by Novel Steroidal Compounds, Endocrinology, 1999, pages 2891-2897, vol. 140 No. 6	☐
	16	FOSSA, ET AL., Weekly Docetaxel and Prednisone Versus Prednisolone Alone in Androgen-Independent Prostate Cancer: A Randomized Phase II Study, European Urology, 2007, pp 1691-1699, Volume 52	☐
	17	GERBER, ET AL., Prostate Specific Antigen for Assessing Response to Ketoconazole and Prednisone in Patients with Hormone Refractory Metastatic Prostate Cancer, The Journal of Urology, 1990, pp 1177-1179, Volume 144, Number 5	☐
	18	HAKKI ET AL, CYP17- and CYP11B-dependent steriod hydroxylases as drug development targets, Elsevier, 2006, pages 27-52, vol. 11	☐
	19	HARRIS, ET AL., Low Dose Ketoconazole with Replacement Doses of Hydrocortisone in Patients with Progressive Androgen Independent Prostate Cancer, The Journal of Urology, 2002, pp 542-545, Volume 168	☐
	20	MOREIRA ET AL, Synthesis and evaluation of novel 17-indazole androstene derivatives designed as CYP17 inhibitors, Elsevier, 2007, pages 939-948, vol. 72	☐
	21	NEWELL ET AL, The Cancer Research UK experience of pre-clinical toxicology studies to support early clinical trials with novel cancer therapies, Elsevier, 2004, pages 899-906, vol. 40	☐
	22	PETRYLAK, ET AL., Future Directions in the Treatment of Androgen-Independent Prostate Cancer, Urology, 2005, pp 8-13, Volume 65, Supplement 6A	☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	ALAN H. AUERBACH
	Art Unit	1629
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	23	SCHOLZ, ET AL., Long-Term Outcome for Men with Androgen Independent Prostate Cancer Treated with Ketoconazole and Hydrocortisone, The Journal of Urology, 2005, pp 1947-1952, Volume 173	☐
	24	SMALL ET AL, The Case for Socondary Hormaonal Therapies in the Chemotherapy Age, The Journal of Urology, 2006, pages S66 - S71, vol. 176	☐
	25	WIKIPEDIA, Corticosteriod, undated, website 2013	☐
	26		☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature	/San Ming Hui/	Date Considered	10/21/2013

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

CPC						
Symbol					**Type**	**Version**
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			

CPC Combination Sets							
Symbol					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	20	
/SAN-MING HUI/ Primary Examiner.Art Unit 1629	10/21/2013	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	1

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
514	170	A	6	1	K	31 / 56 (2006.0)						

CROSS REFERENCE(S)					
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)				
514	180				

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	20	
/SAN-MING HUI/ Primary Examiner.Art Unit 1629	10/21/2013	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	1

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

☒ **Claims renumbered in the same order as presented by applicant** ☐ **CPA** ☐ **T.D.** ☐ **R.1.47**

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 20	
/SAN-MING HUI/ Primary Examiner.Art Unit 1629 (Primary Examiner)	10/21/2013 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 1

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
514	170, 182	1/27/11	SH
514	170, 182	9/5/12	SH
514	170, 182	2/25/13	SH
514	170, 182	6/28/13	SH
514	170, 182	10/21/13	SH

SEARCH NOTES		
Search Notes	Date	Examiner
EAST search and inventor search in PALM	1/27/11	SH
EAST search and inventor search in PALM	9/5/12	SH
EAST search and inventor search in PALM	2/25/13	SH
EAST search and inventor search in PALM	6/28/2013	SH
EAST search and inventor search in PALM	10/21/13	SH

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
514	170, 182	6/28/13	SH
514	170, 182	10/21/13	SH

SUBMISSION UNDER MPEP 609.06 Page 1 of 1		
	Confirmation Number	1597
	Application Number	13/034,340
	Filing Date	February 24, 2011
	First Named Inventor	Alan H. Auerbach
	Group Art Unit	1629
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	U.S. Patent Document Number	Kind Code[2] (if known)	Pages, Columns, Lines, where relevant passages or relevant figures appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	Foreign Patent Document Office[3]	Number[4]	KindCode[5]	Pages, Columns, Lines, where relevant passages or relevant figures appear	T[6]

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Third Party Observations dated October 18, 2012 for EP Appln. No. 07837326.3	
		Third Party Observations dated March 28, 2013 for EP Appln. No. 07837326.3	
		Third Party Observations dated July 1, 2013 for EP Appln. No. 07837326.3	

Examiner Signature	/San Ming Hui/	Date Considered	10/21/2013

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2352	abiraterone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L2	3	prdnisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L3	33161	prednisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L4	146800	prostate	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L5	1956	L1 and L4	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L6	139	L1 same L4	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L7	1184	514/170.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L8	2617	514/182.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L9	501671	cancer	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L10	2313	L1 and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L11	1181	L1 same L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L12	0	"9320097".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L13	2	"9509178".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32
L14	0	"9509178".pn. and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/10/21 11:32

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L15	2292	514/182.ccls.	US-PGPUB; USPAT	OR	ON	2013/10/21 11:32
L16	1029	514/170.ccls.	US-PGPUB; USPAT	OR	ON	2013/10/21 11:32

10/21/2013 11:37:54 AM
C:\Users\shui\Documents\EAST\Workspaces\13-034340.wsp

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	13034340	Filing Date	2011-02-24	Docket Number (if applicable)	CGR5001USCNT1	Art Unit	1629
First Named Inventor	Alan H. Auerbach			Examiner Name	San Ming R. Hui		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____

☐ Other _____

☒ Enclosed

☐ Amendment/Reply

☒ Information Disclosure Statement (IDS)

☐ Affidavit(s)/ Declaration(s)

☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____
(Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

☒ **The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.**
The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 100750

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

☐ Applicant Signature

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Signature of Registered U.S. Patent Practitioner			
Signature	/Timothy E. Tracy, Reg. No. 39,401/	Date (YYYY-MM-DD)	2014-01-10
Name	Timothy E. Tracy	Registration Number	39401

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PTO/SB/08A (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 2

Application Number	13/034,340
Filing Date	February 24, 2011
First Named Inventor	Alan H. Auerbach
Group Art Unit	1629
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	U.S. Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document mm-dd-yyyy	Pages, Columns, Lines, where relevant passages or relevant figures appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Foreign Patent Document Office[3]	Number[4]	KindCode[5]	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document mm-dd-yyyy	Pages, Columns, Lines, where relevant passages or relevant figures appear	T[6]

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Unique citation designation number. 2 See attached Kinds of U.S. Patent Documents. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS,SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

PTO/SB/08A (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 2 of 2

Application Number	13/034,340
Filing Date	February 24, 2011
First Named Inventor	Alan H. Auerbach
Group Art Unit	1629
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Berry, W. et al. Phase III Study of Mitoxantrone Plus Low Dose Prednisone Versus Low Dose Prednisone Alone in Patients with Asymptomatic Hormone Refractory Prostate Cancer, The Journal of Urology, 2002, pages 2439-2443, Volume 168.	
		Chang, Ching-Yi, et al. Glucocorticoids Manifest Androgenic Activity in a Cell Derived from a Metastatic Prostate Cancer, Cancer Research, 2001, pages 8712-8717, Volume 61.	
		Dorff, TB, Crawford, ED. Management and challenges of corticosteroid therapy in men with metastatic castrate-resistant prostate cancer, Annals of Oncology, 2013, pages 31-8, Volume 24(1).	
		Efstathiou, Eleni, et al. Effects of Abiraterone Acetate on Androgen Signaling in Castrate-Resistant Prostate Cancer in Bone, American Society of Clinical Oncology, Journal of Clinical Oncology, 2011, pages 1-8.	
		Huggins, Charles, et al. Studies on Prostatic Cancer.I. The Effect of Castration, of Estrogen and of Androgen Injection on Serum Phosphatases in Metastatic Carcinoma of the Prostate, Cancer Research, 1941, pages 293-297, Volume 1.	
		Mostaghel, EA. et al. Molecular Pathways: Targeting resistance in the androgen receptor for therapeutic benefit, Clin Cancer Res, 2013 Dec 4. [Epub ahead of print].	
		Nishimura, Kazuo, et al. Potential Mechanism for the Effects of Dexamethasone on Growth of Androgen-Independent Prostate Cancer, Journal of the National Cancer Institute, 2001, pages 1739-1746, Volume 93.	
		Oudar, Stephane, et al. Actualite dans le cancer de la prostate, Synthese, Bull Cancer 2005; 92 (10), pgs. 865-873 (relevance in English abstract)	
		Petrylak, et al. Docetaxel and Estramustine Compared with Mitoxantrone and Prednisone for Advanced Refractory Prostate Cancer, The New England Journal of Medicine, 2004, pages 1513-20, Volume 351.	
		Ryan, et al., Aberaterone Acetate in Metastatic Prostate Cancer Without Previous Chemotherapy, The New England Journal of Medicine, 2013, 368:138-148.	
		Sartor, et al, Abiraterone Prolongs Survival in Metastatic Prostate Cancer, Nature Reviews Clinical Oncology, 2011, pages 515-16, Volume 8.	
		Tannock, IF, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer, The New England Journal of Medicine, 2004, pages 1502-1512, Volume 351(15).	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Unique citation designation number. 2 Applicant is to place a check mark here if English language Translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Confirmation Number	1597
Application Number	13/034340
Filing Date	February 24, 2011
First Named Inventor	Alan H. Auerbach
Group Art Unit	1629
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ Attached are copies of search report(s) from corresponding patent application(s), which are listed on the attached Submission Under MPEP 609.06.

☒ In accordance with §1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified national application (other than a continued prosecution application under §1.53(d)), within three months of the date of entry into the national stage of the above identified application as set forth in §1.491, or before the mailing date of a first Office Action on the merits of the above-identified application, or before the mailing date of a first Office Action after the filing of a request for continued examination under §1.114, no additional fee is required.

☒ Please charge any deficiency or credit any overpayment to Deposit Account No. 10- 0750/ CGR5001USCNT1/TET.

☐ None

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Timothy E. Tracy, Reg. No. 39,401/	Date (YYYY-MM-DD)	2014-01-10
Name/Print	Timothy E. Tracy	Registration Number	39,401

CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being electronically filed via EFS-Web to the Commissioner for Patents with the U.S. Patent and Trademark Office on: January 14, 2014

Name (print/type)	Denise Mattos-Bosque		
Signature	/Denise Mattos-Bosque/	Date	January 10, 2014

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Electronic Patent Application Fee Transmittal

Application Number:	13034340
Filing Date:	24-Feb-2011
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Request for Continued Examination	1801	1	1200	1200
		Total in USD ($)		**1200**

Electronic Acknowledgement Receipt

EFS ID:	17881759
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	10-JAN-2014
Filing Date:	24-FEB-2011
Time Stamp:	15:22:34
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1200
RAM confirmation Number	2016
Deposit Account	100750
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Continued Examination (RCE)	sb0030e_RCE_10Jan14.pdf	80018 8f8e039dbf5b96f6ef9af22f0bf8b2dbb657ca12	no	3
Warnings:					
This is not a USPTO supplied RCE SB30 form.					
Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	CGR5001USCNT1_1449_10Jan14.pdf	366077 c33f3b49b1452fea1fe45efdec9fc3b59ce65784	no	2
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Information Disclosure Statement (IDS) Form (SB08)	IDSCertifStm_1449wRCE_10Jan14.pdf	274569 ba987bab7cb6a266d828ae1dd52eb61a7dd2dcdc	no	1
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
4	Non Patent Literature	Berry_JUrol_2002.pdf	63925 d00379d301e5cf2a664c0de8b564bbb852c14c16	no	5
Warnings:					
Information:					
5	Non Patent Literature	Chang_CancerRes_2001.pdf	522795 947e4f3c917d3e85d840bc345d37d57126307248	no	7
Warnings:					
Information:					
6	Non Patent Literature	Dorff_AnnOnc_2012.pdf	214205 94cb53fa2bbe20d047ff33a15890e93528af27db	no	8
Warnings:					
Information:					
7	Non Patent Literature	Efstathiou_JournClinOncol_2011.pdf	205288 2e665457b94e97bb281c6a748c03207ee5a5388c	no	8
Warnings:					
Information:					

8	Non Patent Literature	Huggins_CancerRes_1941.pdf	1449687 5adb5593f9d6eeebd0e83f8060454b36f0968dac	no	6
Warnings:					
Information:					
9	Non Patent Literature	Mostaghel_ClinCancerRes_2013.pdf	4351720 45ea516ea40668a6b3bcc3896fe1259b48f00814	no	15
Warnings:					
Information:					
10	Non Patent Literature	Nishimura_NatlCancerInst_2001.pdf	336227 8114009bffc2be36cd1c56d294d2b4ec77d48a30	no	8
Warnings:					
Information:					
11	Non Patent Literature	Oudard_BullCancer_2005.pdf	2891641 a1b43d93f4d7cb05a4882b758975686be7a441ad	no	10
Warnings:					
Information:					
12	Non Patent Literature	Petrylak_NEnglJMed_2004.pdf	183846 f5da5013fac650bc692b644a354944c4c763df67	no	8
Warnings:					
Information:					
13	Non Patent Literature	Ryan_NewEnglJMed_2013.pdf	229013 149bc3a0015c890ee644fd0d7dbd52807c0f0bd6	no	11
Warnings:					
Information:					
14	Non Patent Literature	Sartor_ROA_2012.pdf	70195 927a901d5d35608499b5693f77b94ae418efb436	no	2
Warnings:					
Information:					
15	Non Patent Literature	Tannock_NEnglJMed_2004.pdf	142400 4064489b6579cf249c1e6113af7edd86926d9dcd	no	11
Warnings:					
Information:					
16	Fee Worksheet (SB06)	fee-info.pdf	30231 407e1fd9e6954f8d8c743539dcc2d8d15d47285d	no	2
Warnings:					
Information:					

Total Files Size (in bytes):	11411837

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

27777 7590 02/11/2014

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1621	

DATE MAILED: 02/11/2014

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR TREATING CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$960	$0	$0	$960	05/12/2014

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

27777 7590 02/11/2014
PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR TREATING CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$960	$0	$0	$960	05/12/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
HUI, SAN MING R	1621	514-170000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ Applicant certifying micro entity status. See 37 CFR 1.29 — NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27 — NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status. — NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 02/11/2014

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1621	

DATE MAILED: 02/11/2014

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 13/034,340	Applicant(s) AUERBACH ET AL.	
	Examiner SAN-MING HUI	Art Unit 1621	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *1/10/2014*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *37-56*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☒ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/SAN-MING HUI/
Primary Examiner, Art Unit 1621

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 1/10/2014 has been entered.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: the herein claimed method of treating prostate cancer is essentially the same as the notice of allowance mailed 7/30/2013. The commercial success of the combination of prednisone and abiraterone to treat prostate cancer obviate the rejection under 35 USC 103(a).

Claims 37-56 are allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAN-MING HUI whose telephone number is (571)272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Melenie McCormick can be reached on (571) 272-8037. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1621

/SAN-MING HUI/
Primary Examiner, Art Unit 1621

PTO/SB/08A (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 2

Application Number	13/034,340
Filing Date	February 24, 2011
First Named Inventor	Alan H. Auerbach
Group Art Unit	1629
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	U.S. Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document mm-dd-yyyy	Pages, Columns, Lines, where relevant passages or relevant figures appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Foreign Patent Document Office[3]	Number[4]	KindCode[5]	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document mm-dd-yyyy	Pages, Columns, Lines, where relevant passages or relevant figures appear	T[6]

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number. [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS,SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

PTO/SB/08A (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 2 of 2

Application Number	13/034,340
Filing Date	February 24, 2011
First Named Inventor	Alan H. Auerbach
Group Art Unit	1629
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Berry, W. et al. Phase III Study of Mitoxantrone Plus Low Dose Prednisone Versus Low Dose Prednisone Alone in Patients with Asymptomatic Hormone Refractory Prostate Cancer, The Journal of Urology, 2002, pages 2439-2443, Volume 168.	
		Chang, Ching-Yi, et al. Glucocorticoids Manifest Androgenic Activity in a Cell Derived from a Metastatic Prostate Cancer, Cancer Research, 2001, pages 8712-8717, Volume 61.	
		Dorff, TB, Crawford, ED. Management and challenges of corticosteroid therapy in men with metastatic castrate-resistant prostate cancer, Annals of Oncology, 2013, pages 31-8, Volume 24(1).	
		Efstathiou, Eleni, et al. Effects of Abiraterone Acetate on Androgen Signaling in Castrate-Resistant Prostate Cancer in Bone, American Society of Clinical Oncology, Journal of Clinical Oncology, 2011, pages 1-8.	
		Huggins, Charles, et al. Studies on Prostatic Cancer.I. The Effect of Castration, of Estrogen and of Androgen Injection on Serum Phosphatases in Metastatic Carcinoma of the Prostate, Cancer Research, 1941, pages 293-297, Volume 1.	
		Mostaghel, EA. et al. Molecular Pathways: Targeting resistance in the androgen receptor for therapeutic benefit, Clin Cancer Res, 2013 Dec 4. [Epub ahead of print].	
		Nishimura, Kazuo, et al. Potential Mechanism for the Effects of Dexamethasone on Growth of Androgen-Independent Prostate Cancer, Journal of the National Cancer Institute, 2001, pages 1739-1746, Volume 93.	
		Oudar, Stephane, et al. Actualite dans le cancer de la prostate, Synthese, Bull Cancer 2005; 92 (10), pgs. 865-873 (relevance in English abstract)	
		Petrylak, et al. Docetaxel and Estramustine Compared with Mitoxantrone and Prednisone for Advanced Refractory Prostate Cancer, The New England Journal of Medicine, 2004, pages 1513-20, Volume 351.	
		Ryan, et al., Aberaterone Acetate in Metastatic Prostate Cancer Without Previous Chemotherapy, The New England Journal of Medicine, 2013, 368:138-148.	
		Sartor, et al, Abiraterone Prolongs Survival in Metastatic Prostate Cancer, Nature Reviews Clinical Oncology, 2011, pages 515-16, Volume 8.	
		Tannock, IF, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer, The New England Journal of Medicine, 2004, pages 1502-1512, Volume 351(15).	

Examiner Signature	/San Ming Hui/	Date Considered	01/29/2014

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Unique citation designation number. 2 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1629

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012	09/05/2012	02/25/2013	06/28/2013	10/21/2013	01/29/2014		
	1	÷								
	2	÷								
	3	÷								
	4	÷								
	5	÷								
	6	÷								
	7	÷								
	8	÷								
	9	÷								
	10	÷								
	11	÷								
	12	÷								
	13	÷								
	14	÷								
	15	÷								
	16	÷								
	17	÷								
	18	÷								
	19	÷								
	20	÷								
	21	÷								
	22	÷								
	23	÷								
	24	÷								
	25	÷								
	26	÷								
	27	÷								
	28	÷								
	29	÷								
	30	÷								
	31	÷								
	32	÷								
	33	÷								
	34	÷								
	35	÷								
	36	÷								

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/21/2011	01/27/2012	09/05/2012	02/25/2013	06/28/2013	10/21/2013	01/29/2014		
	37		✓	✓	✓	=	=	=		
	38		✓	✓	✓	=	=	=		
	39		✓	✓	✓	=	=	=		
	40		✓	✓	✓	=	=	=		
	41		✓	✓	✓	=	=	=		
	42		✓	✓	✓	=	=	=		
	43		✓	✓	✓	=	=	=		
	44		✓	✓	✓	=	=	=		
	45		✓	✓	✓	=	=	=		
	46		✓	✓	✓	=	=	=		
	47		✓	✓	✓	=	=	=		
	48		✓	✓	✓	=	=	=		
	49		✓	✓	✓	=	=	=		
	50		✓	✓	✓	=	=	=		
	51		✓	✓	✓	=	=	=		
	52		✓	✓	✓	=	=	=		
	53		✓	✓	✓	=	=	=		
	54		✓	✓	✓	=	=	=		
	55		✓	✓	✓	=	=	=		
	56		✓	✓	✓	=	=	=		

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
514	170, 182	1/27/11	SH
514	170, 182	9/5/12	SH
514	170, 182	2/25/13	SH
514	170, 182	6/28/13	SH
514	170, 182	10/21/13	SH
514	170, 182	1/29/14	SH

SEARCH NOTES		
Search Notes	Date	Examiner
EAST search and inventor search in PALM	1/27/11	SH
EAST search and inventor search in PALM	9/5/12	SH
EAST search and inventor search in PALM	2/25/13	SH
EAST search and inventor search in PALM	6/28/2013	SH
EAST search and inventor search in PALM	10/21/13	SH
EAST search and inventor search in PALM	1/29/14	SH

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
514	170, 182	6/28/13	SH
514	170, 182	10/21/13	SH

INTERFERENCE SEARCH			
US Class/ CPC Symbol	**US Subclass / CPC Group**	**Date**	**Examiner**
514	170, 182	1/29/14	SH

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

CPC		
Symbol	**Type**	**Version**

CPC Combination Sets				
Symbol	**Type**	**Set**	**Ranking**	**Version**

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	20	
/SAN-MING HUI/ Primary Examiner.Art Unit 1621	01/29/2014	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	1

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
514	170	A	6	1	K	31 / 56 (2006.0)						

CROSS REFERENCE(S)					
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)				
514	180				

NONE	Total Claims Allowed:
(Assistant Examiner) (Date)	20
/SAN-MING HUI/ Primary Examiner.Art Unit 1621 01/29/2014 (Primary Examiner) (Date)	O.G. Print Claim(s): 1 / O.G. Print Figure: 1

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 20	
/SAN-MING HUI/ Primary Examiner.Art Unit 1621 (Primary Examiner)	01/29/2014 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 1

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L3	2482	abiraterone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L4	3	prdnisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L5	34327	prednisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L6	151075	prostate	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L7	2066	L3 and L6	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L8	152	L3 same L6	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L9	1237	514/170.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L10	2750	514/182.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L11	514610	cancer	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L12	2438	L3 and L11	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L13	1260	L3 same L11	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L14	0	"9320097".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L15	2	"9509178".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40
L16	0	"9509178".pn. and L11	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/01/29 09:40

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2340	514/182.ccls.	US-PGPUB; USPAT	OR	ON	2014/01/29 09:40
L2	1048	514/170.ccls.	US-PGPUB; USPAT	OR	ON	2014/01/29 09:40
L17	2340	514/182.ccls.	US-PGPUB; USPAT	OR	ON	2014/01/29 09:40
L18	1048	514/170.ccls.	US-PGPUB; USPAT	OR	ON	2014/01/29 09:40

1/29/2014 9:41:34 AM
C:\Users\shui\Documents\EAST\Workspaces\13-034340.wsp

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	13034340	Filing Date	2011-02-24	Docket Number (if applicable)	CGR5001USCNT1	Art Unit	1629
First Named Inventor	Alan H. Auerbach			Examiner Name	San Ming R. Hui		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____

☐ Other _____

☒ Enclosed

☐ Amendment/Reply

☒ Information Disclosure Statement (IDS)

☐ Affidavit(s)/ Declaration(s)

☒ Other
MPEP609D

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____
(Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.

☒ The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 100750

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

☐ Applicant Signature

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Signature of Registered U.S. Patent Practitioner			
Signature	/Timothy E. Tracy, Reg. No. 39,401/	Date (YYYY-MM-DD)	2014-05-09
Name	Timothy E. Tracy	Registration Number	39401

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13034340
Filing Date	2011-02-24
First Named Inventor	Alan H. Auerbach
Art Unit	1621
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20060030608	A1	2006-02-09	Nelson, et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2478907	EP		2012-07-25	Cougar Biotechnology, Inc.		☐
	2	2006027266	WO		2006-03-16	Nitec Pharma AG		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

NON-PATENT LITERATURE DOCUMENTS

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	Alan H. Auerbach
	Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Assessment Report for Zytiga (abiraterone) published 2011 by the CHMP of the EMA	☐
	2	AUCHUS, R.J., "The genetics, pathophysiology, and the management of human deficiencies of P450c17", Endocrinol Metab Clin North Am (2001), 30, p.101-119	☐
	3	AYUB, M., "Inhibition of testicular 17a-hydroxylase and 17,20-lyase but not 3B-hydroxysteroid dehydrogenase-isomerase or 17B-hydroxysteroid oxidoreductase by ketoconazole and other imidazole drugs, Journal of Steroid Biochemistry (1987) 28(5), p.521-531	☐
	4	Campbell-Walsh Urology, Ninth Edition, Saunders, Vol. 3, Chapters 104 and 105	☐
	5	Cecil Textbook of Medicine, Wyngaarden & Smith 18th edition; Chapter on "Glucocorticosteroid Therapy", Wyngaarden & Smith 18th edition, (1988) p.128-131	☐
	6	Cougar Biotechnology Inc. with the U.S. Securities and Exchange Commission, Form 10-QSB	☐
	7	CZOCK, et al., "Pharmacokinetics and Pharmacodynamics of Systemically Administered Glucocorticoids", Pharmacokinet (2005), 44(1), p.61-98	☐
	8	ERGUN-LONGMIRE, Berrin, et al., "Two Novel Mutations Found in a Patient with 17a-Hydroxylase Enzyme Deficiency", The Journal of Clinical Endocrinology & Metabolism (2006), 91(10), p.4179-4182	☐
	9	FAKIH, et al., Urology (2002) 60, p.553-561	☐
	10	FRIEL, Patrick N., et al., "Suppression of adrenal function by low-dose prednisone: assessment with 24-hour urinary steroid hormone profiles-A review of five cases", Alternative Medicine Review (2006), 11(1)	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	Alan H. Auerbach
	Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	11	Internet article: http://clinicaltrials.gov/archive/NCT00485303/2007_06_11	☐
	12	Information concerning Zytiga (abiraterone acetate) from http://www.kompendium.ch/prod/pnr/1183238/de?Platform=Desktop as of March 25, 2014	☐
	13	Internet article: http://clinicaltrials.gov/ct2/show/study/NCT00485303?sec=X501	☐
	14	MOSTAGHEL, E.A., "Abiraterone in the treatment of metastatic castration-resistant prostate cancer", Cancer Management Res. (2014) 6, p.39-51	☐
	15	OSABA, D., et al., "Health-Related Quality of Life in Men with Metastatic Prostate Cancer Treated with Prednisone alone or Mitoxantrone and Prednisone", J. Clin. Oncol. (1999), 17(6), p.1654-1663	☐
	16	PETRYLAK, D.P., "New Paradigms for Advanced Prostate Cancer", Rev. Urol. (2007), 9, Suppl. 2, S3-S12	☐
	17	Prostate Cancer Principles and Practice, Taylor & Francis (2006) Chapter 93	☐
	18	REID, A., et al., "Annals of Oncology", Educational and Abstract Book of the ESMO Conference Lugano (ECLU), (2007), 18(Supplement 9), ix173-ix174. Abstract 50PD	☐
	19	REMINGTON, "The Science and Practice of Pharmacy, 20th Edition (2000), p.1363-1370	☐
	20	RUNGE, Marschall S., et al., "Principles of Molecular Medicine; Second edition; (2006) Humana Press Inc. ISBN: 1-58829-202-9. pgs.365-376 and 482-484	☐
	21	SILLS, Irene N., et al., "17a-hydroxylase deficiency in a genetic male and female sibling pair", Int. J. Gynaecol. Obstet., (1981), 19, p.473-479	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	Alan H. Auerbach
	Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	22	Summary of Product Characteristics for Zytiga 250mg tablets (16Jan2014)	☐
	23	TANNOCK., et al., "Docetaxel Plus Prednisone or Mitoxantrone Plus Prednisone for Advanced Prostate Cancer", Journal of Urology (2005), 173(2), p.456	☐
	24	The reply of applicant (i.e. the Proprietor of herein opposed patent) dated June 4, 2013 in relation to the corresponding US2011/0144016A1 US proceedings.	☐
	25	WANG, C., et al., "Hypertension due to 17a-Hydroxylase deficiency", Australian and New Zealand Journal of Medicine (1978), 8(3), p.295-299	☐
	26	YANO, A., et al., "Glucocorticoids Suppress Tumor Angiogensis and In vivo Growth of Prostate Cancer Cells", Clin. Cancer Res., (2006) 12, 3003-3009	☐
	27		☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Sheet 1 of 1

Confirmation Number	1597
Application Number	13/034,340
Filing Date	February 24, 2011
First Named Inventor	Alan H. Auerbach
Group Art Unit	1629
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☒ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement (See 37 CFR 1.97(e)(1)), or before the mailing date of a first Office Action on the merits of the above-identified application, or before the mailing date of a first Office Action after the filing of a request for continued examination under §1.114, no additional fee is required.

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ Identification of Prior Application in which some of the listed information was already cited and for which no copies are submitted or need to be submitted. This application relies, under 35 U.S.C. §120, on the earlier filing date of prior application serial no.: . If any of the foregoing publications are not available to the Examiner, Applicant will endeavor to supply copies at the Examiner's request.

☒ **REMINDER TO THE EXAMINER**
In view of, and pursuant to, the holdings of the Federal Circuit Court of Appeals in the cases *Dayco Products, Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 66 U.S.P.Q.2d 1801 (Fed. Cir. 2003); *McKesson Info. Sol'ns v. Bridge Med.*, 487 F.3d 897, 927 (Fed. Cir. 2007); and related cases, Applicants hereby inform the Examiner of the existence of commonly owned pending U.S. Patent Application Serial Nos. 11/844,440. This application has published and is therefore publicly available in PAIR. Moreover, the Patent Office has issued one or more Office Actions in this application. The Examiner is invited to review the prosecution of this application to determine its impact, if any, on the prosecution of the present application. In an effort not to overwhelm the Examiner with an overly large IDS, Applicants are not submitting copies of these publicly available documents. Of course, Applicants would be happy to do so at the Examiner's request.

In addition, submitted herewith are Third Party Observations that were submitted in the European Patent Office for the corresponding European Application to the captioned application.

☒ Attached are copies of the statement(s) from any corresponding document(s), which are listed on the attached Submission Under MPEP 609.06.

☐ The relevance of those listed references which are not in the English language is as follows:

☒ Copies of copyrighted material were made and delivered to the government under license from Copyright Clearance Center, Inc. No further reproduction is permitted.

☒ Any fee set forth in 37 CFR 1.17 (p) has been submitted herewith. The Commissioner is hereby authorized to charge any additional fees which may be required in connection with the filing of this communication, or credit any overpayment, to Account No. 10-0750.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Timothy E. Tracy, Reg. No. 39,401/	Date (YYYY-MM-DD)	May 9, 2014
Name/Print	Timothy E. Tracy	Registration Number	39,401

CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being electronically filed via EFS-Web to the Commissioner for Patents with the U.S. Patent and Trademark Office on: May 9, 2014

Name (print/type)	Denise Mattos-Bosque		
Signature	/Denise Mattos-Bosque/	Date	May 9, 2014

SUBMISSION UNDER MPEP 609.06 Page 1 of 1		
	Confirmation Number	1597
	Application Number	13/034340
	Filing Date	02-24-2014
	First Named Inventor	Alan H. Auerbach
	Group Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	U.S. Patent Document Number	Kind Code[2] (if known)	Pages, Columns, Lines, where relevant passages or relevant figures appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	Foreign Patent Document Office[3]	Number[4]	KindCode[5]	Pages, Columns, Lines, where relevant passages or relevant figures appear	T[6]

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner 's Initials*	Cite No.[1]	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Statement of Opposition, Actavis Group PTC ehf	
		Statement of Opposition, Alfred E. Tiefenbacher	
		Statement of Opposition, Alison Gallafent	
		Statement of Opposition, Arnold Siedsma	
		Statement of Opposition, Cabinet Lavoix	
		Statement of Opposition, Galenicum Health, S.L.	
		Statement of Opposition, Generics Ltd.	
		Statement of Opposition, Helm AG	
		Statement of Opposition, Hetero Drugs	
		Statement of Opposition, Isenbruck Bosl Horschler LLP	
		Statement of Opposition, Laboratorios Leon Farma, S.A.	
		Statement of Opposition, Maiwald Patentanwalts GmbH	
		Statement of Opposition, Stada Arzneimittel	
		Statement of Opposition, Synthon B.V.	
		Statement of Opposition, Teva Pharmaceutical Industries, Ltd.	
		Statement of Opposition, Zentiva k.s.	

Examiner Signature		Date Considered	

Electronic Patent Application Fee Transmittal

Application Number:	13034340
Filing Date:	24-Feb-2011
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
RCE - 2nd and Subsequent Request	1820	1	1700	1700
		Total in USD ($)		**1880**

Electronic Acknowledgement Receipt

EFS ID:	18992805
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	09-MAY-2014
Filing Date:	24-FEB-2011
Time Stamp:	16:24:59
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1880
RAM confirmation Number	2725
Deposit Account	100750
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Continued Examination (RCE)	sb0030e_RCE2_09May14.pdf	80038 022dbee9319cc76e673583cafb8c1f3e456344d9	no	3
Warnings:					
This is not a USPTO supplied RCE SB30 form.					
Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	CGR5001USCNT1_1449_09May14.pdf	73362 41d7563e714cd88a172c2d81f8abd5cb5d948b43	no	5
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Transmittal Letter	CGR5001USCNT1_IDSCertStmt_09May14.pdf	247253 659830135f59e684de6a0c5c5e9bc810de1a04e5	no	1
Warnings:					
Information:					
4	Other Reference-Patent/App/Search documents	CGR5001USCNT1_MPEP609_09May14.pdf	204276 c062117564099b729dcb03f6db52817a76164aa0	no	1
Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	31846 e4b96e56fd1461cc51f1ae1d62ffdbbe835254c1	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	636775		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 2 478 907 A2

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
25.07.2012 Bulletin 2012/30

(21) Application number: **12160586.9**

(22) Date of filing: **23.08.2007**

(51) Int Cl.:
A61K 31/573 *(2006.01)* ***A61K 31/58*** *(2006.01)*
A61K 45/06 *(2006.01)* ***A61P 35/00*** *(2006.01)*

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC MT NL PL PT RO SE SI SK TR
Designated Extension States:
AL BA HR MK RS

(30) Priority: **25.08.2006 US 921506 P**

(62) Document number(s) of the earlier application(s) in accordance with Art. 76 EPC:
07837326.3 / 2 061 561

(71) Applicant: **Cougar Biotechnology, Inc.**
Los Angeles CA 90024 (US)

(72) Inventor: **The designation of the inventor has not yet been filed**

(74) Representative: **Carpmaels & Ransford**
One Southampton Row
London
WC1B 5HA (GB)

Remarks:
•This application was filed on 21-03-2012 as a divisional application to the application mentioned under INID code 62.
•Claims filed after the date of filing of the application (Rule 68(4) EPC).

(54) Methods and compositions for treating cancer

(57) Methods and compositions for treating cancer are described herein. More particularly, the methods for treating cancer comprise administering a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate (i.e., 3β-acetoxy-17-(3-pyridyl) androsta-5, 16-diene), in combination with at least one additional therapeutic agent such as an anti-cancer agent or a steroid. Furthermore, disclosed are compositions comprising a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, and at least one additional therapeutic agent, such as an anti-cancer agent or a steroid.

EP 2 478 907 A2

Description

FIELD OF THE INVENTION

[0001] Methods and compositions for treating cancer are described herein. More particularly, the methods for treating cancer comprise administering a 17α-hydroxylase/$C_{17,\ 20}$-lyase inhibitor, such as abiraterone acetate (*i.e.,* 3β-acetoxy-17-(3-pyridyl) androsta-5, 16-diene), in combination with at least one additional therapeutic agent, such as an anti-cancer agent or a steroid. Furthermore, disclosed are compositions comprising a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, and at least one additional therapeutic agent such as an anti-cancer agent or a steroid, e.g., a corticosteroid or, more specifically, a glucocorticoid.

BACKGROUND

[0002] The number of people diagnosed with cancer has significantly increased. Of special interest are individuals diagnosed with androgen-dependent disorders, such as prostate cancer, and estrogen-dependent disorders, such as breast cancer since such diagnoses are increasing in number at an alarming rate.

[0003] Prostate cancer is currently the most common non-skin cancer and the second leading cause of cancer-related death in men after lung cancer. The primary course of treatment for patients diagnosed with organ-confined prostate cancer is usually prostatectomy or radiotherapy. Not only are these treatments highly invasive and have undesirable side effects, such localized treatments are not effective on prostate cancer after it has metastasized. Moreover, a large percent of individuals who receive localized treatments will suffer from recurring cancer.

[0004] Additionally, breast cancer incidence in women has increased from one out of every 20 women in 1960 to one out of every eight women in 2005. Moreover, it is the most common cancer among white and African-American women. Similar to treating prostate cancer, most options for women diagnosed with breast cancer are highly invasive and have significant side-effects. Such treatments include surgery, radiation and chemotherapy.

[0005] Hormone therapy is another treatment option for individuals diagnosed with prostate or breast cancer. Hormone therapy is a form of systemic treatment for prostate or breast cancer wherein hormone ablation agents are used to suppress the production or block the effects of hormones, such as estrogen and progesterone in the body, which are believed to promote the growth of breast cancer, as well as testosterone and dihydrotestosterone, which are believed to promote the growth of prostate cancer. Moreover, hormone therapy is less invasive than surgery and does not have many of the side effects associated with chemotherapy or radiation. Hormone therapy can also be used by itself or in addition to localized therapy and has shown to be effective in individuals whose cancer has metastasized.

[0006] Even though hormone therapy is less invasive and can be used on more advanced stages of cancer, some individuals administered current hormone therapy treatments may not show a significant response or may not show any response at all to such treatments. Additionally, some patients treated with current hormone therapy treatments may also suffer from relapsing or recurring cancer. Currently, such refractory cancer patients are left with very few treatment options.

[0007] Despite the progress made in the treatment of cancer, there remains a need for more effective ways to treat cancer such as, but not limited to, prostate cancer and breast cancer. Additionally, there is a need for effective anti-cancer treatment options for patients who are not responding to current anti-cancer treatments. Also, there is a need for effective anti-cancer treatment options for patients whose cancer has recurred.

SUMMARY OF THE INVENTION

[0008] Described herein are methods for treating a cancer in which a therapeutically effective amount of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate (*i.e.* 3β-acetoxy-17-(3-pyridyl)androsta-5,16-diene), is administered to a patient, e.g., a patient in need thereof, in combination with a therapeutically effective amount of at least one additional therapeutic agent including, but not limited to, an anti-cancer agent or steroid. Such methods can also provide an effective treatment for individuals with a refractory cancer, including individuals who are currently undergoing a cancer treatment. Therefore, in certain embodiments, the method is directed to treating a refractory cancer in a patient, in which a therapeutically effective amount of 17α-hydroxylase/$C_{17,20}$-lyase inhibitor is administered to a patient currently receiving an anti-cancer agent.

[0009] For example, in certain embodiments, the method for the treatment of a cancer in a mammal comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 0. 1 mg/m^2 to about 20 mg/m^2 of mitoxantrone.

[0010] In another embodiment, the method for the treatment of a cancer in a mammal comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/m^2 to about 175 mg/m^2 of paclitaxel.

[0011] In still other embodiments, the method for the treatment of a cancer in a mammal comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/m^2 to about 100 mg/m^2 of docetaxel.

[0012] Furthermore, described herein is a method for the treatment of a cancer in a mammal comprising administering an amount of about 0.01 mg/kglday to about 100 mg/kg/day of abiraterone acetate; and an amount of about 0.01 mg to about 200 mg of leuprolide, wherein the leuprolide is administered over a period of about 3 days to about 12 months.

[0013] In other embodiments, the method for the treatment of a cancer in a mammal comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 0.01 mg to about 20 mg of goserelin, wherein the goserelin is administered over a period of about 28 days to about 3 months.

[0014] Additionally, in another embodiment, the method for the treatment of a cancer in a mammal comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 0.01 mg to about 20 mg of triptorelin, wherein the triptorelin is administered over a period of about 1 month.

[0015] The method for the treatment of a cancer in a mammal can also comprise administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 0.1 μg/day to about 500 μg/day of seocalcitol, such as about 100 μg/day of seocalcitol.

[0016] Also, the method for the treatment of a cancer in a mammal can comprise administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/day to about 300 mg/day of bicalutamide.

[0017] In yet another embodiment, the method for the treatment of a cancer in a mammal can comprise administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/day to about 2000 mg/day of flutamide.

[0018] Moreover, the method for the treatment of a cancer in a mammal can comprise administering an amount of about 50 mg/day to about 2000 mg/day of abiraterone acetate and an amount of about 0.01 mg/day to about 500 mg/day of a glucocorticoid including, but not limited to, hydrocortisone, prednisone or dexamethasone.

[0019] Also described herein are compositions for the treatment of cancer that comprise a combination of a therapeutically effective amount of at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and a therapeutically effective amount of at least one additional anti-cancer agent, such as, but not limited to, mitoxantrone, paclitaxel, docetaxel, leuprolide, goserelin, triptorelin, seocalcitol, bicalutamide, flutamide, or a steroid including, but not limited to, hydrocortisone, prednisone, or dexamethasone.

[0020] Finally, single unit dosage forms comprising abiraterone acetate and a glucocorticoid, optionally with carriers, diluents or excipients, are contemplated. Also, kits comprising at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and an additional anti cancer agent or steroid are contemplated. For example, the kit may include a vial containing abiraterone acetate and another vial containing a glucocorticoid.

Definitions

[0021] As used herein and unless otherwise defined the word "cancer," refers to the growth, division or proliferation of abnormal cells in the body. Cancers that can be treated with the methods and the compositions described herein include, but are not limited to, prostate cancer, breast cancer, adrenal cancer, leukemia, lymphoma, myeloma, Waldenström's macroglobulinemia, monoclonal gammopathy, benign monoclonal gammopathy, heavy chain disease, bone and connective tissue sarcoma, brain tumors, thyroid cancer, pancreatic cancer, pituitary cancer, eye cancer, vaginal cancer, vulvar cancer, cervical cancer, uterine cancer, ovarian cancer, esophageal cancer, stomach cancer, colon cancer, rectal cancer, liver cancer, gallbladder cancer, cholangiocarcinoma, lung cancer, testicular cancer, penal cancer, oral cancer, skin cancer, kidney cancers, Wilms' tumor and bladder cancer.

[0022] As used herein, and unless otherwise defined, the terms "treat," "treating" and "treatment" include the eradication, removal, modification, management or control of a tumor or primary, regional, or metastatic cancer cells or tissue and the minimization or delay of the spread of cancer.

[0023] As used herein, and unless otherwise defined, the term "patient" means an animal, including but not limited to an animal such as a human, monkey, cow, horse, sheep, pig, chicken, turkey, quail, cat, dog, mouse, rat, rabbit, or guinea pig. In one embodiment, the patient is a mammal and in another embodiment the patient is a human. In certain embodiments, the patient can be an adult male or female. In some embodiments, the patient is a male of age about 30 years to about 85 years. In other embodiments, the patient is a female of age about 30 years to about 85 years. In a particular embodiment, the patient has or is susceptible to having (e.g., through genetic or environmental factors) cancer. In a further embodiment, the patient has or is susceptible to having (e.g., through genetic or environmental factors) a tumor. In other embodiments, the patient can be castrated or non-castrated.

[0024] The term "17α-hydroxylase/$C_{17,20}$-lyase inhibitor" as used herein refers to an inhibitor of 17α-hydroxylase/$C_{17,20}$-lyase, (which is an enzyme in testosterone synthesis), an analog thereof, derivative thereof, metabolite thereof or pharmaceutically acceptable salt thereof. Also, unless otherwise noted, reference to a particular 17α-hydroxyla-

se/$C_{17,20}$-lyase inhibitor can include analogs, derivatives, metabolites or pharmaceutically acceptable salts of such particular 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0025] The term "anti-cancer agent" as used herein refers to any therapeutic agent that directly or indirectly kills cancer cells or directly or indirectly prohibits stops or reduces the proliferation of cancer cells. It should be noted that even though throughout this specification and in the claims the phrase "anti-cancer agent" is written as a singular noun, for example; "an anti-cancer agent" or "the anti-cancer agent," the phrase "anti-cancer agent" should not be interpreted as being limited to the inclusion of a single anti-cancer agent.

[0026] As used herein, and unless otherwise defined, the phrase "therapeutically effective amount" when used in connection with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor or therapeutic agent means an amount of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor or therapeutic agent effective for treating a disease or disorder disclosed herein, such as cancer.

[0027] As used herein and unless otherwise defined the phrase "refractory cancer," means cancer that is not responding to an anti-cancer treatment or cancer that is not responding sufficiently to an anti-cancer treatment. Refractory cancer can also include recurring or relapsing cancer.

[0028] As used herein and unless otherwise defined the phrase "refractory patient," means a patient who has refractory cancer.

[0029] As used herein and unless otherwise defined the phrase "relapse cancer," means cancer that was at one time responsive to an anti-cancer treatment but has become no longer responsive to such treatment or is no longer responding sufficiently to such treatment.

[0030] As used herein and unless otherwise defined the phrase "recurring cancer," means cancer that has returned after a patient has been earlier diagnosed with cancer, under gone treatment or had been previously diagnosed as cancer-free.

[0031] As used herein and unless otherwise defined the term "derivative" refers to a chemically modified compound wherein the chemical modification takes place at one or more functional groups of the compound. The derivative may retain or improve the pharmacological activity of the compound from which it is derived.

[0032] As used herein and unless otherwise defined the term "analog" refers to a chemical compound that is structurally similar to another but differs slightly in composition (as in the replacement of one atom by an atom of a different element or in the presence of a particular functional group).

[0033] As used herein and unless otherwise defined the phrase "pharmaceutically acceptable salt" refers to any salt of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor which retains the biological effectiveness of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor. Examples of pharmaceutically acceptable salts include, but are not limited to, acetates, sulfates, pyrosulfates, bisulfates, sulfites, bisulfites, phosphates, monohydrogenphosphates, dihydrogenphosphates, metaphosphates, pyrophosphates, chlorides, bromides, iodides, acetates, propionates, decanoates, caprylates, acrylates, formates, isobutyrates, caproates, heptanoates, propiolates, oxalates, malonates, succinates, suberates, sebacates, fumarates, maleates, butyne-1,4-dioates, hexyne-1,6-dioates, benzoates, chlorobenzoates, methylbenzoates, dinitrobenzoates, hydroxybenzoates, methoxybenzoates, phthalates, sulfonates, xylenesulfonates, phylacetates, phenylpropionates, phenylbutyrates, citrates, lactates, gamma-hydroxybutyrates, glycollates, tartarates, alkanesulfonates (e.g. methane-sulfonate or mesylate), propanesulfonates, naphthalene-1-sulfonates, naphthalene-2-sulfonates, and mandelates. Several of the officially approved salts are listed in Remington: The Science and Practice of Pharmacy, Mack Publ. Co., Easton.

DETAILED DESCRIPTION OF THE INVENTION

[0034] The methods described herein for treating cancer comprise administering to a mammal, preferably a human, a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor in addition to at least one therapeutic agent, such as an anti-cancer agent or steroid, particularly a glucocorticoid. The compositions described herein comprise a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and at least one additional therapeutic agent, such as an anti-cancer agent or steroid, particularly a corticosteroid or glucocorticoid. Other anti-cancer treatments such as, administration of yet another anti-cancer agent, radiotherapy, chemotherapy, photodynamic therapy, surgery or other immunotherapy, can be used with the methods and compositions.

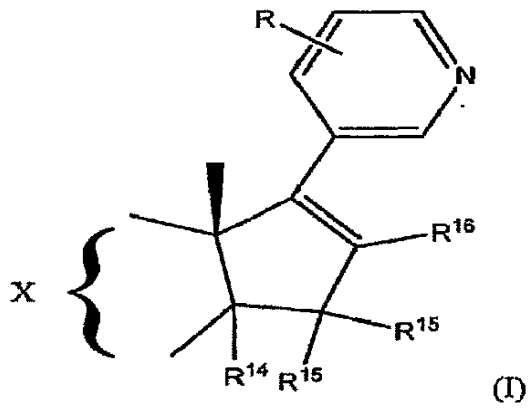
17α-hydroxylase/$C_{17,20}$-lyase Inhibitors

[0035] 17α-hydroxylase/$C_{17,20}$-lyase inhibitors have been shown to be useful in the treatment of cancer, specifically hormone-dependent disorders such as, androgen-dependent and estrogen-dependent disorders like prostate cancer and breast cancer respectively, as described in United States Patent No. 5,604,213 to Barrie *et al.,* which is herein incorporated by reference in its entirety.

[0036] In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be 17-(3-pyridyl)androsta-5,16-dien-3β-ol; 17-(3-pyridyl)androsta-3,5,16-triene; 17-(3-pyridyl)androsta-4,16-dien-3-one; 17-(3-pyridyl)estra-l,3,5[10],16-tetraen-3-ol; 17-(3-pyridyl)-5α-androst-16-en-3a-ol; 17-(3-pyridyl)-5α -androst-16-en-3-one; 17-(3-pyridyl)-androsta-4,16-diene-3,11-dione; 17-(3-pyridyl)-androsta-3,5,16-trien-3-ol; 6α-and 6β-fluoro-17-(3-pyridyl)androsta-4,16-dien-3-

one; 17-(3-pyridyl)androsta-4,16-dien-3,6-dione; 3α-trifluoromethyl-17-(3-pyridyl)androst-16-en-3β-ol or their acid addition salts and 3-esters as well as metabolites, analogs, derivatives or a pharmaceutically acceptable salt thereof.

[0037] In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can have the structure of formula (I):



(I)

wherein X represents the residue of the A, B and C rings of a steroid which can be, without limitation, androstan-3α- or 3β-ol; androst-5-en-3α- or 3β-ol; androst-4-en-3-one; androst-2-ene; androst-4-ene; androst-5-ene; androsta-5,7-dien-3α or 3β-ol; androsta-1,4-dien-3-one; androsta-3,5-diene; androsta-3,5-diene-3-ol; estra-1,3,5[10]-triene; estra-1,3,5 [10]-trien-3-ol; 5α -androstan-3-one; androst-4-ene-3, 11-dione; 6-fluoroandrost-4-ene-3-one; or androstan-4-ene-3,6-dione; each of which, where structurally permissible, can be further derivatized in one or more of the following ways, including, but not limited to, to form 3-esters; to have one or more carbon or carbon ring double bonds in any of the 5,6-, 6,7-, 7,8-, 9,11- and 11,12-positions; as 3-oximes; as 3-methylenes; as 3-carboxylates; as 3-nitriles; as 3-nitros; as 3-desoxy derivatives; to have one or more hydroxy, halo, C_{1-4} -alkyl, trifluoromethyl, C_{1-4} -alkoxy, C_{1-4} -alkanoyloxy, benzoyloxy, oxo, methylene or alkenyl substituents in the A, B, or C-ring; or to be 19-nor;

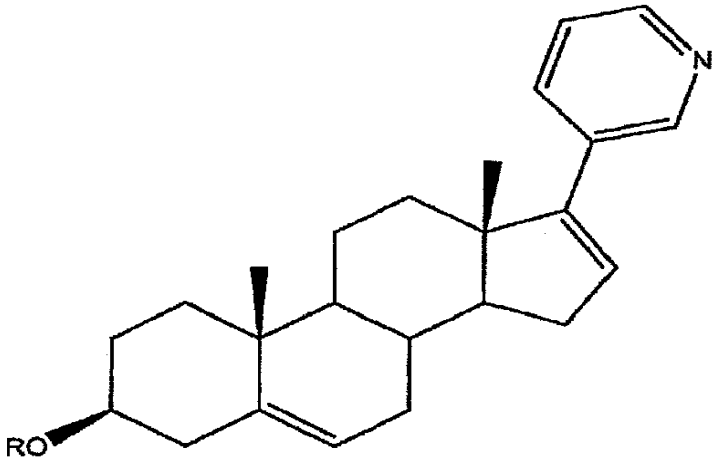
R represents a hydrogen atom or an alkyl group of 1-4 carbon atoms;

R^{14} represents a hydrogen atom, a halogen atom or an alkyl group of 1 to 4 carbon atoms;

each of the R^{15} substituents independently represents a hydrogen atom or an alkyl or alkoxy group of 1-4 carbon atoms, a hydroxy group or an alkylcarbonyloxy group of 2 to 5 carbon atoms or together represent an oxo or methylene group or R^{14} and one of the R^{15} groups together represent a double bond and the other R^{15} group represents a hydrogen atom or an alkyl group of 1 to 4 carbon atoms; and

R^{16} represents a hydrogen atom, halogen atom, or an alkyl group of 1 to 4 carbon atoms, in the form of the free bases or pharmaceutically acceptable acid addition salts, but excluding 3β-acetoxy-17-(3-pyridyl)androsta-5,14,16-triene, 3β, 15α- and 3β,15β-diacetoxy-17-(3-pyridyl)androsta-5,16-diene and 3β-methoxy-17-(3-pyridyl-5α-androst-16-ene. Suitable inhibitors also include metabolites, derivatives, analogs, or pharmaceutically acceptable salts of formula (I).

[0038] In another embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can have the structure of formula (I):

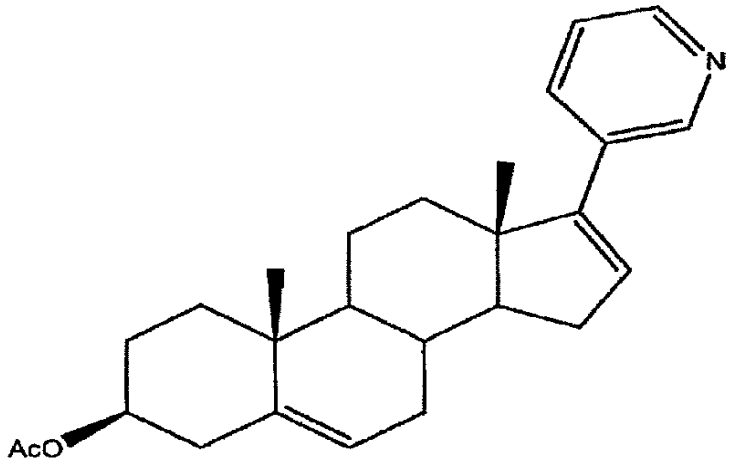


(I)

wherein R represents hydrogen or a lower acyl group having 1 to 4 carbons. Suitable inhibitors also include derivatives, analogs, or pharmaceutically acceptable salts of formula (I).

[0039] In still another embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be a 3β-alkanoyloxy-17-(3-pyridyl) androsta-5, 16-diene in which the alkanoyloxy group has from 2 to 4 carbon atoms.

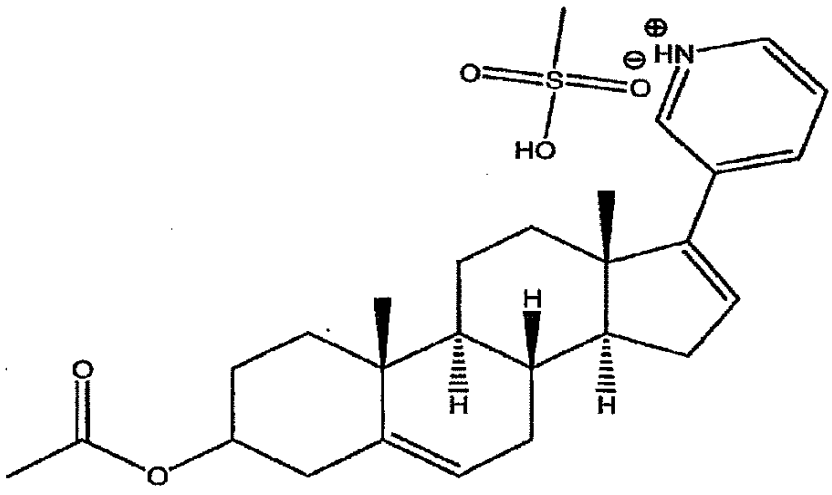
[0040] In a preferred embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises abiraterone acetate or 3β-acetoxy-17-(3-pyridyl)androsta-5,16-diene which has the following structural formula:



(II)

and pharmaceutically acceptable salts thereof.

[0041] Preferred salts of abiraterone acetate and methods of making such salts are also disclosed in United States Provisional Application No. 60/603,559 to Hunt, which is incorporated by reference in its entirety. Preferred salts include, but are not limited to, acetates, citrates, lactates, alkanesulfonates (e.g. methane-sulfonate or mesylate) and tartarates. Of special interest is the abiraterone acetate mesylate salt (*i.e.* 3β-acetoxy-17-(3'-pyridyl)androsta-5,16-diene mesylate salt) which has the following structural formula:



(III)

[0042] The 17α-hydroxylase/$C_{17,20}$-lyase inhibitors can be made according to any method known to one skilled in the art. For example, such inhibitors can be synthesized according to the method disclosed in United States Patent Nos. 5,604,213 and 5,618,807 to Barrie et al., herein incorporated by reference. Another method of making 17α-hydroxylase/$C_{17,20}$-lyase inhibitors is disclosed in United States provisional application 60/603,558 to Bury, herein incorporated by reference.

[0043] The amount of 17α-hydroxylase/$C_{17,20}$-lyase inhibitor administered to a mammal having cancer is an amount that is sufficient to treat the cancer, whether the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor is administered alone or in

combination with an additional anti-cancer treatment, such as an additional anti-cancer agent.

Additional Therapeutic Agents

[0044] Suitable compounds that can be used in addition to 17α-hydroxylase/$C_{17,20}$-lyase inhibitors as an anti-cancer agent include, but are not limited to, hormone ablation agents, anti-androgen agents, differentiating agents, anti-neoplastic agents, kinase inhibitors, anti-metabolite agents, alkylating agents, antibiotic agents, immunological agents, interferon-type agents, intercalating agents, growth factor inhibitors, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response modifiers, mitotic inhibitors, matrix metalloprotease inhibitors, genetic therapeutics, and anti-androgens. The amount of the additional anti-cancer agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor. Below are lists of examples of some of the above classes of anti-cancer agents. The examples are not all inclusive and are for purposes of illustration and not for purposes of limitation. Many of the examples below could be listed in multiple classes of anti-cancer agents and are not restricted in any way to the class in which they are listed in.

[0045] Suitable hormonal ablation agents include, but are not limited to, androgen ablation agents and estrogen ablation agents. In preferred embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor is administered with a hormonal ablation agent, such as deslorelin, leuprolide, goserelin or triptorelin. Even though throughout this specification and in the claims the phrase "hormonal ablation agent" is written as a singular noun, for example; "a hormonal ablation agent" or "the hormonal ablation agent," the phrase "hormonal ablation agent" should not be interpreted as being limited to the inclusion of a single hormonal ablation agent. The amount of the hormonal ablation agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0046] Suitable anti-androgen agents include but are not limited to bicalutamide, flutamide and nilutamide. The amount of the anti-androgen agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0047] In another embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor may be administered with a differentiating agent. Suitable differentiating agents include, but are not limited to, polyamine inhibitors; vitamin D and its analogs, such as, calcitriol, doxercalciferol and seocalcitol; metabolites of vitamin A, such as, ATRA, retinoic acid, retinoids; short-chain fatty acids; phenylbutyrate; and nonsteroidal anti-inflammatory agents. The amount of the differentiating agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0048] In another preferred embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor may be administered with an anti-neoplastic agent, including, but not limited to, tubulin interacting agents, topoisomerase inhibitors and agents, acitretin, alstonine, amonafide, amphethinile, amsacrine, ankinomycin, anti-neoplaston, aphidicolin glycinate, asparaginase, baccharin, batracylin, benfluron, benzotript, bromofosfamide, caracemide, carmethizole hydrochloride, chlorsulfaquinoxalone, clanfenur, claviridenone, crisnatol, curaderm, cytarabine, cytocytin, dacarbazine, datelliptinium, dihaematoporphyrin ether, dihydrolenperone, dinaline, distamycin, docetaxel, elliprabin, elliptinium acetate, epothilones, ergotamine, etoposide, etretinate, fenretinide, gallium nitrate, genkwadaphnin, hexadecylphosphocholine, homoharringtonine, hydroxyurea, ilmofosine, isoglutamine, isotretinoin, leukoregulin, lonidamine, merbarone, merocyanlne derivatives, methylanilinoacridine, minactivin, mitonafide, mitoquidone, mitoxantrone, mopidamol, motretinide, N-(retinoyl)amino acids, N-acylated-dehydroatanines, nafazatrom, nocodazole derivative, ocreotide, oquizanocine, paclitaxel, pancratistatin, pazelliptine, piroxantrone, polyhaematoporphyrin, polypreic acid, probimane, procarbazine, proglumide, razoxane, retelliptine, spatol, spirocyclopropane derivatives, spirogermanium, strypoldinone, superoxide dismutase, teniposide, thaliblastine, tocotrienol, topotecan, ukrain, vinblastine sulfate, vincristine, vindesine, vinestramide, vinorelbine, vintriptol, vinzolidine, and withanolides. The amount of the anti-neoplastic agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0049] The 17α-hydroxylase/$C_{17,20}$-lyase inhibitors may also be used with a kinase inhibitor including p38 inhibitors and CDK inhibitors, TNF inhibitors, metallomatrix proteases inhibitors (MMP), COX-2 inhibitors including celecoxib, rofecoxib, parecoxib, valdecoxib, and etoricoxib, SOD mimics or $\alpha_v\beta_3$ inhibitors. The amount of the kinase inhibitor administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0050] In another embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor may be administered with an anti-metabolite agent. Suitable anti-metabolite agents may be selected from, but not limited to, 5-FU-fibrinogen, acanthifolic acid, aminothiadiazole, brequinar sodium, carmofur, cyclopentyl cytosine, cytarabine phosphate stearate, cytarabine conjugates, dezaguanine, dideoxycytidine, dideoxyguanosine, didox, doxifluridine, fazarabine, floxuridine, fludarabine phosphate, 5-fluorouracil, N-(2'-furanidyl)-5-fluorouracil, isopropyl pyrrolizine, methobenzaprim, methotrexate, norspermidine, pentostatin, piritrexim, plicamycin, thioguanine, tiazofurin, trimetrexate, tyrosine kinase inhibitors, and uricytin. The amount

of the anti-metabolite agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0051] In another embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor may be administered with an alkylating agent. Suitable alkylating agents may be selected from, but not limited to, aldo-phosphamide analogues, altretamine, anaxirone, bestrabucil, budotitane, carboplatin, carmustine, chlorambucil, cisplatin, cyclophosphamide, cyplatate, diphenylspiromustine, diplatinum cytostatic, elmustine, estramustine phosphate sodium, fotemustine, hepsul-fam, ifosfamide, iproplatin, lomustine, mafosfamide, mitolactol, oxaliplatin, prednimustine, ranimustine, semustine, spiromustine, tauromustine, temozolomide, teroxirone, tetraplatin and trimelamol. The amount of the alkylating agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer, whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0052] In another preferred embodiment, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor may be administered with an antibiotic agent. Suitable antibiotic agents may be selected from, but not limited to, aclarubicin, actinomycin D, actinoplanone, adriamycin, aeroplysinin derivative, amrubicin, anthracycline, azino-mycin-A, bisucaberin, bleomycin sulfate, bryostatin-1, calichemycin, chromoximycin, dactinomycin, daunorubicin, ditrisarubicin B, dexamethasone, doxorubicin, doxorubicin-fibrinogen, elsamicin-A, epirubicin, erbstatin, esorubicin, esperamicin-Al, esperamicin-Alb, fostriecin, glidobactin, gregatin-A, grincamycin, herbimycin, corticosteroids such as hydrocortisone, idarubicin, illudins, kazusamycin, kesarirhodins, menogaril, mitomycin, neoenactin, oxalysine, oxaunomycin, peplomycin, pilatin, pirarubicin, porothramycin, prednisone, prednisolone, pyrindanycin A, rapamycin, rhizoxin, rodorubicin, sibanomicin, siwenmycin, sorangicin-A, sparsomycin, talisomycin, terpentecin, thrazine, tricrozarin A, and zorubicin. The amount of the antibiotic agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0053] Alternatively the 17α-hydroxylase/$C_{17,20}$-lyase inhibitors may also be used with other anti-cancer agents, including but not limited to, acemannan, aclarubicin, aldesleukin, alemtuzumab, alitretinoin, altretamine, amifostine, amsacrine, anagrelide, anastrozole, ancestim, bexarotene, broxuridine, capecitabine, celmoleukin, cetrorelix, cladribine, clotrimazole, daclizumab, dexrazoxane, dilazep, docosanol, doxifluridine, bromocriptine, carmustine, cytarabine, diclofenac, edelfosine, edrecolomab, eflornithine, emitefur, exemestane, exisulind, fadrozole, filgrastim, finasteride, fludarabine phosphate, formestane, fotemustine, gallium nitrate, gemcitabine, glycopine, heptaplatin, ibandronic acid, imiquimod, iobenguane, irinotecan, irsogladine, lanreotide, leflunomide, lenograstim, lentinan sulfate, letrozole, liarozole, lobaplatin, lonidamine, masoprocol, melarsoprol, metoclopramide, mifepristone, miltefosine, mirimostim, mitoguazone, mitolactol, molgramostim, nafarelin, nartograstim, nedaplatin, nilutamide, noscapine, oprelvekin, osaterone, oxaliplatin, pamidronic acid, pegaspargase, pentosan polysulfate sodium, pentostatin, picibanit, pirarubicin, porfimer sodium, raloxifene, raltitrexed, rasburicase, rituximab, romurtide, sargramostim, sizofiran, sobuzoxane, sonermin, suramin, tasonermin, tazarotene, tegafur, temoporfin, temozolomide, teniposide, tetrachlorodecaoxide, thalidomide, thymalfasin, thyrotropin alfa, topotecan, toremifene, trastuzumab, treosulfan, tretinoin, trilostane, trimetrexate, ubenimex, valrubicin, verteporfin, vinorelbine. The amount of the anti-cancer agent administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0054] The 17α-hydroxylase/$C_{17,20}$-lyase inhibitors may also be administered or combined with steroids, such as corticosteroids or glucocorticoids. The 17α-hydroxylase/$C_{17,20}$-lyase inhibitors and the steroid may be administered in the same or in different compositions. Non-limiting examples of suitable steroids include hydrocortisone, prednisone, or dexamethasone. The amount of the steroid administered to a mammal having cancer is an amount that is sufficient to treat the cancer whether administered alone or in combination with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0055] In one embodiment, provided herein are methods and compositions comprising both abiraterone acetate and a steroid particularly a corticosteroid, or more particularly a glucocorticoid. Steroids within the scope of the disclosure include, but are not limited to, (1) hydrocortisone (cortisol; cyprionate (*e.g.,* CORTEF), oral; sodium phosphate injection (HYDROCORTONE PHOSPHATE); sodium succinate (e.g., A-HYDROCORT, Solu-CORTEF); cortisone acetate oral or injection forms, etc.), (2) dexamethasone (e.g., Decadron, oral; Decadron-LA injection, etc.), (3) prednisolone (e.g., Delta-CORTEF, prednisolone acetate (ECONOPRED), prednisolone sodium phosphate (HYDELTRASOL), prednisolone tebutate (HYDELTRA-TBA, etc.)), or (4) prednisone (e.g., DELTASONE, etc.) and combinations thereof. See, e.g., GOODMAN & GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, 10TH EDITION 2001.

[0056] In a specific embodiment, single unit solid oral dosage forms which comprise an amount from about 50 mg to about 300 mg of abiraterone acetate and an amount from about 0.5 mg to about 3.0 mg of a steroid, e.g., glucocorticoid in a single composition, optionally with excipients, carriers, diluents, etc. is contemplated. For instance, the single unit dosage form can comprise about 250 mg of abiraterone acetate and about 1.0 mg, 1.25 mg, 1.5 mg, or 2.0 mg of a steroid, such as but not limited to corticosteroids or glucocorticoids.

Administration of the 17α-hydroxylase/$C_{17,20}$-lyase Inhibitor and an Additional Therapeutic Agent

[0057] The 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the additional therapeutic agent, such as an anti-cancer agent or a steroid can be administered by any method known to one skilled in the art. In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the additional therapeutic agent can be in separate compositions prior to administration. In the alternative, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the additional therapeutic agent can be combined into a single composition for administration.

[0058] The 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the additional therapeutic agent can be administered sequentially or simultaneously. If administered sequentially, the order of administration is flexible. For instance, 17α-hydroxylase/$C_{17,20}$-lyase inhibitor acetate can be administered prior to administration of the additional therapeutic agent. Alternatively, administration of the additional therapeutic agent can precede administration of 17α-hydroxylase/$C_{17,20}$-lyase inhibitor.

[0059] Whether they are administered as separate compositions or in one composition, each composition is preferably pharmaceutically suitable for administration. Moreover, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the therapeutic agent, if administered separately, can be administered by the same or different modes of administration. Examples of modes of administration include parenteral (e.g., subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, intradermal, intraperitoneal, intraportal, intra-arterial, intrathecal, transmucosal, intra-articular, and intrapleural,), transdermal (e.g., topical), epidural, and mucosal (e.g., intranasal) injection or infusion, as well as oral, inhalation, pulmonary, and rectal administration. In specific embodiments, both are oral.

[0060] For example, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be administered transdermally and the additional therapeutic agent can be administered parenterally. Alternatively, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be administered orally, such as in a tablet, caplet or capsule, while the additional therapeutic agent can be administered intravenously. Such intravenous administered therapeutic agents include, but are not limited to, docetaxel injections, such as Taxotere®; paclitaxel injections, such as Paclitaxel® and mitoxantrone injections, such as Novantrone®. Also, the additional therapeutic agent can be in the form of depots or implants such as leuprolide depots and implants, e.g. Viadur® and Lupron Depot®; triptorelin depots, e.g. Trelstar®; goserelin implants, e.g. Zoladex®.

[0061] The suitable daily dosage of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor depends upon a number of factors, including, the nature of the severity of the condition to be treated, the particular inhibitor, the route of administration and the age, weight, and response of the individual patient. Suitable daily dosages of 17α-hydroxylase/$C_{17,20}$-lyase inhibitors can generally range from about 0.0001 mg/kg/day to about 1000 mg/kg/day, or from about 0.001 mg/kg/day to about 200 mg/kg/day, or from about 0.01 mg/kg/day to about 200 mg/kg/day, or from about 0.01 mg/kg/day to about 100 mg/kg/day in single or multiple doses.

[0062] In some embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be administered in an amount from about 0.004 mg/day to about 5,000 mg/day, or from about 0.04 mg/day to about 3,000 mg/day, or from about 0.4 mg/day to about 1500 mg/day. In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor can be administered in an amount from about 0.1 mg/day to about 2000 mg/day or from about 1 mg/day to about 2000 mg/day or from about 50 mg/day to about 2000 mg/day or from about 100 mg/day to about 1500 mg/day or from about 5 mg/day to about 1,000 mg/day or from about 5 mg/day to about 900 mg/day or from about 10 mg/day to about 800 mg/day or from about 15 mg/day to about 700 mg/day or from about 20 mg/day to about 600 mg/day or from about 25 mg/day to about 500 mg/day in single or multiple doses.

[0063] In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor is co-administered with an additional anti-cancer agent such as mitoxantrone, paclitaxel or docetaxel. For example, a method for the treatment of a cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of mitoxantrone. For example, the abiraterone acetate can be administered in an amount of about 0.01 mg/kg/day to about 100 mg/kg/day and the mitoxantrone can be administered in an amount of about 0.1 mg/m^2 to about 20 mg/m^2. Preferably, the mitoxantrone is administered over a period of between about 10 to about 20 minutes once every 21 days.

[0064] Also, a method for the treatment of a cancer in a mammal can comprise administering an amount of abiraterone acetate and an amount of paclitaxel. In one embodiment, the abiraterone acetate can be administered in an amount of about 0.01 mg/kg/day to about 100 mg/kg/day and the paclitaxel can be administered in the amount of about 1 mg/m^2 to about 175 mg/m^2. Preferably, the paclitaxel is administered over a period of between about 2 to about 5 hours once every three months.

[0065] Additionally, a method for the treatment of a cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of docetaxel. For example, the abiraterone acetate can be administered in an amount of about 0.01 mg/kg/day to about 100 mg/kg/day and the docetaxel can be administered in an amount of about 1 mg/m^2 to about 100 mg/m^2. Preferably, the docetaxel is administered over a period of between about 1 to about 2 hours once every three weeks.

[0066] In certain embodiments, the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor is administered along with an anti-cancer agent that comprises a hormonal ablation agent, including, but not limited to, leuprolide, goserelin, or triptorelin. For

example, one method for the treatment of a cancer in a mammal also comprises administering an amount of abiraterone acetate and an amount of leuprolide. The amount of abiraterone acetate can be about 0.01 mg/kg/day to about 100 mg/kg/day and the amount of leuprolide can be about 0.01 mg to about 200 mg over a period of about 3 days to about 12 months. Preferably, the leuprolide is administered in the amount of about 3.6 mg of leuprolide over a period of about 3 days to about 12 months.

[0067] Additionally, the methods for the treatment of cancer in a mammal include administering an amount of abiraterone acetate and an amount of goserelin. For example, the amount of abiraterone acetate can be about 0.01 mg/kg/day to about 100 mg/kg/day and the amount of goserelin can be about 0.01 mg to about 20 mg over a period of about 28 days to about 3 months. Preferably, the goserelin is administered in the amount of about 3.6 mg to about 10.8 mg over a period of about 28 days to about 3 months.

[0068] In certain embodiments the methods for the treatment of cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of triptorelin. For example, the amount of abiraterone acetate can be about 0.01 mg/kg/day to about 100 mg/kg/day and the amount of triptorelin can be about 0.01 mg to about 20 mg, over a period of about 1 month, preferably the triptorelin is administered in the amount of about 3.75 mg over a period of about 1 month.

[0069] Also, in one embodiment, the method for the treatment of a cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of seocalcitol. For instance, the method involves administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 0.1 μg/day to about 500 μg/day of seocalcitol, such as about 100 μg/day of seocalcitol.

[0070] In another embodiment, the method for the treatment of a cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of bicalutamide. For instance, the method involves administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/day to about 300 mg/day of bicalutamide.

[0071] In yet another embodiment, the method for the treatment of a cancer in a mammal comprises administering an amount of abiraterone acetate and an amount of flutamide. For example, the method comprises administering an amount of about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and an amount of about 1 mg/day to about 2000 mg/day of flutamide.

[0072] Moreover, the method for the treatment of a cancer in a mammal can comprise administering an amount of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor such as abiraterone acetate and an amount of a glucocorticoid including, but not limited to, hydrocortisone, prednisone or dexamethasone. For example, the method can comprise administering an amount of about 50 mg/day to about 2000 mg/day of abiraterone acetate and an amount of about 0.01 mg/day to about 500 mg/day of hydrocortisone. In other instances, the method can comprise administering an amount of about 500 mg/day to about 1500 mg/day of abiraterone acetate and an amount of about 10 mg/day to about 250 mg/day of hydrocortisone.

[0073] The method for the treatment of a cancer can also comprise administering an amount of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate, and an amount of a glucocorticoid, such as prednisone. For example, the method can comprise administering an amount of about 50 mg/day to about 2000 mg/day of abiraterone acetate and an amount of about 0.01 mg/day to about 500 mg/day of prednisone. Also, the method can comprise administering an amount of about 500 mg/day to about 1500 mg/day of abiraterone acetate and an amount of about 10 mg/day to about 250 mg/day of prednisone.

[0074] In addition, the method for the treatment of a cancer can also comprise administering an amount of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate, and an amount of a glucocorticoid, such as dexamethasone. For example, the method can comprise administering an amount of about 50 mg/day to about 2000 mg/day of abiraterone acetate and an amount of about 0.01 mg/day to about 500 mg/day of dexamethasone. Also, the method can comprise administering an amount of about 500 mg/day to about 1500 mg/day of abiraterone acetate and an amount of about 0.5 mg/day to about 25 mg/day of dexamethasone.

Compositions Containing a 17α-hydroxylase/$C_{17,20}$-lyase Inhibitor and an Additional Therapeutic Agent

[0075] In certain embodiments, the compositions can contain a combination of a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, preferably abiraterone acetate, and any of the therapeutic agents recited above. Whether the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and the additional therapeutic agent are administered in separate compositions or as a single composition, the compositions can take various forms. For example, the compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders or sustained-release formulations, depending on the intended route of administration.

[0076] For topical or transdermal administration, the compositions can be formulated as solutions, gels, ointments, creams, suspensions or salves.

[0077] For oral administration, the compositions may be formulated as tablets, pills, dragees, troches, capsules, liquids,

gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated.

[0078] The composition may also be formulated in rectal or vaginal compositions such as suppositories or retention enemas that contain conventional suppository bases such as cocoa butter or other glycerides.

[0079] In addition to the formulations described previously, the composition may also be formulated as a depot preparation. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the therapeutic agents may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

[0080] Additionally, the composition may be delivered using a sustained-release system, such as semi-permeable matrices of solid polymers containing the composition. Various forms of sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature can release the composition over a period of hours, days, weeks, months. For example a sustained release capsule can release the compositions over a period of 100 days or longer. Depending on the chemical nature and the biological stability of the composition, additional strategies for stabilization may be employed.

[0081] The compositions can further comprise a pharmaceutically acceptable carrier. The term "carrier" refers to a diluent, adjuvant (e.g., Freund's adjuvant (complete and incomplete)), excipient, or vehicle with which the therapeutic is administered.

[0082] For parenteral administrations, the composition can comprise one or more of the following carriers: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerin, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The parenteral preparation can be enclosed in ampules, disposable syringes or multiple dose vials made of glass or plastic.

[0083] For oral solid formulations suitable carriers include fillers such as sugars, e.g., lactose, sucrose, mannitol and sorbitol; cellulose preparations such as maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, fats and oils; granulating agents; and binding agents such as microcrystalline cellulose, gum tragacanth or gelatin; disintegrating agents, such as cross-linked polyvinylpyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate, Primogel, or corn starch; lubricants, such as magnesium stearate or Sterotes; glidants, such as colloidal silicon dioxide; a sweetening agent, such as sucrose or saccharin; or flavoring agents, such as peppermint, methyl salicylate, or orange flavoring. If desired, solid dosage forms may be sugar-coated or enteric-coated using standard techniques.

[0084] For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy injectability with a syringe. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars; polyalcohols such as mannitol, sorbitol; sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

[0085] Also for intravenous administration, the compositions may be formulated in solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. The solution may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. In a preferred embodiment, the compositions are formulated in sterile solutions.

[0086] For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories.

[0087] For administration by inhalation, the compositions may be formulated as an aerosol spray from pressurized packs or a nebulizer, with the use of a suitable propellant, *e.g.,* dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol, the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the composition and a suitable powder base such as lactose or starch.

[0088] The pharmaceutical compositions may be manufactured by means of conventional mixing, dissolving, granu-

lating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes.

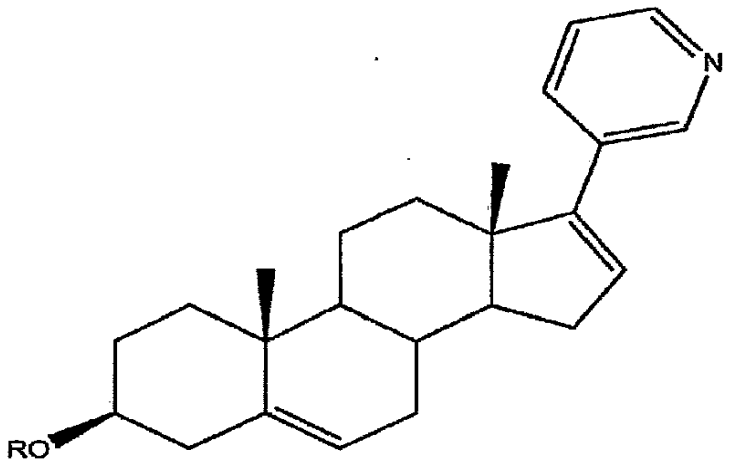
[0089] One example of a composition comprising a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and an additional therapeutic agent is an oral composition or composition suitable for oral administration comprising abiraterone acetate in combination with a steroid. For example, the oral composition can be a solid dosage form such as a pill, a tablet or a capsule. The oral composition can comprise about 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, 450 mg, 500 mg, 550 mg, 600 mg, 650 mg, 700 mg, 750 mg, 800 mg, 850 mg, 900 mg, 950 mg, or 1000 mg of abiraterone acetate. The oral composition can comprises about 0.25 mg, 0.5 mg, 0.75 mg, 1.0 mg, 1.25 mg, 1.5 mg, 1.75 mg, 2.0 mg, 2.25 mg, 2.5 mg, 2.75 mg, 3.0 mg, 3.25 mg, 3.5 mg, 3.75 mg, 4.0 mg, 4.25 mg, 4.5 mg, 4.75 mg, 5.0 mg, 7.5 mg, 10 mg, 20 mg, 30 mg, 40 mg or 50 mg of a steroid, such as a glucocorticoid.

[0090] In one embodiment, the oral composition can comprise about 50 mg to about 500 mg of abiraterone acetate and an amount of about 0.25 mg to about 3.5 mg of the steroid, such as hydrocortisone, prednisone or dexamethasone. In other instances, the composition can comprise about 50 mg to about 300 mg of abiraterone acetate and an amount of about 1.0 mg to about 2.5 mg of the steroid, such as hydrocortisone, prednisone or dexamethasone. In another embodiment the composition can comprise about 50 mg to about 300 mg of abiraterone acetate and about 0.5 mg to about 3.0 mg of a steroid. For example, the oral composition can be a tablet containing 250 mg of abiraterone acetate; 1.25 mg or 2.0 mg of a steroid, such as hydrocortisone, prednisone or dexamethasone; and one or more carriers, excipients, diluents or additional ingredients. Additionally, the oral composition can be a capsule containing 250 mg of abiraterone acetate; 1.25 mg or 2.0 mg of a steroid, such as hydrocortisone, prednisone or dexamethasone; and one or more carriers, excipients, diluents or additional ingredients.

[0091] The description contained herein is for purposes of illustration and not for purposes of limitation. The methods and compositions described herein can comprise any feature described herein either alone or in combination with any other feature(s) described herein. Changes and modifications may be made to the embodiments of the description. Furthermore, obvious changes, modifications or variations will occur to those skilled in the art. Also, all references cited above are incorporated herein, in their entirety, for all purposes related to this disclosure.

The invention also encompasses the following embodiments.

1. A method for the treatment of a cancer in a mammal comprising administering a therapeutically effective amount of at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor and a therapeutically effective amount of at least one additional therapeutic agent to a patient having a cancer; wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises a compound of the formula (I) or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

2. The method of embodiment 1, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises abiraterone acetate or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof.

3. The method of embodiment 2, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises the mesylate salt of abiraterone acetate.

4. The method of embodiment 1, wherein the therapeutically effective amount of the 17α-hydroxylase/$C_{17,20}$-lyase

inhibitor comprises about 50 mg/day to about 2000 mg/day.

5. The method of embodiment 1, wherein the additional therapeutic agent comprises an anti-neoplastic agent, an alkylating agent, an anti-metabolite agent, an antibiotic agent, a hormonal ablation agent, an androgen ablation agent, an anti-androgen agent, or a steroid.

6. The method of embodiment 1, wherein the additional therapeutic agent comprises mitoxantrone, paclitaxel, docetaxel, leuprolide, goserelin, triptorelin, seocalcitol, bicalutamide, flutamide, hydrocortisone, prednisone or dexamethasone.

7. The method of embodiment 1, wherein the 17-hydroxylase/$C_{17,20}$ lyase inhibitor and the additional therapeutic agent are administered to the mammal in a single composition comprising the 17-hydroxylase/$C_{17,20}$ lyase inhibitor and the additional therapeutic agent.

8. The method of embodiment 1, wherein the 17-hydroxylase/$C_{17,20}$ lyase inhibitor and the additional therapeutic agent are administered separately to the mammal.

9. The method of embodiment 1, wherein the cancer is prostate cancer or breast cancer.

10. The method of embodiment 1, wherein the therapeutically effective amount of the at least one 17-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100. mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 0.1 mg/m^2 to about 20 mg/m^2 of mitoxantrone.

11. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 1 mg/m^2 to about 175 mg/m^2 of paclitaxel.

12. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 1 mg/m^2 to about 100 mg/m^2 of docetaxel.

13. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 0.01 to about 200 mg of leuprolide over a period of about 3 days to about 12 months.

14. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxy/ase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 20 mg of goserelin over a period of about 28 days to about 3 months.

15. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 0.01 mg to about 20 mg of triptorelin over a period of about 1 month.

16. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 0.1 μg/day to about 500 μg/day of seocalcitol.

17. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 1 mg/day to about 300 mg/day of bicalcutamide.

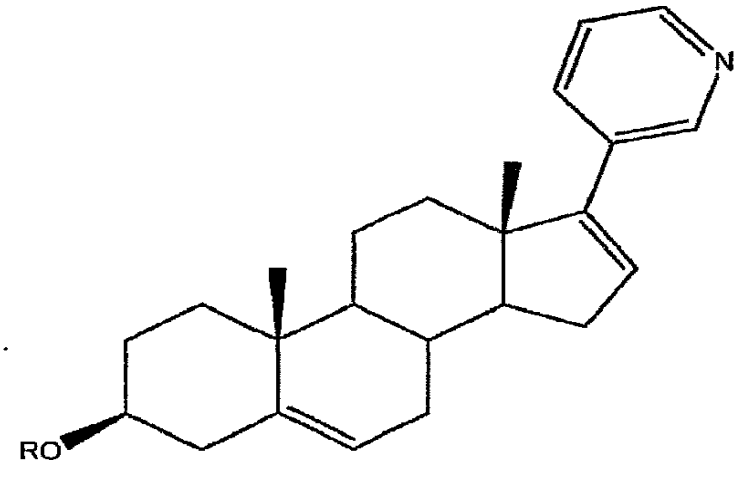
18. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 0.01 mg/kg/day to about 100 mg/kg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 1 mg/day to about 2000 mg/day flutamide.

19. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg/day to about 2000 mg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 10 mg/day to about 250 mg/day of hydrocortisone.

20. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg/day to about 2000 mg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 10 mg/day to about 250 mg/day prednisone.

21. The method of embodiment 1 wherein the therapeutically effective amount of the at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg/day to about 2000 mg/day of abiraterone acetate and the therapeutically effective amount of the at least one additional therapeutic agent comprises about 0.5 mg/day to about 25 mg/day dexamethasone.

22. A method for treating a patient having a refractory prostate or breast cancer who is currently receiving at least one treatment for cancer, the method comprising administering a therapeutically effective amount of at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor in addition to the at least one treatment the patient is currently receiving, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises a compound of the formula (I) or an analog, a derivative, a metabolite or pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

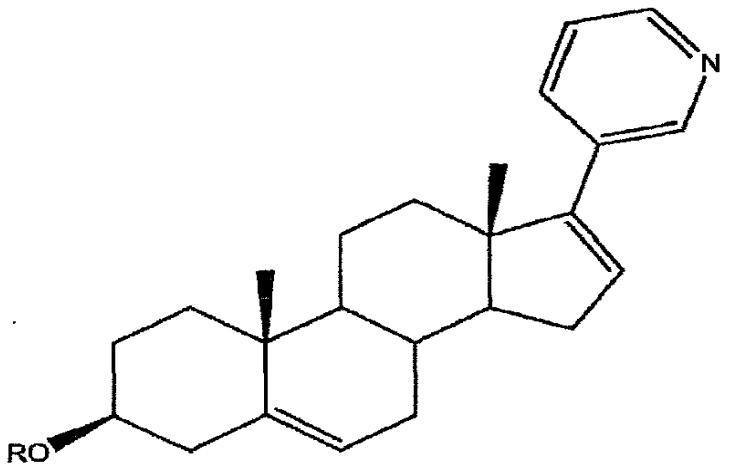
23. The method of embodiment 22, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises abiraterone acetate or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof.

24. The method of embodiment 23, wherein the 17α-hydroxylasc/$C_{17,20}$-lyase inhibitor comprises the mesylate salt of abiraterone acetate.

25. The method of embodiment 22, wherein the therapeutically effective amount of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg/day to about 2000 mg/day.

26. The method of embodiment 22, wherein the treatment for cancer comprises the administration of an anti-cancer agent, chemotherapy, radiation or surgery.

27. A pharmaceutical composition for the treatment of a cancer in a mammal comprising a therapeutically effective amount of at least one 17α-hydroxylase/$C_{17,20}$-lyase inhibitor; and at least one additional therapeutic agent; wherein the 17α-hydroxytase/$C/_{17,20}$-lyase inhibitor comprises a compound of the formula (I) or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

28. The composition of embodiment 27, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises abiraterone acetate or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof.

29. The composition of embodiment 28, wherein the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises the mesylate salt of abiraterone acetate.

30. The composition of embodiment 27, wherein the therapeutically effective amount of the 17α-hydroxylase/$C_{17,20}$-lyase inhibitor comprises about 50 mg to about 500 mg.

31. The composition of embodiment 27, wherein the additional therapeutic agent comprises mitoxantrone, paclitaxel, docetaxel, leuprolide, goserelin, triptorelin, seocalcitol, bicalutamide, flutamide, hydrocortisone, prednisone or dexamethasone.

32. A pharmaceutical composition for the treatment of a cancer in a mammal comprising a therapeutically effective amount of abiraterone acetate; and a therapeutically effective amount of a steroid, wherein the composition is suitable for oral administration.

33. The composition of embodiment 32 wherein the composition is a solid dosage form.

34. The composition of embodiment 32, wherein the composition comprises about 50 mg to about 500 mg of abiraterone acetate, and about 0.25 mg to about 3.5 mg of the steroid.

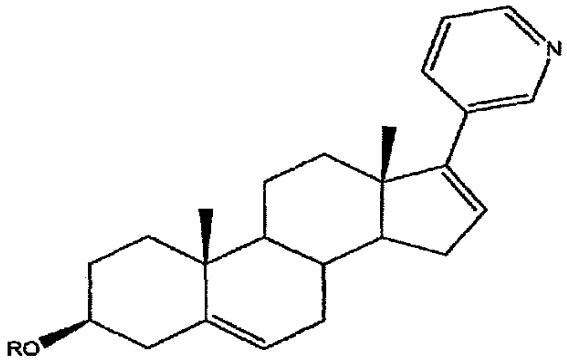
35. The composition of embodiment 32, wherein the steroid comprises hydrocortisone, prednisone, or dexamethasone.

36. The composition of embodiment 32, wherein the composition is in the form of a pill, tablet or capsule.

Claims

1. A therapeutic agent for use in a method of treating cancer, said method comprising administering the therapeutic agent in combination with a therapeutically effective amount of at least one 17α-hydroxylase/$C_{17\text{-}20}$-lyase inhibitor, wherein the 17α-hydroxylase/$C_{17\text{-}20}$-lyase inhibitor comprises a compound of the formula (I) or an analog, a deriv-

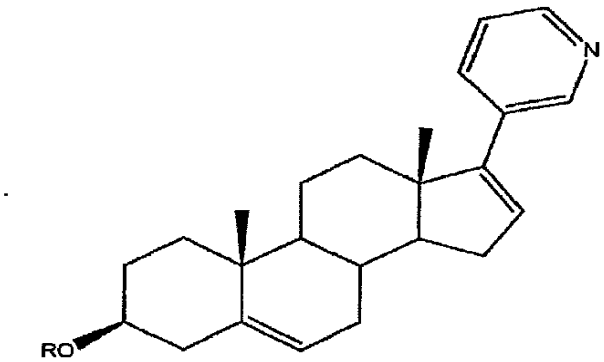
ative, a metabolite or a pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

2. A 17α-hydroxylase/C_{17-20}-lyase inhibitor for use in a method of treating cancer, said method comprising administering the 17α-hydroxylase/C_{17-20}-lyase inhibitor in combination with an additional therapeutic agent, wherein the 17α-hydroxylase/C_{17-20}-lyase inhibitor comprises a compound of the formula (I) or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

3. The therapeutic agent as claimed in claim 1 or the 17α-hydroxylase/C_{17-20}-lyase inhibitor as claimed in claim 2, wherein the 17α-hydroxylase/C_{17-20}-lyase inhibitor comprises abiraterone acetate or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof, optionally, wherein the the 17α-hydroxylase/C_{17-20}-lyase inhibitor comprises the mesylate salt of abiraterone acetate.

4. The therapeutic agent as claimed in claim 1 or the 17α-hydroxylase/C_{17-20}-lyase inhibitor as claimed in claim 2, wherein the therapeutically effective amount of the 17α-hydroxylase/C_{17-20}-lyase inhibitor comprises about 50 mg/day to about 2000 mg/day.

5. The therapeutic agent or the 17α-hydroxylase/C_{17-20}-lyase inhibitor as claimed in any one of claims 1 to 4, wherein the therapeutic agent is a steroid, a corticosteroid or a glucocorticoid.

6. The therapeutic agent or the 17α-hydroxylase/C_{17-20}-lyase inhibitor as claimed in claim 5, wherein the therapeutic agent is selected from the group consisting of hydrocortisone, dexamethasone, prednisolone, prednisone and combinations thereof.

7. The therapeutic agent or the 17α-hydroxylase/C_{17-20}-lyase inhibitor as claimed in claim 6, wherein the therapeutic agent is prednisolone or predinsone.

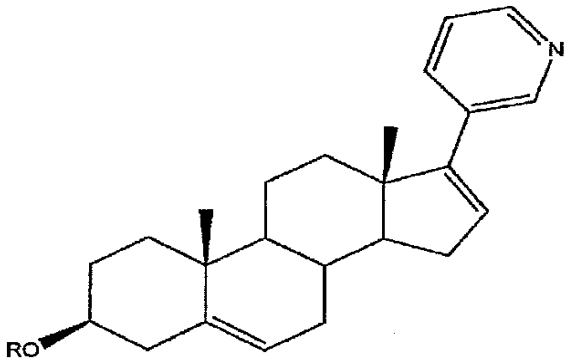
8. The therapeutic agent or the 17α-hydroxylase/C_{17-20}-lyase inhibitor as claimed in any one of claims 1 to 7, wherein the therapeutic agent and the 17α-hydroxylase/C_{17-20}-lyase inhibitor are administered in a single composition.

9. The therapeutic agent or the 17α-hydroxylase/C_{17-20}-lyase inhibitor as claimed in any one of claims 1 to 7, wherein the therapeutic agent and the 17α-hydroxylase/C_{17-20}-lyase inhibitor are administered separately to the mammal.

10. The therapeutic agent or the 17α-hydroxylase/C_{17-20}-lyase inhibitor as claimed in any one of claims 1 to 9, wherein the cancer is prostate cancer or breast cancer.

11. The therapeutic agent as claimed in claim 1 or the 17α-hydroxylase/C_{17-20}-lyase inhibitor as claimed in claim 2, wherein the therapeutically effective amount of the 17α-hydroxylase/C_{17-20}-lyase inhibitor comprises 50 mg/day to 2000 mg/day of abiraterone acetate and the therapeutically effective amount of the therapeutic agent comprises about 10 mg/day to about 250 mg/day prednisone.

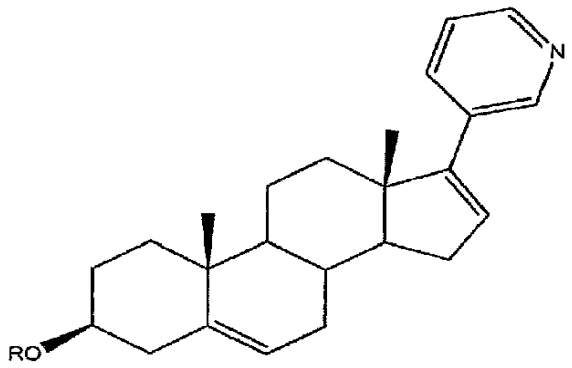
12. A pharmaceutical composition for use in a method of treating cancer comprising a therapeutically effective amount of 17a-hydroxylase/C_{17-20}-lyase inhibitor and an additional therapeutic agent, wherein the 17α-hydroxylase/C_{17-20}-lyase inhibitor comprises a compound of the formula (I) or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

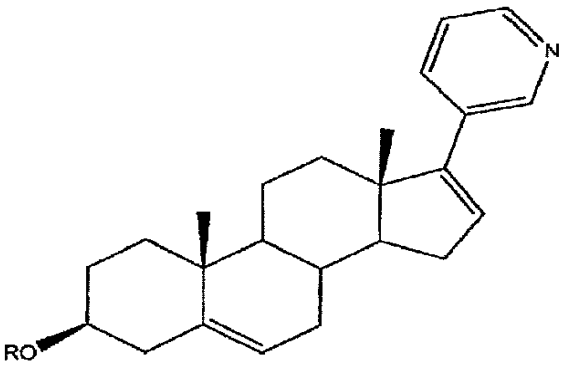
13. Use of a therapeutic agent in the manufacture of a medicament for use in a method of treating cancer, said method comprising administering the therapeutic agent in combination with a therapeutically effective amount of at least one 17α-hydroxylase/C_{17-20}-lyase inhibitor, wherein the 17α-hydroxylase/C_{17-20}-lyase inhibitor comprises a compound of the formula (I) or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

14. Use of a 17α-hydroxylase/C_{17-20}-lyase inhibitor in the manufacture of a medicament for use in a method of treating cancer, said method comprising administering the 17α-hydroxylase/C_{17-20}-lyase inhibitor in combination with a an additional therapeutic agent, wherein the 17α-hydroxylase/C_{17-20}-lyase inhibitor comprises a compound of the formula (I) or an analog, a derivative, a metabolite or a pharmaceutically acceptable salt thereof,



(I)

wherein R represents a hydrogen, or an acyl group having 1-4 carbons.

15. The pharmaceutical composition as claimed in claim 12 or the use as claimed in claims 13 or 14, comprising the features of any one of claims 2 to 11.

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 5604213 A **[0035] [0042]**
- US 60603559 B, Hunt **[0041]**
- US 5618807 A, Barrie **[0042]**
- US 60603558 B, Bury **[0042]**

Non-patent literature cited in the description

- Remington: The Science and Practice of Pharmacy. Mack Publ. Co, **[0033]**

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 2 478 907 A3

(12) EUROPEAN PATENT APPLICATION

(88) Date of publication A3:
01.08.2012 Bulletin 2012/31

(43) Date of publication A2:
25.07.2012 Bulletin 2012/30

(21) Application number: **12160586.9**

(22) Date of filing: **23.08.2007**

(51) Int Cl.:
A61P 35/00 *(2006.01)* ***A61K 31/58*** *(2006.01)*
A61K 45/06 *(2006.01)*

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC MT NL PL PT RO SE SI SK TR
Designated Extension States:
AL BA HR MK RS

(30) Priority: **25.08.2006 US 921506 P**

(62) Document number(s) of the earlier application(s) in accordance with Art. 76 EPC:
07837326.3 / 2 061 561

(71) Applicant: **Cougar Biotechnology, Inc.**
Los Angeles CA 90024 (US)

(72) Inventor: **The designation of the inventor has not yet been filed**

(74) Representative: **Carpmaels & Ransford**
One Southampton Row
London
WC1B 5HA (GB)

(54) Methods and compositions for treating cancer

(57) Methods and compositions for treating cancer are described herein. More particularly, the methods for treating cancer comprise administering a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate (i.e., 3β-acetoxy-17-(3-pyridyl) androsta-5, 16-diene), in combination with at least one additional therapeutic agent such as an anti-cancer agent or a steroid. Furthermore, disclosed are compositions comprising a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, and at least one additional therapeutic agent, such as an anti-cancer agent or a steroid.

EP 2 478 907 A3

Europäisches Patentamt
European Patent Office
Office européen des brevets

EUROPEAN SEARCH REPORT

Application Number
EP 12 16 0586

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	O'DONNELL A ET AL: "Hormonal impact of the 17[alpha]-hydroxylase/C17,20-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer", BRITISH JOURNAL OF CANCER 14 JUN 2004 UNITED KINGDOM, vol. 90, no. 12, 14 June 2004 (2004-06-14), pages 2317-2325, XP002464868, ISSN: 0007-0920 * page 2318, right-hand column, paragraph 1 * * page 2319, left-hand column, paragraph 7 - right-hand column, paragraph 13 * * page 2320, right-hand column, paragraph 2 * * page 2323, right-hand column, paragraph 4 *	1,2,4,9, 10,12-15	INV. A61P35/00 A61K31/58 A61K45/06
X	WO 2004/037269 A (PANTARHEI BIOSCIENCE B V [NL]; COELINGH BENNINK HERMAN JAN TI [NL]; BU) 6 May 2004 (2004-05-06) * claims 14-19 * * page 12, line 11 - page 13, line 32 *	1,2,5, 8-10, 12-15	TECHNICAL FIELDS SEARCHED (IPC) A61P A61K
X	US 2006/030608 A1 (NELSON RICHARD M [US] ET AL) 9 February 2006 (2006-02-09) * paragraph [0186] * * paragraph [0197] * * paragraph [0241] * * paragraph [0191] * * paragraph [0193] * * paragraph [0196] *	1,2, 8-10, 12-15	

-/--

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
The Hague	28 June 2012	Gradassi, Giulia

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent doument, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

2

Europäisches Patentamt
European Patent Office
Office européen des brevets

EUROPEAN SEARCH REPORT

Application Number
EP 12 16 0586

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	WO 02/053138 A (SHANAHAN-PRENDERGAST ELISABETH [IE]) 11 July 2002 (2002-07-11) * page 12, line 20 - page 13, line 31 * * page 14, line 29 - page 19, line 25 * * page 16, line 30 * * page 21, line 9 - page 22, line 21 * * page 26, lines 28-29 * * claims 1,7-9, 13, 52 * -----	1,2, 8-10, 12-15	
Y,D	WO 2006/021776 A (BTG INT LTD [GB]; HUNT NEIL JOHN [GB]) 2 March 2006 (2006-03-02) * the whole document * -----	1-15	
Y	MADAN RAVI A ET AL: "Abiraterone Cougar Biotechnology", IDRUGS, CURRENT DRUGS LTD, GB, vol. 9, no. 1, January 2006 (2006-01), pages 49-55, XP008087480, ISSN: 1369-7056 * the whole document * -----	1-15	
	-/--		TECHNICAL FIELDS SEARCHED (IPC)

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
The Hague	28 June 2012	Gradassi, Giulia

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

2

Europäisches Patentamt
European Patent Office
Office européen des brevets

EUROPEAN SEARCH REPORT

Application Number
EP 12 16 0586

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
Y	SCHOLZ M ET AL: "LONG-TERM OUTCOME FOR MEN WITH ANDROGEN INDEPENDENT PROSTATE CANCER TREATED WITH KETOCONAZOLE AND HYDROCORTISONE", JOURNAL OF UROLOGY, LIPPINCOTT WILLIAMS & WILKINS, BALTIMORE, MD, US, vol. 173, no. 6, 1 June 2005 (2005-06-01), pages 1947-1952, XP027855453, ISSN: 0022-5347 [retrieved on 2005-06-01] * abstract * * page 1947, left-hand column, paragraph 1 * * page 1947, right-hand column, paragraph 2 * * page 1950, right-hand column, paragraph 2 - page 1951, right-hand column, last paragraph * -----	1-15	
Y	HARRIS ET AL: "Low Dose Ketoconazole With Replacement Doses of Hydrocortisone in Patients With Progressive Androgen Independent Prostate Cancer", JOURNAL OF UROLOGY, LIPPINCOTT WILLIAMS & WILKINS, BALTIMORE, MD, US, vol. 168, no. 2, 1 August 2002 (2002-08-01), pages 542-545, XP005540121, ISSN: 0022-5347, DOI: 10.1016/S0022-5347(05)64675-7 * abstract * * page 542, left-hand column, paragraph 1 - page 543, left-hand column, paragraph 2 * * page 544, right-hand column, paragraph 2 - page 545, left-hand column, last paragraph * ----- -/--	1-15	TECHNICAL FIELDS SEARCHED (IPC)

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
The Hague	28 June 2012	Gradassi, Giulia

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

Europäisches Patentamt
European Patent Office
Office européen des brevets

EUROPEAN SEARCH REPORT

Application Number
EP 12 16 0586

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
Y	GERBER G S ET AL: "Prostate specific antigen for assessing response to ketoconazole and prednisone in patients with hormone refractory metastatic prostate cancer", JOURNAL OF UROLOGY, LIPPINCOTT WILLIAMS & WILKINS, BALTIMORE, MD, US, vol. 144, no. 5, 1 January 1990 (1990-01-01), pages 1177-1179, XP008151701, ISSN: 0022-5347 * abstract * * page 1177, left-hand column, paragraph 1 - right-hand column, paragraph 1 * * page 1179, left-hand column, paragraph 5 - right-hand column, paragraph 2 *	1-15	
Y	DE COSTER R ET AL: "EFFECTS OF HIGH-DOSE KETOCONAZOLE AND DEXAMETHASONE ON ACTH-STIMULATED ADRENAL STEROIDOGENESIS IN ORCHIECTOMIZED PROSTATIC CANCER PATIENTS", ACTA ENDOCRINOLOGICA, vol. 115, no. 2, 1987, pages 265-271, XP008153090, ISSN: 0001-5598 * abstract * * page 265, right-hand column, paragraph 1 - page 266, left-hand column, paragraph 5 * * page 270 *	1-15	TECHNICAL FIELDS SEARCHED (IPC)

-/--

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
The Hague	28 June 2012	Gradassi, Giulia

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

Europäisches Patentamt
European Patent Office
Office européen des brevets

EUROPEAN SEARCH REPORT

Application Number
EP 12 16 0586

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
Y,P	FOSSA ET AL: "Weekly Docetaxel and Prednisolone versus Prednisolone Alone in Androgen-Independent Prostate Cancer: A Randomized Phase II Study", EUROPEAN UROLOGY, ELSEVIER BV, NL, vol. 52, no. 6, 21 November 2007 (2007-11-21), pages 1691-1699, XP022356374, ISSN: 0302-2838, DOI: 10.1016/J.EURURO.2007.01.104 * abstract * -----	1-15	

TECHNICAL FIELDS SEARCHED (IPC)

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
The Hague	28 June 2012	Gradassi, Giulia

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

2

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 12 16 0586

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

28-06-2012

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004037269 A	06-05-2004	AT 380552 T	15-12-2007
		AU 2003274823 A1	13-05-2004
		CA 2503549 A1	06-05-2004
		CN 1732007 A	08-02-2006
		DE 60318092 T2	27-11-2008
		DK 1556058 T3	03-03-2008
		EP 1556058 A1	27-07-2005
		ES 2298570 T3	16-05-2008
		PT 1556058 E	20-03-2008
		SI 1556058 T1	29-02-2008
		US 2006247221 A1	02-11-2006
		WO 2004037269 A1	06-05-2004
US 2006030608 A1	09-02-2006	NONE	
WO 02053138 A	11-07-2002	AU 2002219472 A1	16-07-2002
		EP 1351678 A2	15-10-2003
		US 2004092583 A1	13-05-2004
		WO 02053138 A2	11-07-2002
WO 2006021776 A	02-03-2006	AT 472553 T	15-07-2010
		AU 2005276298 A1	02-03-2006
		BR PI0514543 A	17-06-2008
		CA 2576922 A1	02-03-2006
		CN 101044155 A	26-09-2007
		DK 1789432 T3	16-08-2010
		EP 1789432 A1	30-05-2007
		ES 2345345 T3	21-09-2010
		HK 1103091 A1	24-12-2010
		JP 2008510780 A	10-04-2008
		KR 20070049171 A	10-05-2007
		NZ 553085 A	27-08-2010
		PT 1789432 E	09-08-2010
		SI 1789432 T1	29-10-2010
		US 2007249836 A1	25-10-2007
		US 2010152437 A1	17-06-2010
		US 2012053340 A1	01-03-2012
		WO 2006021776 A1	02-03-2006
		ZA 200701533 A	27-08-2008

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

D9

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

PCT

(43) International Publication Date
16 March 2006 (16.03.2006)

(10) International Publication Number
WO 2006/027266 A1

(51) International Patent Classification:
A61K 9/28 (2006.01) *A61K 31/573* (2006.01)

(21) International Application Number:
PCT/EP2005/009726

(22) International Filing Date:
9 September 2005 (09.09.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10 2004 043 863.3
10 September 2004 (10.09.2004) DE
11/216,469 1 September 2005 (01.09.2005) US

(71) Applicant *(for all designated States except US)*: NITEC PHARMA AG [CH/CH]; Rüschenzerstrasse 9, 4153 Reinach (CH).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: SCHÄFFLER, Achim [DE/DE]; Schillerstrasse 7, 64743 Beerfelden (DE).

(74) Agent: WEICKMANN & WEICKMANN; Postfach 860 820, 81635 München (DE).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2006/027266 A1

(54) Title: TABLETS WITH SITE TIME-CONTROLLED GASTROINTESTINAL RELEASE OF ACTIVE INGREDIENT

(57) Abstract: The present invention describes a pharmaceutical dosage form with site and time-controlled gastrointestinal release of active ingredient.

Tablets with site and time-controlled gastrointestinal release of active ingredient

Description

Background of the invention

1. Field of the invention

The present invention describes a pharmaceutical dosage form with site- and time-controlled gastrointestinal release of active ingredient.

2. Description of the Related Art

Release of non-steroidal anti-inflammatory drugs in the stomach frequently causes ulcers of the gastric mucosa. This is why tablets with a gastro-resistant coating are now employed almost exclusively. The disadvantage is often that the active ingredient is released very quickly on entry into the intestine. Thus, it is possible with this technology to achieve control only of the site, but not of the timing, of active ingredient release.

Absorption of some active ingredients is possible only in certain sections of the gastrointestinal tract (absorption window). Active ingredient entry/transfer into the plasma is often desired only when the pathological state becomes particularly manifest at certain periods of the day (circadian rhythm). This is the case for example with asthma or ischemias in the early morning, joint pain in the morning, etc. On the other hand, the effect of some medicaments is often desired only locally in the gastrointestinal tract, such as for inflammations (e.g. in ulcerative colitis or Crohn's disease) or infections in the gastrointestinal tract.

Coated tablets have been described frequently, especially with the aim of delayed release of active ingredient, in which case an initial phase without release of the active ingredient (lag phase) is followed by the active ingredient leaving the tablet.

Thus, WO 02/072033 discloses that the amount of coating material applied determines the lag phase. The coating consists of a swellable material through the pores of which the active ingredient is then released. In this case, the diffusion through the swellable matrix of the coating becomes the release-determining factor. However, release through the pores often does not take place spontaneously after the desired lag phase; on the contrary, there is onset of more or less rapid release. In addition, the influences of food on swelling and eroding coatings are very important.

US 5 464 633 describes a tablet for delayed release of an active substance. The tablet consists of a core which comprises the active ingredient and a polymer, and of a polymer-containing coating.

EP 0 463 877 describes a pharmaceutical preparation for controlled release of an active ingredient, which comprises a core and a coating layer, where the coating layer comprises a water-repellent salt and a copolymer.

A pharmaceutical preparation consisting of a core and of a multilayer coating for release of the active ingredient in the lower part of the gastrointestinal tract (colon) is known for example from EP 0 366 621. Film coatings which are degraded only in the colon by bacteria present therein are, however, unsuitable for releasing the active ingredient in upper sections of the intestine.

WO 01/80824 (Eurand) describes a pharmaceutical form having a core which, besides the active ingredient, also comprises a hydrophilic, swelling polymer, and having a surrounding coating consisting of at least one water-insoluble polymer.

EP 0 939 623 B1 and US 6 183 780 (Duphar) describe an oral dosage form with delayed release consisting of a core and of a coating, where the coating consists of one or more polymers, of a water-soluble plasticizer and of a

substance which increases the brittleness of the coating. The disadvantages of this form are, in particular, that influences of food are possible.

EP 1 067 910 (Bar-Shalom) describes an oral dosage form having at least one erodable surface. EP 1 275 381 (Yamanouchi) likewise describes a core tablet with coating, the latter consisting of a swellable hydrophilic polymer. The effects of food in these cases are also great.

Administration of dilitiazem in the form of biologically inert pellets with a plurality of layers is described in US 6 620 439 (Elite Labs). In this case, the active ingredient is released some hours after intake to treat arterial occlusions in the morning.

US Patent 5 792 476 describes a pharmaceutical composition for peroral administration for rheumatoid arthritis, which comprises a glucocorticoid as active ingredient and which leads to release in the small intestine. The composition is a granulate which is laminated with an inner layer which is resistant to a pH of 6.8, and with an outer layer which is resistant to a pH of 1.0.

US Patent 6 488 960 describes a pharmaceutical dosage form for controlled release of corticoids, reference being made to the formulations described in US Patent 5 792 476.

WO 01/08421 describes a tablet having a core which is coated by at least two layers, one of which completely encloses the other. The coating layers can be produced by spray coating and/or pressing.

WO 01/68056 discloses a pharmaceutical preparation having a release profile with a time delay, comprising a core and at least one hydrophilic or lipophilic coating surrounding the core, where the coating is slowly swollen, dissolved, eroded or changed in its structure in another way through the water present in the release medium, so that the core or parts of the core

become accessible to the release medium. The coating may be formed for example as pressed coating.

WO 02/072034 discloses a pharmaceutical dosage form for delayed release, having a core which comprises as active ingredient a glucocorticoid and a material which brings about delayed release and includes at least one natural or synthetic gum.

WO 2004/093843, the content of which is incorporated herein by reference, discloses a tablet with a specific core geometry to release the active ingredient in a specific delayed release manner.

Brief summary of the invention

The problem underlying the present invention was to provide a pharmaceutical dosage form with site- and time-controlled release of active ingredient, which makes reproducible *in vivo* release possible in the particular desired sections of the intestine irrespective of the patient's food intake. It was further intended also for the active ingredient release process itself to be controllable as optimally as possible depending on the relevant medical indication.

This problem is solved by a pharmaceutical dosage form with site- and time-controlled gastrointestinal release of active ingredient, comprising

(a) a core having at least one active ingredient and having at least one swellable adjuvant such that the active ingredient is rapidly released from the dosage form when the core is contacted with gastrointestinal fluids; and

(b) an inert coating pressed onto the core, said coating being capable of preventing substantial release of the active ingredient for a defined time period following ingestion of the dosage form.

In another aspect, the present invention is directed to a method for the

treatment of a patient in need of therapy with an active ingredient in a site- and time-controlled dosage form, said method comprising administering to said patient the pharmaceutical dosage form described herein.

In another aspect, the present invention is directed to a kit comprising at least one unit dosage of a dosage form described herein with site- and time-controlled gastrointestinal release of active ingredient. The kit optionally contains instructional material for use of the unit dosage form.

In one aspect, the present invention relates to a method of producing a tablet which releases a corticosteroid active ingredient at a predetermined variable location in the GI tract, said method comprising:

determining the location in the GI tract at which it is desired to deliver the corticosteroid;

forming a coated tablet having a core comprising the corticosteroid and a swellable adjuvant, and an inert outer coating; and

compressing the coating of said tablet at a pressure chosen to result in the release of the corticosteroid at said predetermined position.

In another aspect, the present invention relates to a coated tablet having a core of a corticosteroid active ingredient and a coating, capable of releasing the corticosteroid at a predetermined variable location the GI tract, the coating being compressed to a degree which results in the release of the corticosteroid at said predetermined location.

In another aspect, the present invention relates to a method of producing a tablet which releases a corticosteroid active ingredient at a predetermined variable location in the GI tract, said method comprising:

determining the location in the GI tract at which it is desired to deliver the corticosteroid;

forming a coated tablet having a core comprising the corticosteroid and a swellable adjuvant, and an inert outer coating;

compressing the coating of said tablet at a pressure chosen to result in the release of the corticosteroid at said predetermined position; and

testing the in vitro release characteristics in a dissolution apparatus in order to confirm release of the active ingredient at a specific lag time.

In another aspect, the present invention relates to a method for the treatment of a local bowel disorder in the lower sections of the intestine, which comprises administering to a patient in need thereof a coated tablet having a core of a corticosteroid active ingredient and a coating, the coating being compressed to a degree that results in the release of the corticosteroid in the lower sections of the intestine.

Brief description of the drawings

Figure 1 shows the *in vitro* release of the novel tablet containing 5 mg of prednisone ("Prednisone TR") with a lag phase of about 4 h (500 ml of water, paddle, USP)

Figure 2 shows the *in vivo* plasma level of prednisone after administration of

A) standard "Prednisone IR" (=immediate release) tablet (intake 2 am) with 5 mg of prednisone,
B) Novel "Prednisone TR"tablet, "semi-fasted" (intake 8 pm) with 5 mg of prednisone
C) Novel "Prednisone TR" tablet, fed-state (intake 8 pm) with 5 mg of prednisone.

Figure 3 shows the *in vivo* plasma level of prednisolone after administration of

A) standard "Prednisone IR" tablet (intake 2 am) with 5 mg of prednisone,
B) Novel "Prednisone TR" tablet, "semi-fasted" (intake 8 pm) with 5 mg of prednisone
C) Novel "Prednisone TR" tablet, fed-state (intake 8 pm) with 5 mg of

prednisone.

Figure 4 shows the *in vitro* release of a "Prednisone TR" tablet containing 5 mg of prednisone with a lag phase of 6 h (500 ml of water, paddle, USP)

Figure 5 shows an *in vivo* plasma level profile after administration of prednisone tablets.

1) "Prednisone IR"standard tablet (intake 8 am)
2) "Prednisone IR" standard tablet (intake 2 am)
3) Novel "Prednisone TR" tablet with 6 h lag phase ("semi-fasted")(intake 8 pm)
4) Novel "Prednisone TR" tablet with 6 h lag phase (fed state) (intake 8 pm)

Detailed description of the invention

It is possible for the site- and time-linked gastrointestinal release of active ingredient to differentiate two preferred embodiments:

1) Release in the upper sections of the intestine with the following aims:
   - avoidance of instabilities of the active ingredient in contact with gastric juice,
   - avoidance of side effects, such as ulcers, on release of the active ingredient in the stomach,
   - optimal site and timing of absorption of the active ingredient and its entry into the plasma after release of the active ingredient in the upper section of the small intestinal region,
   - achievement of the systemic effect at the ideal time,
   - display of a local effect in the upper sections of the intestine.

2) Release in the lower sections of the intestine with the following aims:
   - local and targeted gastrointestinal release of active ingredients,
   - avoidance of side effects by active ingredients after (unwanted) absorption has taken place.

It is common to both embodiments to increase markedly the medicament efficacy and to reduce the side effects thereof.

A first preferred embodiment therefore provides a pharmaceutical dosage form with a release of active ingredient in the upper sections of the intestine within a period of 2-6 hours. A second preferred embodiment provides a pharmaceutical dosage form with a site- and time-controlled release of active ingredient in the lower sections of the intestine within a period of 6-10 hours after intake.

The invention described herein relates to a novel timed-release ("TR") dosage form which releases the active ingredient or the combination of active ingredients, depending on the composition, the geometry and the production conditions, at a particular site and/or at a particular time, and thus makes it possible to ensure an optimal effect with reduced side effects.

Thus, experiments have already been carried out with prednisone as model substance ("Prednisone TR") and can, because of the comparable properties, also be applied to other active ingredients, e.g. corticosteroids.

The novel "TR" dosage form described herein differs from prior art preparations. It surprisingly shows with a specific geometry of the press coating with inert adjuvants and accurately adjusted production process parameters a reproducible lag phase and subsequent rapid release (drug release phase) of the active ingredient or the active ingredient combination.

The inert coating initially prevents release of the active ingredient or the active ingredient combination over an exactly defined period, so that no absorption can occur. The water present in the gastrointestinal tract penetrates slowly in through the coating and, after a time which is previously fixed by the pressure for compression, reaches the core. The coating ingredients show neither swelling nor erosion of parts of the coating. When

the core is reached, the water penetrating in is very rapidly absorbed by the hydrophilic ingredients of the core, so that the volume of the core increases greatly and, as a consequence thereof, the coating completely bursts open, and the active ingredient and the active ingredient combination respectively is released very rapidly.

A particularly advantageous embodiment of this press-coated "TR" tablet is achieved when a previously compressed core tablet is subsequently compressed with a multilayer tablet press to a press-coated tablet.

The tablet coating typically consists of the following materials in order to achieve a delayed release profile:

- polymer or copolymer of acrylic acid, methacrylic acid etc. (e.g. Eudragits or Carbopol),
- cellulose derivatives such as hydroxypropylmethylcellulose, hydroxypropylcellulose, carboxymethylcellulose, ethylcellulose, cellulose acetate,
- polyvinyl alcohol,
- polyethylene glycol,
- salts of higher fatty acids, esters of monohydric or polyhydric alcohols with short-, medium- or long-chain, saturated or unsaturated fatty acids. Specifically, stearic acid triglycerides (e.g. Dynersan) or glycerol behenate (e.g. Compritol) are used.

In addition, further adjuvants should also be added to these materials so that the tablet coating can be compressed. Typically used here are fillers such as lactose, various starches, celluloses and calcium hydrogen phosphate. The glidant used is normally magnesium stearate, and in exceptional cases also talc and glycerol behenate. A plasticizer is often also added to the coating material, preferably from the group of polyethylene glycol, dibutyl phthalate, Diethyl citrate or triacetin.

In order to achieve an optimal release profile, the tablet core must also fulfil

certain tasks and exhibit certain properties. Thus, after the lag phase has elapsed, a rapid release profile is achieved if typical disintegrants are added to the inner core, which are derived for example from the group of the following substances: cellulose derivatives, starch derivatives, crosslinked polyvinylpyrrolidone. The use of a blowing agent, for example resulting from a combination of a weak acid and a carbonate or bicarbonate, may also promote rapid release. The tablet core typically consists additionally of matrix or filling ingredients (e.g. lactose, cellulose derivatives, calcium hydrogen phosphate or other substances known from the literature) and lubricant or glidant (usually magnesium stearate, in exceptional cases also talc and glycerol behenate).

The size of the core tablet preferably should not exceed 6 mm (preferably 5 mm) in diameter, because otherwise the press-coated tablet becomes too large for convenient ingestion. As a result thereof, the dosages of the active ingredients are in the range from 0.1 to 50 mg, very particularly between 1 and 20 mg.

The *in vitro* release profile of the "TR" dosage form according to the invention is preferably such that less than 5% of the active ingredient is released during the lag phase. After the release phase has started, preferably ≥80%, particularly preferably ≥90%, of the active ingredient is released within one hour. The *in vitro* release is preferably determined using the USP paddle dissolution model in water.

The employed active ingredients are preferably derived from the group of glucocorticoids and all show comparable physicochemical properties. Such include cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, budesonide, dexamethasone, fludrocortisone, fluocortolone, cloprednole, deflazacort, triamcinolone, and the corresponding salts and esters thereof. This applies in particular to prednisone, prednisolone, methylprednisolone, budesonide, dexamethasone, fluocortolone, cloprednole, and deflazacort and the corresponding salts and

esters thereof.

In the present case of the "TR" tablet, the following combination of core materials and coating materials has proved to be particularly suitable for achieving a time- and site-controlled release with exclusion of pH and food influences:

The coating preferably comprises:

- hydrophobic, waxy substances with an HLB value of less than about 5, preferably around 2. Carnauba wax, paraffins, cetyl ester waxes are preferably employed therefor. Glycerol behenate has proved to be particularly suitable. The use of about 20-60%, in particular about 30-50%, in the coating has proved to be very advantageous;
- non-fatty, hydrophobic filling materials such as calcium phosphate salts, e.g. dibasic calcium phosphate. The use of about 25-75% of these filling materials, in particular of about 40-60%, in the coating has proved to be very advantageous here;
- in addition, the tablet coating preferably also consists of binders, e.g. polyvinylpyrrolidone (PVP), typically in concentrations of about 4-12%, specifically about 7-10%, and glidants such as magnesium stearate, in concentrations of about 0.1-2%, in the specific case of about 0.5-1.5%. Colloidal silicon dioxide can for example be used as flow regulator, normally in concentrations of about 0.25-1%. In addition, to distinguish different dosages, a colorant can be added to the tablet coating, preferably an iron oxide pigment in concentrations of about 0.001-1%.

The core tablet preferably comprises:

- an active ingredient or an active ingredient combination from the group of glucocorticoids, preferably prednisone, prednisolone, methylprednisolone, budesonide, dexamethasone, fludrocortisone, fluocortolone, cloprednole, deflazacort, and triamcinolone, and the corresponding salts and esters thereof. The dosages of the active

ingredients are in the region of about 0.1-50 mg, very especially between about 1 and 20 mg;

- in addition, the core tablet preferably comprises a filler such as, for example, lactose, starch derivatives or cellulose derivatives. Lactose is preferably employed. The filler is typically present in concentrations of about 50-90%, specifically of about 60-80%. A disintegrant is additionally present and is typically crosslinked PVP or sodium carboxymethylcellulose, typically in concentrations of about 10-20%. It is additionally possible for a binder, e.g. PVP, to be present, typically in concentrations of about 2-10%, specifically of about 5.5-9%, and a lubricant such as magnesium stearate, in concentrations of about 0.1-2%, in the specific case of about 0.5-1.5%. Colloidal silicon dioxide is normally used as flow regulator, normally in concentrations of about 0.25-1%. It is additionally possible, for visually distinguishing the core from the coating, to add a colorant, preferably an iron oxide pigment in concentrations of about 0.01-1%.

The pharmaceutical dosage form according to the invention is preferably distinguished by the *in vitro* release and the *in vivo* release (on oral intake) of the active ingredient not differing by more than about one hour, particularly preferably not more than about 30 minutes. It is further preferred for the *in vitro* release to be substantially independent of the pH of the release medium or/and of additions in the release medium which simulate high-fat and low-fat food, i.e. to vary by preferably not more than about ±20%. It is further preferred for the *in vivo* release to be substantially independent of food intake, with the time to reach the maximum plasma concentration (t_{max}) varying by not more than about ±20%. The plasma level reached on *in vivo* release is preferably independent of the gastrointestinal pH and of food intake.

On *in vivo* release in the upper sections of the intestine, preferably equivalent parameters, in particular a maximum plasma level (C_{max}) reached

or/and an area reached under the plasma curve (AUC), as for a rapid-release dosage form are achieved. It is particularly preferred for a C_{max} of at least about 70%, preferably of at least about 80%, of the C_{max} of a rapid-release dosage form, and an AUC which does not vary by more than about ±25%, to be achieved. On release in lower sections of the intestine, the *in vivo* plasma levels reached are much lower, this likewise being substantially independent of the gastrointestinal pH and of food intake. The latter embodiment of the invention is thus particularly suitable for the treatment of local inflammatory bowel disease such as Crohn's disease or ulcerative colitis, where a systemic effect is not desired. The first-mentioned embodiment, with which absorption takes place in the upper sections of the intestine, is by contrast suitable in particular for the treatment of inflammatory diseases of the joints, associated with pain, such as, for example, rheumatoid arthritis, allergies and nocturnal severe asthmatic attacks, where a systemic effect is desired.

The process for producing the tablet takes place under usual conditions of the pharmaceutical industry. Thus, standard technologies are used in the production of the core tablet, such as weighing, sieving, mixing, aqueous granulation in a high-speed mixer, fluidized-bed drying of the granules, mixing and compression. Comparable methods are employed to produce the coating, namely weighing, sieving, mixing, aqueous granulation in a high-speed mixer, fluidized-bed drying of the granules, mixing and compression to press-coated tablets.

The geometry of the press-coated tablet has, in addition to the composition, a very great importance. It can be achieved only using a tablet machine for producing press-coated tablets; spray coatings are unsuitable.

The ratio of the thickness of the press-coating on the sides of the tablets to the upper side or lower side is preferably about 2.2-2.6 mm (for the side edges):about 1.2-1.6 mm for the upper side of the tablet and about 1.0-1.4 mm (for the lower side of the tablet), particularly preferably about

2.35-2.45 mm:about 1.35-1.45 mm (upper side of the tablet) and about 1.15-1.25 mm (lower side). This geometry results in the tablet remaining sufficiently small to avoid problems with swallowing.

Tablets with a hardness of about 60-90 N, measured as specified in the European Pharmacopoeia 4, 2.9.8, are thus achieved.

The timed-release ("TR") of active ingredient can be controlled by setting the compressive forces during the application of the coating to the tablet core. Thus, the compressive forces used for release in the upper sections of the intestine are preferably up to about 600 kg, particularly preferably about 250-600 kg, whereas the compressive forces used for release of the active ingredient in the lower sections of the intestine are preferably above about 600 kg, particularly preferably about 600-800 kg.

The pharmaceutical dosage form is particularly preferably in the form of a tablet, but it is also possible to produce the dosage form as capsule.

The present invention is further illustrated by the following examples.

Examples

Example 1: Formulas

Core tablet consisting of:

Corticosteroid[1]	1 mg
Lactose	42.80 mg
Povidone	4 mg
Carboxymethylcellulose, Na	11 mg
Iron oxide, red	0.3 mg
Magnesium stearate	0.6 mg
Silicon dioxide	0.3 mg

or

Corticosteroid[1]	5 mg
Lactose	38.80 mg
Povidone	4 mg
Carboxymethylcellulose, Na	11 mg
Iron oxide, red	0.3 mg
Magnesium stearate	0.6 mg
Silicon dioxide	0.3 mg

or

Corticosteroid[1]	10 mg
Lactose	33.80 mg
Povidone	4 mg
Carboxymethylcellulose, Na	11 mg
Iron oxide, red	0.3 mg
Magnesium stearate	0.6 mg
Silicon dioxide	0.3 mg

Coating consisting of:

Calcium phosphate	50%
Glycerol behenate	40%
Povidone	8.4%
Iron oxide, yellow	0.1%
Magnesium stearate	1.0%
Silicon dioxide	0.5%

[1] Corticosteroid from the group of substances including cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, budesonide, dexamethasone, fludrocortisone, fluocortolone, cloprednole, deflazacort, triamcinolone and the corresponding salts and esters thereof.

The composition of the tablets ensures that the influences of food, pH and motility of the gastrointestinal tract have no influence, and the active ingredient escapes very rapidly from the tablet after completion of the lag phase.

Example 2: Production process and *in vitro* release

With a fixed tablet geometry, the lag phase of active ingredient release is determined exclusively by the variably adjustable compressive force. Prednisone was used as active ingredient in this case.

Thus, an average pressure of 400 kg for compression leads for example to a lag phase of 4 hours. Table 1 summarizes the lag phases as a function of the compressive force:

Table 1: Dependence of the lag phase [h] on the average compressive force [kg]

Compressive force [kg]	lag phase [h]
300	3
340	3.5
400	3.9
460	4.5
580	5

The lag phase is determined by means of the USP paddle dissolution model with 100 rpm in water at a temperature of 37°C. Figure 1 shows typical release behaviour (batch G360).

Surprisingly, the lag phases and drug release phases in hours are comparable in different release media for this formulation, with fixed geometry and identical compressive force. This is evident from Table 2 (batch: G360).

Table 2: Lag phases and drug release phases [h] of the novel "Prednisone TR" tablet with the active ingredient prednisone in different release media, *in vitro* dissolution release, 500 ml, paddle, USP

Medium	Average lag phase [h]	Average drug release phase [h]
Water	4.1	0.7
pH 1.2	3.6	0.8
pH 4.5	3.8	0.9
pH 6.8	4.0	0.9
FaSSIF	4.2	0.8
FeSSIF	4.1	0.9

This surprising finding is very important because the aim which it is intended to pursue is to achieve site- and time-controlled release without the influence of food.

Further experiments to correlate the compressive force with the lag phase were undertaken with respect to 1 mg and 5 mg tablets containing prednisone as the active ingredient. The results are summarized below:

Compressive Force	Average lag phase 1 mg tablet	Average lag phase 5 mg tablet
150 kg	2.2	2.2
200 kg	2.4	2.7
400 kg	3.4	3.9
600 kg	4.2	5.1
800 kg	4.8	5.6
1200 kg	6.0	

Surprisingly, there are some differences in the required compression forces between TR tablets of different strengths. Therefore, testing of the in-vitro characteristics of each batch in a dissolution apparatus is preferred to confirm release of the active at a specific lag-time. This can easily be monitored by a color change of the dissolution medium. The color is released from the colored core tablets.

Example 3: *In vivo* release

It was surprisingly possible to confirm *in vivo* exactly the delay, measured *in vitro*, of prednisone release.

It was possible to show in a pharmacokinetics study that with a delay of 4 hours in active ingredient release *in vitro*, the delay *in vivo* is exactly the same, and there is subsequently a very rapid rise in level. The resulting plasma levels of prednisone after administration of the novel "Prednisone TR" tablet are depicted in Figure 2. They agree very well in terms of time with the *in vitro* release profile. It was additionally found that simultaneous intake of food evidently likewise has no influence *in vivo*, and comparable plasma levels are found as in the "semi-fasted" state. This is surprising because food normally influences the motility of the gastrointestinal tract, the pH, the luminal metabolism, and normally interacts with the dose form. The Guidance for Industry "Food Effect Bioavailability and Fed Bioequivalence Studies" of the US FDA, Department of Health of December 2002 mentions that a difference in reaching the t_{max} ought to be of no clinical relevance.

It is therefore very gratifying that the lag phase for the present "Prednisone TR" tablet *in vitro* is 4 hours and this is also found *in vivo* with and without food. In addition, food evidently has no influence on the maximum plasma levels (C_{max}) reached and the areas reached under the plasma curve (AUC) either. The time until the maximum plasma concentration (t_{max}) is reached is likewise independent of the intake of food.

The difference in t_{max} between the tablet in the semi-fasted state compared with simultaneous food intake is a maximum of ±20% and is thus clinically insignificant.

To demonstrate the influence of food on the release of the active ingredient from the novel "Timed-Release" dosage form, the applicant has carried out a pharmacokinetics study on 27 subjects. Three arms were compared: administration in the evening (8 pm) of the novel "Prednisone TR" tablet with standardized supper (fed state), administration in the evening (8 pm) of the novel "Prednisone TR" tablet with light supper around 17.30 h (semi-fasted), administration at night (2 am) of a standard Prednisone Immediate Release tablet (Decortin, Merck, Germany). The study was carried out randomized, in

cross-over design as single dose administration and thus complies with the usual regulatory requirements.

The aim of the kinetics study was to achieve comparable plasma level profiles in relation to C_{max} and AUC for the novel tablet "Prednisone TR" "semi-fasted" compared with "fed state" in relation to a standard "Prednisone IR" tablet (with rapid release of active ingredient). The novel tablet described herein with the active ingredient prednisone showed that comparable plasma level profiles can be achieved.

The plasma samples were taken at intervals of 0.5 and later of 1 hour.

The prednisone plasma levels found are depicted graphically in Figure 2, and the principal pharmacokinetic characteristics are summarized in Table 3.

Table 3: Pharmacokinetic parameters for prednisons after administration of a single dose of 5 mg of prednisone as "Prednisone IR" or "Prednisone TR" tablet in 27 healthy male volunteers

Parameter	Prednisone IR at 2 am	Prednisone TR;semi-fasted at 8 pm	Predisone TR; fed state at 8 pm	p*
C_{max} (ng/mL)	20.9 (19.2-22.7)	20.3 (18.6-22.1)	22.0 (20.1-23.9)	0.54
t_{max} (h)	2 (1.0-4.0)	6.0 (4.5-10.0)	6.5 (4.5-9.0)	<0.0001
t_{lag} (h)	0.0 (0.0-0.5)	3.5 (2.0-5.5)	4.0 (3.5-5.0)	<0.0001
AUC_{0-t} (h.ng/mL)	107 (98.8-116)	108 (99.1-117)	121 (111-132)	0.16
$AUC_{0-\infty}$ (h.ng/mL)	109 (101-118)	110 (102-119)	123 (114-134)	0.15
$t_{1/2}$ (h)	2.57 (2.51-2.63)	2.41 (2.36-2.47)	2.41 (2.36-2.47)	0.002

t_{max} and t_{lag} values are means (range). The other values are geometric means (90% CI) obtained from ANOVA.
*: probability associated with the hypothesis, that there is no difference between the formulations (ANOVA, except for t_{max} and t_{lag}: Friedman test)

It was also possible to confirm these results for prednisolone, a metabolite of prednisone, after administration of the novel "Prednisone TR" tablet.

Thus, it was also possible to show for prednisolone a comparability between C_{max} and AUC of the novel "Prednisone TR" tablet "semi-fasted" with "fed state". The plasma level profile of the metabolite prednisolone is therefore also independent of food intake.

The plasma samples for determining prednisolone were taken at intervals of 0.5 and later of 1 hour.

The plasma levels found for prednisolone are depicted graphically in Figure 3, and the principal pharmacokinetic characteristics are summarized in Table 4.

Table 4: Pharmacokinetic parameters for prednisolone after administration of a single dose of 5 mg of prednisone as "Prednisone IR" or "Prednisone TR" tablet in 27 healthy male volunteers

Parameter	Prednisone IR at 2 am	Prednisone TR; semi-fased at 8 pm	Prednisone TR; fed state at 8 pm	p*
C_{max} (ng/mL)	135 (124-147)	113 (104-123)	132 (121-143)	0.036
t_{max} (h)	1.0 (0.5-3.0)	5.0 (4.0-9.0)	5.5 (4.5-9.0)	<0.0001
t_{lag} (h)	0.0 (0.0-0.5)	3.5 (2.0-5.5)	3.5 (3.0-5.0)	<0.0001

AUC_{0-t} (h.ng/mL)	614 (571-661)	561 (520-605)	647 (599-698)	0.081
$AUC_{0-\infty}$ (h.ng/mL)	624 (582-670)	573 (533-616)	658 (612-707)	0.0076
$t_{1/2}$ (h)	2.66 (2.63-2.70)	2.66 (2.62-2.69)	2.71 (2.68-2.75)	0.11

t_{max} and t_{lag} values are means (range). The other values are geometric means (90% CI) obtained from ANOVA.

*: probability associated with the hypothesis, that there is no difference between the formulations (ANOVA, except for t_{max} and t_{lag} Friedman test)

Typical achieved C_{max} values for 5 mg prednisone tablets after ingestion will be in the range of from about 15 to about 25 ng/ml, and the AUC of prednisone is from about 75 to about 150 h*ng/mL. The achieved C_{max} values for the prednisolone metabolite will be in the range of from about 100 to about 160 ng/ml, and the AUC of prednisolone is from about 500 to about 700 h*ng/mL.

It should additionally be mentioned that the coefficients of variation for C_{max}, t_{max} and AUC for prednisone after administration of the standard tablet "Prednisone IR" (at 2 am) and of the novel tablet "Prednisone TR" (at 8 pm) with and without food are approximately comparable. This has not previously been described for a tablet with modified release of active ingredient. Table 5 summarizes the coefficients of variation for prednisone.

Table 5: Coefficients of variation for C_{max}, t_{max}, AUC for prednisone plasma levels after administration of a standard tablet "Prednisone IR", of the novel tablet "Prednisone TR" "semi-fasted" and in "fed state"

		Prednisone IR at 2 am	Prednisone TR; semi-fasted at 8 pm	prednisone TR; fed state at 8 pm
N		26	26	26

C_{max} (ng/ml)	Average	21.1	21.4	22.2
	SD	3.56	5.65	3.66
	Median	20.8	21.4	22.2
	CV	16.9	26.4	16.4
t_{max} (h)	Average	2.06	6.21	6.5
	SD	0.68	1.22	1.11
	Median	2	6	6.5
	CV	33.1	19.6	17.1
$AUC_{0-\infty}$ (ng/ml*h)	Average	111	116	126
	SD	17.5	31	24.3
	Median	106	122	130
	CV (%)	15.8	26.6	19.2

The coefficients of variation of the pharmacokinetic parameters for the metabolite prednisolone likewise differ negligibly when the standard tablet is compared with the novel tablet.

Table 6: Coefficients of variation for C_{max}, t_{max}, AUC for prednisolone plasma levels after administration of a standard tablet "Prednisone IR", of the novel tablet "Prednisone TR" "semi-fasted" and in fed state

		Prednisone IR at 2 am	Prednisone TR semi-fasted at 8 pm	Prednisone TR; fed state at 8 pm
N		26	26	26
C_{max} (ng/ml)	Average	138	121	135
	SD	22.9	32.3	24.5
	Median	140	130	135
	CV	16.6	26.8	18.2
t_{max} (h)	Average	1.12	5.58	5.81
	SD	0.67	1.2	1.16
	Median	1	4	5.5
	CV	59.3	21.5	19.9
$AUC_{0-\infty}$ (ng/ml*h)	Average	638	611	680
	SD	112	178	142
	Median	646	677	713
	CV (%)	17.7	29.2	20.9

The situation is quite different when a tablet with a longer lag phase (6 hours

in vitro) is administered. It is true that release after 6 hours is in this case also found *in vitro*. However, at the same time, the absorption is greatly reduced because the release obviously takes place in lower sections of the intestine, and absorption now takes place only to a smaller extent. This was shown in a second pharmacokinetics study. Figure 5 shows a novel "Prednisone TR" tablet with a lag phase of 6 hours, which can be produced by means of a higher pressure for compression.

Typical achieved C_{max} values for such 5 mg prednisone tablets after ingestion will be in the range of less than 15 ng/ml, and the AUC of prednisone is less than 75 h*ng/mL. The achieved C_{max} values for the prednisolone metabolite will be in the range of less than 100 ng/ml, and the AUC of prednisolone is less than 500 h*ng/mL.

Very interesting novel therapeutic approaches derive therefrom, and this invention relates thereto. Thus, the composition of the tablet, its specific geometry and a compressive force which can be adjusted variably make it possible for the coating of the tablet to release the active ingredient very rapidly from the core tablet after an exactly fixed time. This is very advantageous because the site of release can also be fixed accurately via this precise presetting.

It is possible with a site of release on the one hand to treat local disorders of the gastrointestinal tract locally. For example, ulcerative colitis, an inflammatory disorder of the bowel, may affect different sections of the intestine. This novel timed-release ("TR") tablet is very advantageous especially for disorders of lower sections of the intestine, because there is now mainly local release of the active ingredient, but absorption thereof is only negligible or very limited. It is possible thereby to avoid effects which normally occur after uptake of the active ingredient into the blood.

However, with a precise controlled active ingredient release after an exactly defined lag phase it is also possible to achieve the plasma level profiles

which correspond to those after administration of a rapid-release tablet. However, the precondition for this is that the coating of the novel timed-release ("TR") tablet exposes the active ingredient-containing core after less than 6 hours, and the active ingredient can then be very rapidly dissolved and absorbed. One application thereof is, for example, the administration of corticoids for the treatment of inflammatory disorders to the joints, where pro-inflammatory cytokines are released in the early hours of the morning and are thought to be responsible for the pain in the morning and the stiffness of fingers in the morning. It is now possible through the novel tablet, with intake at 10 pm, to enable release at 2 am, and thus to ensure the optimal effect, described by Arvidson et al. (Annals of Rheumatic Diseases 1997; 56:27-31) of the cortisones on rheumatoid arthritis and, in addition, to contribute to a crucial increase in patient compliance. Consequently, the tablets of the present invention may be ingested once daily at bed-time, for example between about 8 pm and about 12 am, and more preferably between about 9 pm and about 11 pm.

The present invention also provides a method for producing a tablet that releases a corticosteroid active ingredient at a predetermined variable location in the GI tract, said method comprising:

determining the location in the GI tract at which it is desired to deliver the corticosteroid;

forming a coated tablet having a core comprising the corticosteroid and a swellable adjuvant, and an inert outer coating;

compressing the coating of said tablet at a pressure chosen to result in the release of the corticosteroid at said predetermined position; and

testing the in vitro release characteristics in a dissolution apparatus in order to confirm release of the active ingredient at a specific lag time. The in vitro release characteristics can then be correlated to the suitable in vivo release lag time.

In a preferred embodiment, the tablet core comprises a coloring material, and the in vitro release of the active ingredient is determined by a color change. The dissolution apparatus may be any standard apparatus in the

industry, and preferably is in accordance with USP XXVIII.

Claims

1. A method of producing a tablet which releases a corticosteroid active ingredient at a predetermined variable location in the GI tract, said method comprising
determining the location in the GI tract at which it is desired to deliver the corticosteroid;
forming a coated tablet having a core comprising the corticosteroid and a swellable adjuvant, and an inert outer coating; and
compressing the coating of said tablet at a pressure chosen to result in the release of the corticosteroid at said predetermined position.

2. The method of claim 1, wherein the active ingredient is rapidly released when the core is contacted with gastrointestinal fluids; and wherein said coating is capable of preventing substantial release of the active ingredient for a defined time period following ingestion of the dosage form.

3. The method of claim 1, wherein the active ingredient is released in the upper sections of the intestine within a period of about 2 to about 6 hours after ingestion.

4. The method of claim 1, wherein the active ingredient is released in the lower sections of the intestine within a period of about 6 to about 10 hours after ingestion.

5. The method of claim 1, wherein the *in vitro* release and the *in vivo* release of the active ingredient do not differ by more than about 1 hour.

6. The method of claim 1, wherein the *in vitro* release of the active ingredient is substantially independent of the pH of the release medium or/and of additions in the release medium which simulate high-fat and

low-fat food.

7. The method of claim 1, wherein the *in vivo* release is substantially independent of food intake.

8. The method of claim 1, wherein a systemic effect occurs on *in vivo* release of the active ingredient in the upper sections of the intestine.

9. The method of claim 8, wherein the coating is produced by compressive forces of up to about 600 kg.

10. The method of claim 8, wherein the plasma level reached on *in vivo* release of the active ingredient is independent of the gastrointestinal pH and of food intake.

11. The method of claim 8, wherein the *in vivo* biopharmaceutical/ pharmacokinetic profile of the corticosteroid active ingredient or its active metabolite is at least substantially identical to that of an immediate release tablet regarding C_{max} and/or AUC.

12. The method of claim 11 wherein the tablet comprises about 5 mg of prednisone, and wherein the achieved c_{max} of prednisone after ingestion is from about 15 to about 25 ng/mL and/or the AUC of prednisone is from about 75 to about 150 h*ng/mL.

13. The method of claim 11 wherein the tablet comprises about 5 mg of prednisone, and/or wherein the achieved c_{max} of the prednisolone active metabolite after ingestion is from about 100 to about 160 ng/mL and the AUC of the prednisolone active metabolite is from about 500 to about 700 h*ng/mL.

14. The method of claim 8, wherein the achieved t_{max} of the active ingredient is from about 2 to about 8 hours after ingestion.

15. The method of claim 4, wherein a substantially local effect occurs on *in vivo* release of the active ingredient in the lower sections of the intestine.

16. The method of claim 15, wherein the coating is produced by compressive forces above about 600 kg.

17. The method of claim 1, wherein the core comprises
- the corticosteroid;
- from about 50% to about 90% of a filler;
- from about 10% to about 20% of a disintegrant,
- from about 2% to about 10% of a binder;
- from about 0.1% to about 2% of a glidant;
- from about 0.25% to about 1% of a flow regulator; and
- from 0% to about 1% of a pigment;

all based on the total weight of the core.

18. The method of claim 17, wherein the filler comprises lactose; the disintegrant comprises crosslinked polyvinylpyrrolidone, sodium carboxymethylcellulose, or mixtures thereof; the binder comprises uncrosslinked polyvinylpyrrolidone; the lubricant comprises magnesium stearate; the flow regulator comprises colloidal silicon dioxide; and the pigment comprises iron oxide.

19. The method of claim 1, wherein the coating comprises
- from about 20% to about 60% of a hydrophobic waxy substance;
- from about 25% to about 75% of a non-fatty hydrophobic filling material;

- from about 4% to about 12% of a binder;
- from about 0.1% to about 2% of a glidant;
- from about 0.25% to about 1% of a flow regulator; and
- from about 0% to about 1% of a pigment;

all based on the total weight of the coating.

20. The method of claim 19, wherein the hydrophobic waxy substance comprises glycerol behenate and the non-fatty hydrophobic filler comprises calcium phosphate.

21. The method of claim 20, wherein the non-fatty hydrophobic filler comprises dibasic calcium phosphate.

22. The method of claim 21, wherein the non-fatty hydrophobic filler comprises basic calcium phosphate.

23. The method of claim 1, wherein the active ingredient comprises more than one corticosteroid.

24. The method of claim 1, wherein the active ingredient is selected from the group consisting of cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, budesonide, dexamethasone, fludrocortisone, fluocortolone, cloprednole, deflazacort, triamcinolone and pharmaceutically acceptable salts and esters thereof, and mixtures thereof.

25. The method of claim 1, wherein the active ingredient is selected from the group consisting of prednisone, prednisolone, methylprednisolone and budesonide.

26. The method of claim 1, wherein the amount of active ingredient is from about 0.1 mg to about 20 mg.

27. The method of claim 8, wherein the tablet is ingested once daily at bed-time.

28. The method of claim 27, wherein the tablet is ingested between about 8 pm and about 12 am.

29. The method of claim 28, wherein the tablet is ingested between about 9 pm and about 11 pm.

30. The method of claim 8, wherein the active ingredient is effective for the treatment of inflammatory disorders of the joints, pain, allergies or nocturnal severe asthmatic attacks.

31. The method of claim 1, wherein the active ingredient is effective for the treatment of a local inflammatory bowel disorder.

32. The method of claim 31, wherein the disorder is selected from the group

consisting of Crohn's disease and ulcerative colitis.

33. The method of claim 8, wherein the active ingredient is effective for the treatment of a local inflammatory bowel disorder in the upper sections of the intestine.

34. The method of claim 33, wherein the disorder is selected from the group consisting of Crohn's disease and ulcerative colitis.

35. The method of claim 15, wherein the active ingredient is effective for the treatment of a local inflammatory bowel disorder in the lower sections of the intestine.

36. The method of claim 35, wherein the disorder is selected from the group consisting of Crohn's disease and ulcerative colitis.

37. A coated tablet having a core of a corticosteroid active ingredient and a coating, capable of releasing the corticosteroid at a predetermined variable location the GI tract, the coating being compressed to a degree which results in the release of the corticosteroid at said predetermined location.

38. The tablet of claim 37, wherein the active ingredient is rapidly released when the core is contacted with gastrointestinal fluids; and wherein said coating is capable of preventing substantial release of the active

ingredient for a defined time period following ingestion of the dosage form.

39. The tablet of claim 37, wherein the active ingredient is released in the upper sections of the intestine within a period of from about 2 to about 6 hours after ingestion.

40. The tablet of claim 37, wherein the active ingredient is released in the lower sections of the intestine within a period of from about 6 to about 10 hours after ingestion.

41. The tablet of claim 37, wherein the *in vitro* release and the *in vivo* release of the active ingredient do not differ by more than about 1 hour.

42. The tablet of claim 37, wherein the *in vitro* release of the active ingredient is substantially independent of the pH of the release medium and of additions in the release medium which simulate high-fat and low-fat food.

43. The tablet of claim 37, wherein the *in vivo* release of the active ingredient is substantially independent of food intake.

44. The tablet of claim 37, wherein a systemic effect occurs on *in vivo* release of the active ingredient in the upper sections of the intestine.

45. The tablet of claim 44, wherein the coating is produced by compressive forces of up to about 600 kg.

46. The tablet of claim 44, wherein the plasma level reached on *in vivo* release of the active ingredient is independent of the gastrointestinal pH and of food intake.

47. The tablet of claim 44, wherein the *in vivo* biopharmaceutical/ pharmacokinetic profile of the corticosteroid active ingredient or its active metabolite is at least substantially identical to that of an immediate release tablet regarding C_{max} and/or AUC.

48. The tablet of claim 44 which comprises about 5 mg of prednisone, and wherein the achieved C_{max} of prednisone after ingestion is from about 15 to about 25 ng/mL and/or the AUC of prednisone is about 75-150 h*ng/mL.

49. The tablet of claim 44 which comprises about 5 mg of prednisone, and wherein the achieved C_{max} of the prednisolone active metabolite is from about 100 to about 160 ng/mL and/or the AUC of the prednisolone active metabolite is from about 500 to about 700 h*ng/mL.

50. The tablet of claim 44, wherein the achieved t_{max} of the active ingredient is from about 2 to about 8 hours after ingestion.

51. The tablet of claim 37, wherein a substantially local effect occurs on *in vivo* release in the lower sections of the intestine.

52. The tablet of claim 51, wherein the coating is produced by compressive forces above about 600 kg.

53. The tablet of claim 37, wherein the core comprises

- the corticosteroid;
- from about 50% to about 90% of a filler;
- from about 10% to about 20% of a disintegrant,
- from about 2% to about 10% of a binder;
- from about 0.1% to about 2% of a glidant;
- from about 0.25% to about 1% of a flow regulator; and
- from 0% to about 1% of a pigment;

all based on the total weight of the core.

54. The tablet of claim 53, wherein the filler comprises lactose; the disintegrant comprises crosslinked polyvinylpyrrolidone, sodium carboxymethylcellulose, or mixtures thereof; the binder comprises uncrosslinked polyvinylpyrrolidone; the lubricant comprises magnesium stearate; the flow regulator comprises colloidal silicon dioxide; and the pigment comprises iron oxide.

55. The tablet of claim 37, wherein the coating comprises

- from about 20% to about 60% of a hydrophobic waxy substance;

- from about 25% to about 75% of a non-fatty hydrophobic filling material;
- from about 4% to about 12% of a binder;
- from about 0.1% to about 2% of a glidant;
- from about 0.25% to about 1% of a flow regulator; and
- from about 0% to about 1% of a pigment;

all based on the total weight of the coating.

56. The tablet of claim 55, wherein the hydrophobic waxy substance comprises glycerol behenate and the non-fatty hydrophobic filler comprises calcium phosphate.

57. The tablet of claim 56, wherein the non-fatty hydrophobic filler comprises dibasic calcium phosphate dihydrate.

58. The tablet of claim 56, wherein the non-fatty hydrophobic filler comprises basic calcium phosphate.

59. The tablet of claim 37, wherein the active ingredient comprises more than one corticosteroid.

60. The tablet of claim 37, wherein the active ingredient is selected from the group consisting of cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, budesonide, dexamethasone, fludrocortisone, fluocortolone, cloprednole, deflazacort, triamcinolone and

pharmaceutically acceptable salts and esters thereof, and mixtures thereof.

61. The tablet of claim 37, wherein the active ingredient is selected from the group consisting of prednisone, prednisolone, methylprednisolone and budesonide.

62. The tablet of claim 37, wherein the amount of active ingredient is from about 0.1 mg to about 20 mg.

63. The tablet of claim 44, wherein the tablet is ingested once daily at bed-time.

64. The tablet of claim 63, wherein the tablet is ingested between about 8 pm and about 12 am.

65. The tablet of claim 63, wherein the tablet is ingested between about 9 pm and about 11 pm.

66. The tablet of claim 44, wherein the active ingredient is effective for the treatment of inflammatory disorders of the joints, pain, allergies or nocturnal severe asthmatic attacks.

67. The tablet of claim 37, wherein the active ingredient is effective for the treatment of a local inflammatory bowel disorder.

68. The tablet of claim 67, wherein the disorder is selected from the group consisting of Crohn's disease and ulcerative colitis.

69. The tablet of claim 44, wherein the active ingredient is effective for the treatment of a local inflammatory bowel disorder in the upper sections of the intestine.

70. The tablet of claim 69, wherein the disorder is selected from the group consisting of Crohn's disease and ulcerative colitis.

71. The tablet of claim 51, wherein the active ingredient is effective for the treatment of a local inflammatory bowel disorder in the lower sections of the intestine.

72. The tablet of claim 71, wherein the disorder is selected from the group consisting of Crohn's disease and ulcerative colitis.

73. A coated tablet having a core of a corticosteroid active ingredient and a coating, the coating being produced by compressive forces of greater than about 600 kg.

74. The tablet of claim 73, wherein the active ingredient is rapidly released when the core is contacted with gastrointestinal fluids; and wherein said coating is capable of preventing substantial release of the active

ingredient for a defined time period following ingestion of the dosage form.

75. The tablet of claim 73, wherein the active ingredient is released in the lower sections of the intestine within a period of from about 6 to about 10 hours after ingestion.

76. The tablet of claim 73, wherein the *in vitro* release and the *in vivo* release of the active ingredient do not differ by more than about 1 hour.

77. The tablet of claim 73, wherein the *in vitro* release of the active ingredient is substantially independent of the pH of the release medium and of additions in the release medium which simulate high-fat and low-fat food.

78. The tablet of claim 73, wherein the *in vivo* release of the active ingredient is substantially independent of food intake.

79. The tablet of claim 73, wherein the active ingredient is prednisone, and the plasma level reached on *in vivo* release of the prednisone is less than about 15 ng/mL (C_{max}) and/or less than about 75 h*ng/mL (AUC).

80. The tablet of claim 79, wherein the plasma level reached on *in vivo* release of the prednisolone active metabolite is less than about 100 ng/mL (C_{max}) and/or less than about 500 h*ng/mL (AUC).

81. The tablet of claim 73, wherein a substantially local effect occurs on *in vivo* release in the lower sections of the intestine, and wherein a systemic effect is not exhibited.

82. The tablet of claim 73, wherein the core comprises

- the corticosteroid;
- from about 50% to about 90% of a filler;
- from about 10% to about 20% of a disintegrant,
- from about 2% to about 10% of a binder;
- from about 0.1% to about 2% of a glidant;
- from about 0.25% to about 1% of a flow regulator; and
- from 0% to about 1% of a pigment;

all based on the total weight of the core.

83. The tablet of claim 82, wherein the filler comprises lactose; the disintegrant comprises crosslinked polyvinylpyrrolidone, sodium carboxymethylcellulose, or mixtures thereof; the binder comprises uncrosslinked polyvinylpyrrolidone; the lubricant comprises magnesium stearate; the flow regulator comprises colloidal silicon dioxide; and the pigment comprises iron oxide.

84. The tablet of claim 73, wherein the coating comprises

- from about 20% to about 60% of a hydrophobic waxy substance;
- from about 25% to about 75% of a non-fatty hydrophobic filling

material;

- from about 4% to about 12% of a binder;
- from about 0.1% to about 2% of a glidant;
- from about 0.25% to about 1% of a flow regulator; and
- from about 0% to about 1% of a pigment;

all based on the total weight of the coating.

85. The tablet of claim 84, wherein the hydrophobic waxy substance comprises glycerol behenate and the non-fatty hydrophobic filler comprises calcium phosphate.

86. The tablet of claim 85, wherein the non-fatty hydrophobic filler comprises dibasic calcium phosphate dihydrate.

87. The tablet of claim 85, wherein the non-fatty hydrophobic filler comprises basic calcium phosphate.

88. The tablet of claim 73, wherein the active ingredient comprises more than one corticosteroid.

89. The tablet of claim 73, wherein the active ingredient is selected from the group consisting of cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, budesonide, dexamethasone, fludrocortisone, fluocortolone, cloprednole, deflazacort, triamcinolone and pharmaceutically acceptable salts and esters thereof, and mixtures

thereof.

90. The tablet of claim 73, wherein the active ingredient is selected from the group consisting of prednisone, prednisolone, methylprednisolone and budesonide.

91. The tablet of claim 73, wherein the amount of active ingredient is from about 0.1 mg to about 20 mg.

92. The tablet of claim 73, wherein the active ingredient is effective for the treatment of a local inflammatory bowel disorder.

93. The tablet of claim 92, wherein the disorder is selected from the group consisting of Crohn's disease and ulcerative colitis.

94. A method of producing a tablet which releases a corticosteroid active ingredient at a predetermined variable location in the GI tract, said method comprising

determining the location in the GI tract at which it is desired to deliver the corticosteroid;

forming a coated tablet having a core comprising the corticosteroid and a swellable adjuvant, and an inert outer coating;

compressing the coating of said tablet at a pressure chosen to result in the release of the corticosteroid at said predetermined position; and

testing the in vitro release characteristics in a dissolution apparatus in

order to confirm release of the active ingredient at a specific lag time.

95. The method of claim 94, wherein the core comprises a coloring material, and the release of the active ingredient is determined by a color change.

96. A method for the treatment of a local bowel disorder in the lower sections of the intestine, which comprises administering to a patient in need thereof a coated tablet having a core of a corticosteroid active ingredient and a coating, the coating being compressed to a degree that results in the release of the corticosteroid in the lower sections of the intestine.

97. The method of claim 96, wherein the coating has been compressed by a force of greater than about 600 kg.

98. The method of claim 96, wherein the active ingredient is effective for the treatment of a local inflammatory bowel disorder.

99. The method of claim 98, wherein the disorder is selected from the group consisting of Crohn's disease and ulcerative colitis.

100. The method of claim 96, wherein the active ingredient is released in the lower sections of the intestine within a period of about 6 to about 10 hours after ingestion.

101. The method of claim 96, wherein the core comprises

- the corticosteroid;
- from about 50% to about 90% of a filler;
- from about 10% to about 20% of a disintegrant,
- from about 2% to about 10% of a binder;
- from about 0.1% to about 2% of a glidant;
- from about 0.25% to about 1% of a flow regulator; and
- from 0% to about 1% of a pigment;

all based on the total weight of the core.

102. The method of claim 101, wherein the filler comprises lactose; the disintegrant comprises crosslinked polyvinylpyrrolidone, sodium carboxymethylcellulose, or mixtures thereof; the binder comprises uncrosslinked polyvinylpyrrolidone; the lubricant comprises magnesium stearate; the flow regulator comprises colloidal silicon dioxide; and the pigment comprises iron oxide.

103. The method of claim 96, wherein the coating comprises

- from about 20% to about 60% of a hydrophobic waxy substance;
- from about 25% to about 75% of a non-fatty hydrophobic filling material;
- from about 4% to about 12% of a binder;
- from about 0.1% to about 2% of a glidant;
- from about 0.25% to about 1% of a flow regulator; and
- from about 0% to about 1% of a pigment;

all based on the total weight of the coating.

104. The method of claim 103, wherein the hydrophobic waxy substance comprises glycerol behenate and the non-fatty hydrophobic filler comprises calcium phosphate.

105. The method of claim 104, wherein the non-fatty hydrophobic filler comprises dibasic calcium phosphate.

106. The method of claim 104, wherein the non-fatty hydrophobic filler comprises basic calcium phosphate.

107. The method of claim 96, wherein the active ingredient comprises more than one corticosteroid.

108. The method of claim 96, wherein the active ingredient is selected from the group consisting of cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, budesonide, dexamethasone, fludrocortisone, fluocortolone, cloprednole, deflazacort, triamcinolone and pharmaceutically acceptable salts and esters thereof, and mixtures thereof.

109. The method of claim 96, wherein the active ingredient is selected from the group consisting of prednisone, prednisolone, methylprednisolone and budesonide.

110. The method of claim 96, wherein the amount of active ingredient is from about 0.1 mg to about 20 mg.

Figure 1

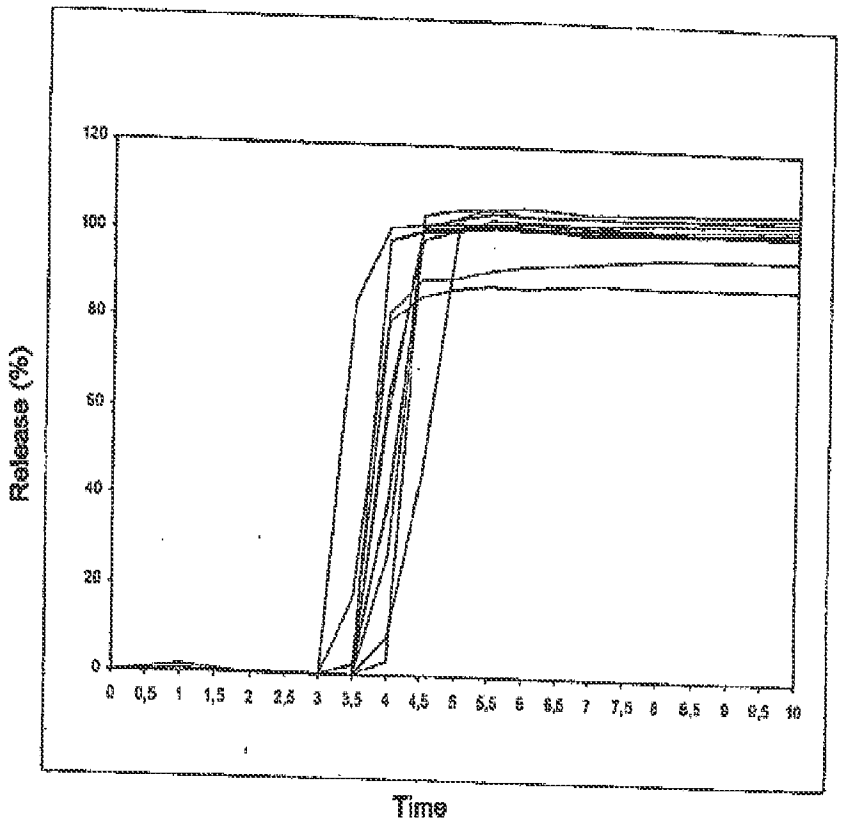


Figure 2

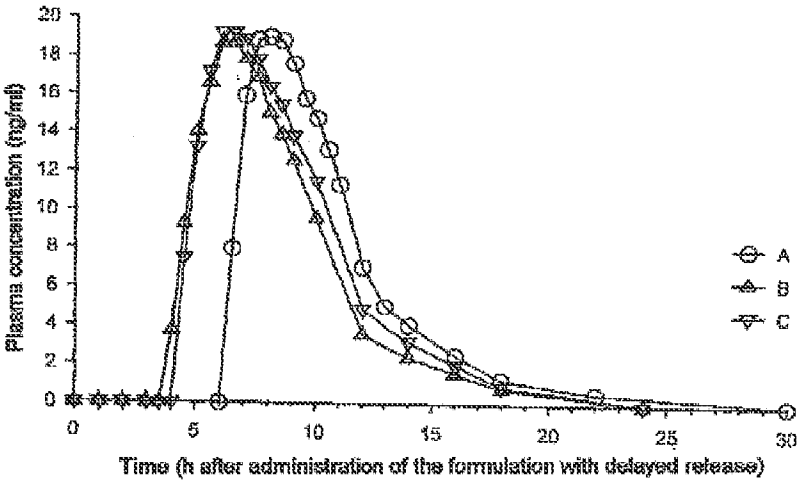


Figure 3

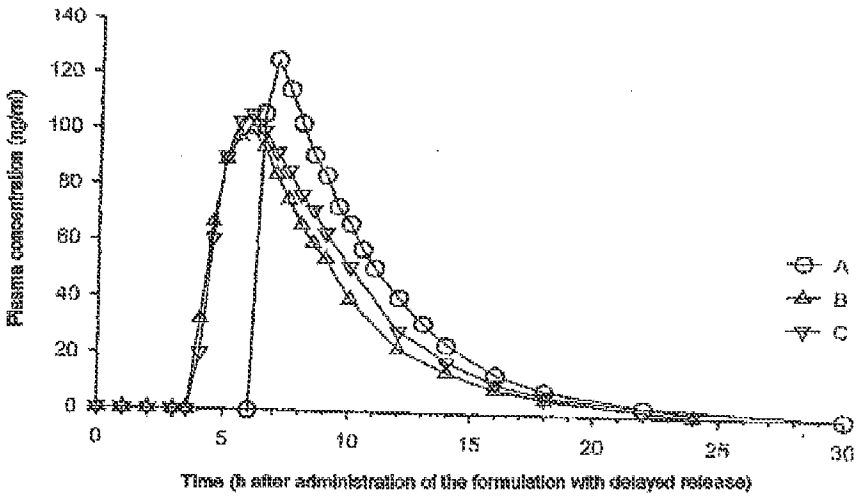


Figure 4

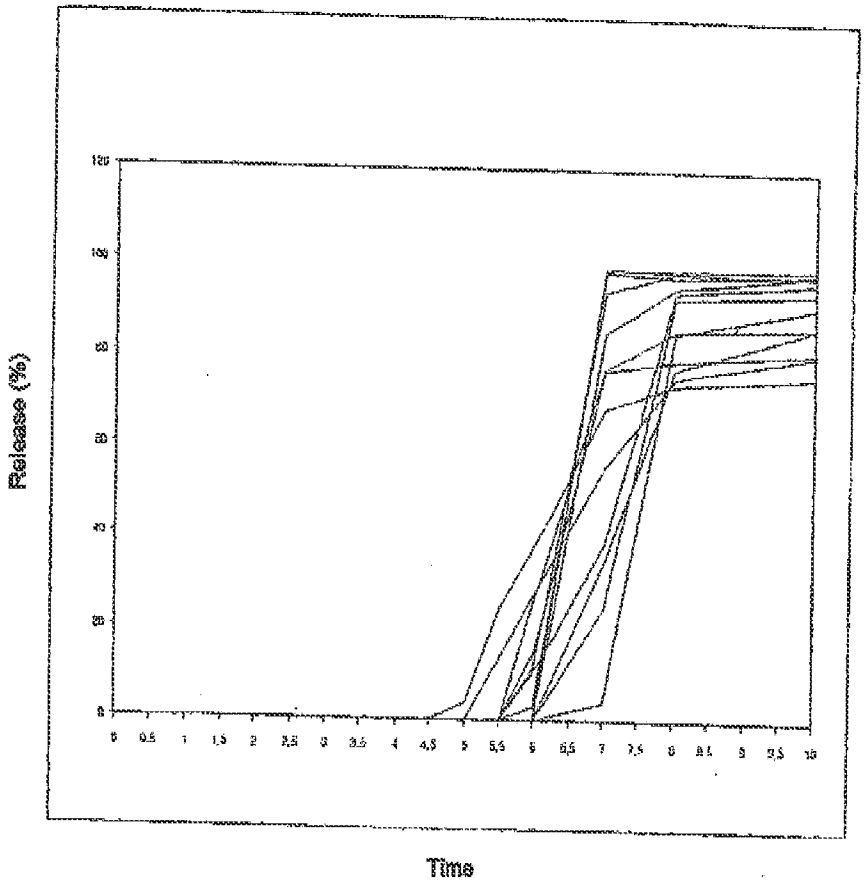
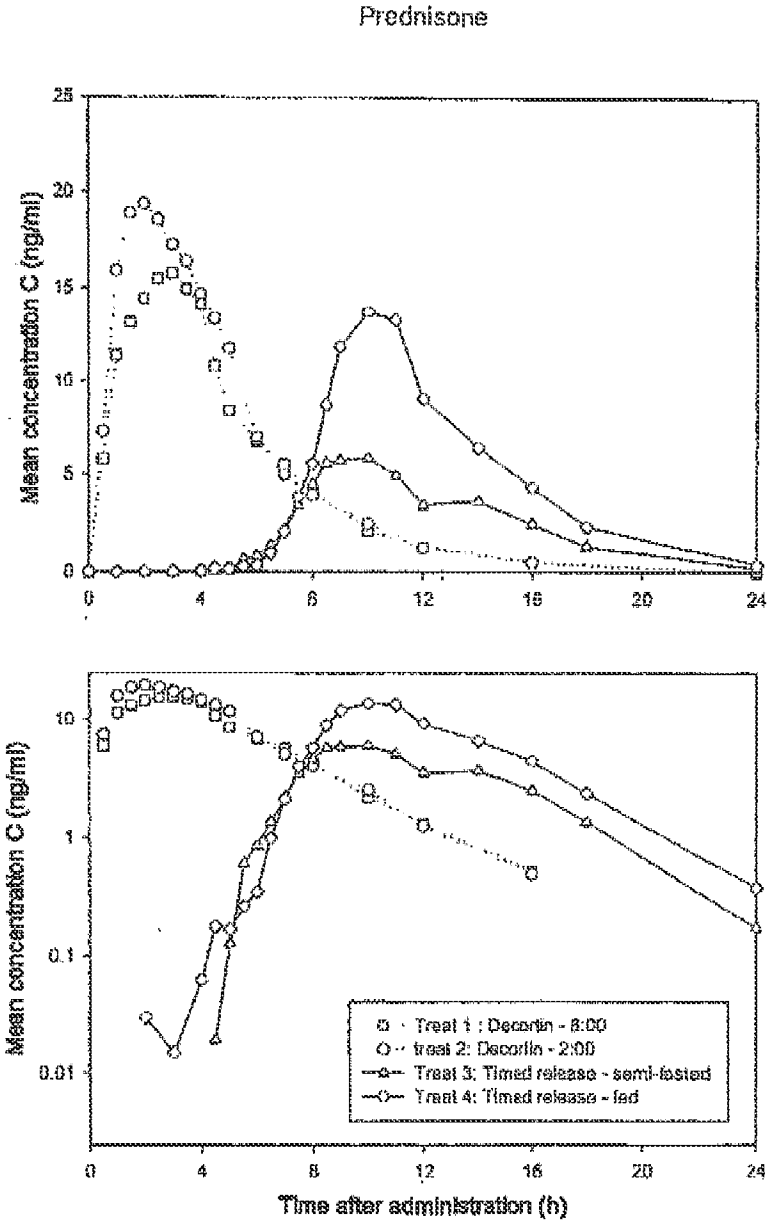


Figure 5



INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/009726

A. CLASSIFICATION OF SUBJECT MATTER
A61K9/28 A61K31/573

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, EMBASE, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/072033 A (PENWEST PHARMACEUTICALS CO; BAICHWAL, ANAND, R; WOODCOCK, PAUL; HIGGIN) 19 September 2002 (2002-09-19) cited in the application examples 37-39 claims 1,45	1-110
X	WO 01/68056 A (MERCK PATENT GMBH; ZOBEL, HANS-PETER; SCHAEFFLER, ACHIN; KRAUS, EDGAR;) 20 September 2001 (2001-09-20) cited in the application page 5, line 26 - line 34 table 2 claims 1,3,5,7	1-110

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 November 2005	01/12/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hedegaard, A

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/009726

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96/40078 A (CIBUS PHARMACEUTICAL, INC) 19 December 1996 (1996-12-19) page 26, line 4 - line 31 examples 1,3 claims 14,21,23-25,37,51	1-110
P,X	WO 2004/093850 A (JAGOTEC AG; VERGNAULT, GUY; GRENIER, PASCAL; DRAGAN, CHRISTOPHE) 4 November 2004 (2004-11-04) page 9, line 14 - page 13, line 24 example 1 claim 1	1-110
P,X	WO 2005/027843 A (PENWEST PHARMACEUTICALS CO; BAICHWAL, ANAND, R; WOODCOCK, PAUL; LABUDZ) 31 March 2005 (2005-03-31) examples 7-12 claims 1,5,6	1-110
A	EP 1 275 381 A (YAMANOUCHI PHARMACEUTICAL CO. LTD) 15 January 2003 (2003-01-15) cited in the application the whole document	1-110
A	LIN K-H ET AL: "Compression forces and amount of outer coating layer affecting the time-controlled disintegration of the compression-coated tablets prepared by direct compression with micronized ethylcellulose" JOURNAL OF PHARMACEUTICAL SCIENCES, AMERICAN PHARMACEUTICAL ASSOCIATION. WASHINGTON, US, vol. 90, no. 12, December 2001 (2001-12), pages 2005-2009, XP002299256 ISSN: 0022-3549 the whole document	1-110
A	CONTE U ET AL: "PRESS-COATED TABLETS FOR TIME-PROGRAMMED RELEASE OF DRUGS" BIOMATERIALS, ELSEVIER SCIENCE PUBLISHERS BV., BARKING, GB, vol. 14, no. 13, 1 October 1993 (1993-10-01), pages 1017-1023, XP000404245 ISSN: 0142-9612 the whole document	1-110

Form PCT/ISA/210 (continuation of second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/009726

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 02072033	A	19-09-2002	CA	2440588 A1	19-09-2002
			CA	2440641 A1	19-09-2002
			CN	1499960 A	26-05-2004
			EP	1368000 A2	10-12-2003
			EP	1368005 A2	10-12-2003
			JP	2004529902 T	30-09-2004
			JP	2005500255 T	06-01-2005
			MX	PA03008292 A	11-12-2003
			MX	PA03008293 A	11-12-2003
			WO	02072034 A2	19-09-2002
WO 0168056	A	20-09-2001	AU	4247001 A	24-09-2001
			DE	10012555 A1	20-09-2001
WO 9640078	A	19-12-1996	AT	280572 T	15-11-2004
			AU	6163096 A	30-12-1996
			CA	2224170 A1	19-12-1996
			DE	69633721 D1	02-12-2004
			EP	0831791 A1	01-04-1998
			ES	2231815 T3	16-05-2005
			JP	11507357 T	29-06-1999
			PT	831791 T	28-02-2005
WO 2004093850	A	04-11-2004	NONE		
WO 2005027843	A	31-03-2005	NONE		
EP 1275381	A	15-01-2003	AU	4876901 A	30-10-2001
			WO	0178686 A1	25-10-2001

Form PCT/ISA/210 (patent family annex) (January 2004)

Electronic Acknowledgement Receipt

EFS ID:	18993227
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	09-MAY-2014
Filing Date:	24-FEB-2011
Time Stamp:	16:43:33
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Non Patent Literature	AssessmentReport_2011.pdf	4441995 6a0d6999bc695824cd4fc42ca4db3beb35ceee56	no	78

Warnings:	
Information:	

2	Non Patent Literature	Auchus_2001.pdf	4644529 e26187a71e1c9d9fecef8a639e9ea7b1d0522cbb	no	19
Warnings:					
Information:					
3	Non Patent Literature	Ayub_1987.pdf	1962615 fa8ff92f55eaef87564c7925738851b0dc50ba97	no	11
Warnings:					
Information:					
4	Non Patent Literature	CampbellWalsh.pdf	12774923 700b960795a8c041f3bd53c058e6b2e4d9a329c2	no	40
Warnings:					
Information:					
5	Non Patent Literature	CecilTxtbk.pdf	779168 e687aa70297a63e2be83746d01b02c61db035f0c	no	7
Warnings:					
Information:					
6	Non Patent Literature	USSecurExchComm_10QSB.pdf	1816157 45f820ffce7383db91adacc98d562b111454ee04	no	21
Warnings:					
Information:					
7	Non Patent Literature	Czock_2005.pdf	8309949 31384c0b3ac0eb9a9cfa83a129f7cd95774bf785	no	38
Warnings:					
Information:					
8	Foreign Reference	EP2478907.pdf	426924 7ed5058ce5d846311c059ba6e0ad449a69726bbe	no	26
Warnings:					
Information:					
9	Non Patent Literature	ErgunLongmire_2006.pdf	1196214 219b4c1316e0c9d2ee1406400a4cd8b1edf7a075	no	4
Warnings:					
Information:					
10	Non Patent Literature	Fakih_2002.pdf	2280887 610b25334cd45b21adffb9eafe4772d4c4a2fbea	no	9
Warnings:					
Information:					

11	Non Patent Literature	Friel_11_1_2006.pdf	1784502 1e0b89563448e523e7f2ba5426311d70fad9f4ef	no	7
Warnings:					
Information:					
12	Non Patent Literature	InternetArticle_X501.pdf	964281 6a60cdb55f2035a0b2ba293423cdfc5a1bc287ad	no	6
Warnings:					
Information:					
13	Non Patent Literature	InternetArticle_2007_6_11.pdf	670778 7fdd951a5e297747d0f90e0eb824c926e5b05108	no	5
Warnings:					
Information:					
14	Non Patent Literature	Info_1183238_2014.pdf	148473 0157bd61b36ec6b827db0ccfcf6ef673110516e1	no	1
Warnings:					
Information:					
15	Non Patent Literature	Mostaghel_2014.pdf	3637858 60fde2076472b177dd9ec08dbb2d3f7001a39201	no	13
Warnings:					
Information:					
16	Non Patent Literature	Osaba_1999.pdf	2121329 961f2d29a3477f8676481d3579307b0c2ff2a48e	no	10
Warnings:					
Information:					
17	Non Patent Literature	Petrylak_2007.pdf	2712885 ed629c08b29e6cd48a7164d0f64b264e836693c5	no	10
Warnings:					
Information:					
18	Non Patent Literature	Prostate_Ch93.pdf	5268997 fb67d7a601a31087dccc28ef009cc1bf4de6123d	no	17
Warnings:					
Information:					
19	Non Patent Literature	Reid_18_9_2007.pdf	757035 e17948f6c5abc249bc06a887966a8821f5168966	no	6
Warnings:					
Information:					

20	Non Patent Literature	Remington_2000.pdf	864892 7a84513387c1f5fc9a10f38cf47a041fa4d243e1	no	11
Warnings:					
Information:					
21	Non Patent Literature	Runge_2006.pdf	1369044 4bdd2c2b9ed4e4c7f19315390a0db2db0c013f5c	no	5
Warnings:					
Information:					
22	Non Patent Literature	Sills_1981.pdf	1901937 f1c833f8f02195978567de00d18d47cd579cc223	no	7
Warnings:					
Information:					
23	Non Patent Literature	SummaryofProductClear.pdf	2742116 0369a35a017d6d15916a1a1886e5dc85bd358dd7	no	14
Warnings:					
Information:					
24	Non Patent Literature	Tannock_456.pdf	50166 1cb2bfd28674938bc92d907e7611da9606678170	no	1
Warnings:					
Information:					
25	Non Patent Literature	ReplyApplic_06042013.pdf	1015955 1b6dadd0caf55f90f05ef8a5be193452ddf3bc9c	no	9
Warnings:					
Information:					
26	Non Patent Literature	Wang_1978.pdf	1164818 0b3cdc4ae12542d33cbaf93321541578f4733601	no	5
Warnings:					
Information:					
27	Foreign Reference	WO2006027266.pdf	1999067 1e2b67e156f9c8a98079eba5d4c9f311551d76da	no	54
Warnings:					
Information:					
28	Non Patent Literature	Yano_12_2006.pdf	2306451 7ce13f914da62f41a1e07c823815b8854334d26a	no	8
Warnings:					
Information:					

29	Other Reference-Patent/App/Search documents	Opponent_ActavisGrp.pdf	676699 b6f200140fe2db21dec9b66173e5fa6caac5b476	no	6
Warnings:					
Information:					
30	Other Reference-Patent/App/Search documents	Opponent_AlfredTiefenbacher.pdf	134477 4bb55102b45b8caccfe9ee647bd9f3d6e7a1753b	no	5
Warnings:					
Information:					
31	Other Reference-Patent/App/Search documents	Opponent_AlisonGallafent.pdf	1198019 2238d26e696a5159449e4ab202896825834efe88	no	37
Warnings:					
Information:					
32	Other Reference-Patent/App/Search documents	Opponent_ArnoldSiedsma.pdf	1411262 87949a632592c184245140a39b6954467632916b	no	19
Warnings:					
Information:					
33	Other Reference-Patent/App/Search documents	Opponent_CabinetLavoix.pdf	155432 4685351c853a3cfcf77cbf3a5bfde95af4bf52f7	no	6
Warnings:					
Information:					
34	Other Reference-Patent/App/Search documents	Opponent_GalenicumHealth.pdf	675270 e1cc89d6304b15e3a75bfd51964eb4d2a292060d	no	6
Warnings:					
Information:					
35	Other Reference-Patent/App/Search documents	Opponent_GenericsLtd.pdf	144213 3dcb5471a8d62bbfe0c8aa707879f9ba51d8bedc	no	6
Warnings:					
Information:					
36	Other Reference-Patent/App/Search documents	Opponent_HelmAG.pdf	134067 84811de1c3228f6152c0aa7defd0eced2e395165	no	5
Warnings:					
Information:					
37	Other Reference-Patent/App/Search documents	Opponent_HeteroDrugs.pdf	118619 549182001e1cca579031432d96b342d9137e69b9	no	5
Warnings:					
Information:					

38	Other Reference-Patent/App/Search documents	Opponent_IsenbruckBosl.pdf	1122897 a8e9a46b281c7c22f0cef44aba9acbc558c8220c	no	24
Warnings:					
Information:					
39	Other Reference-Patent/App/Search documents	Opponent_LaboratoriosLeon.pdf	101596 fa42e343215b21929a665e1a83ebfd63f83f87a8	no	4
Warnings:					
Information:					
40	Other Reference-Patent/App/Search documents	Opponent_Maiwald.pdf	130840 04c7f21d1c8d341e78d5307cd9c80ee1aadcbdd7	no	5
Warnings:					
Information:					
41	Other Reference-Patent/App/Search documents	Opponent_StadaArzneimittel.pdf	734323 ae843daffe97832e99bafc05d0ecf5c12cab761a	no	16
Warnings:					
Information:					
42	Other Reference-Patent/App/Search documents	Opponent_SynthonBV.pdf	487328 195991fff00319b8fb870d208ec2a8cd432cb41a	no	5
Warnings:					
Information:					
43	Other Reference-Patent/App/Search documents	Opponent_Teva.pdf	1268798 6013c8088164726842942cd61b9adc8e0f93efb2	no	27
Warnings:					
Information:					
44	Other Reference-Patent/App/Search documents	Opponent_Zentiva.pdf	102185 fef1351d84190f4bf36087885191977f9bd31c71a	no	4
Warnings:					
Information:					
		Total Files Size (in bytes):	78709970		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13034340
Filing Date	2011-02-24
First Named Inventor	Alan H. Auerbach
Art Unit	1621
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐
	2							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

NON-PATENT LITERATURE DOCUMENTS

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13034340
Filing Date	2011-02-24
First Named Inventor	Alan H. Auerbach
Art Unit	1621
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Carducci, M.A., "What is more exciting? The Activity of Docetaxel in Early Prostate Cancer or the Successful Collaboration between Urologists and Medical Oncologists to complete a study in early Prostate Cancer?", Journal of Clinical Oncology (2005), Vol. 23, No. 15, pg. 3304-3307	☐
	2	Sahu, B., et al., "FoxA1 Specifies Unique Androgen and Glucocorticoid Receptor Binding Events in Prostate Cancer Cells", Cancer Research (2013), Vol. 73, pg. 1570-1580	☐
	3	Storlie, J.A., et al., "Prostate Specific Antigen Levels and Clinical Response to Low Dose Dexamethasone for Hormone-Refractory Metastatic Prostate Carcinoma", Cancer (1995) Vol. 76, No. 1, pg. 96-100	☐
	4	Tanagho, E.A., et al., "The Leading Single-Volume Resource in Urology", Smith's General Urology, 16th Edition, (2004), Chapter 19, pgs. 321-323; Chapter 22, pgs. 380-385	☐
	5	Tomic, R., et al., "Hormonal Effects of High Dose Medroxyprogesterone Acetate Treatment in Males with Renal or Prostatic Adenocarcinoma", (1988), Vol. 22 (1), Abstract	☐
	6	Venkitaraman, R., et al., "Efficacy of Low-Dose Dexamethasone in Castration-Refractory Prostate Cancer", BJU Int (2008), 101, pgs 1756-1764	☐
	7	Vogelzang, N.J., Curriculum Vitae, 15 pages	☐
	8	Yano, A., et al., "Glucocorticoids Suppress Tumor Lymphangiogenesis of Prostate Cancer Cells", Clin Cancer Res (2006), Vol. 12, pgs. 6012-6017	☐
	9		☐
	10		☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	Alan H. Auerbach
	Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	11		☐
	12		☐
	13		☐
	14		☐
	15		☐
	16		☐
	17		☐
	18		☐
	19		☐
	20		☐
	21		☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	Alan H. Auerbach
	Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	22		☐
	23		☐
	24		☐
	25		☐
	26		☐
	27		☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	Alan H. Auerbach
	Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☒ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Timothy E. Tracy, Reg. No. 39,401/	Date (YYYY-MM-DD)	2014-05-30
Name/Print	Timothy E. Tracy	Registration Number	39,401

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

SUBMISSION UNDER MPEP 609.06 Page 1 of 1		
	Confirmation Number	1597
	Application Number	13/034340
	Filing Date	02-24-2014
	First Named Inventor	Alan H. Auerbach
	Group Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	U.S. Patent Document Number	Kind Code[2] (if known)	Pages, Columns, Lines, where relevant passages or relevant figures appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	Foreign Patent Document Office[3]	Number[4]	KindCode[5]	Pages, Columns, Lines, where relevant passages or relevant figures appear	T[6]

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner 's Initials*	Cite No.[1]	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Declaration by Dr. Jacqueline Anne Warner in the matter of Opposition by Northern Rivers Pty Ltd., 25 pages	
		Declaration by Helen Grimes in the matter of Opposition by Northern Rivers Pty Ltd., 43 pages	

Examiner Signature		Date Considered	

Electronic Patent Application Fee Transmittal

Application Number:	13034340
Filing Date:	24-Feb-2011
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
		Total in USD ($)		**180**

Electronic Acknowledgement Receipt

EFS ID:	19171888
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	30-MAY-2014
Filing Date:	24-FEB-2011
Time Stamp:	14:58:28
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$180
RAM confirmation Number	1453
Deposit Account	100750
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	CGR5001USCNT1_1449_30May14.pdf	73001 43dfafd7bad050c70f24add78930e8208c7d13d7	no	6
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
2	Other Reference-Patent/App/Search documents	CGR5001USCNT1_MPEP609_30May14.pdf	203475 2ef92356ba2e401ee2ef51b770cad48e7dc36251	no	1
Warnings:					
Information:					
3	Non Patent Literature	Sahu_2013_73_1570_1570.pdf	1123627 df7a9085fc2fd1a36111da1b84c57551578904a1	no	12
Warnings:					
Information:					
4	Non Patent Literature	Tomic_1988_22_15_18.pdf	104749 759f2154223d543c4b38eb31e97bb16a3b4ce048	no	1
Warnings:					
Information:					
5	Non Patent Literature	Venkitaraman_2008_101_440_3.pdf	79767 9c79ee4b4dafb439b5066ca0a9ac4c5ada74016e	no	4
Warnings:					
Information:					
6	Non Patent Literature	Yano_2006_12_6012_6017.pdf	326833 49b4587b5cc2a2b4122a08358f58d0c49c920c12	no	7
Warnings:					
Information:					
7	Non Patent Literature	Carducci_2005.pdf	480737 2e28aaa66dc823cc443cb024269b8c292e562b85	no	4
Warnings:					
Information:					

8	Non Patent Literature	Storlie_1995.pdf	1525035 c25d21e6d62cb2b29b9d25be7d6bd274ba7a76e4	no	5
Warnings:					
Information:					
9	Non Patent Literature	Tanagho_2004.pdf	1400532 afef92d88f9a23c9c479b15f7f2e6ca50c6f1b63	no	12
Warnings:					
Information:					
10	Non Patent Literature	Vogelzang_Vitae.pdf	1121068 9833f6fe7cec6bf9c2b238dbdb8b16fb331f90ed	no	15
Warnings:					
Information:					
11	Other Reference-Patent/App/Search documents	Declaration_of_HelenGrimes.pdf	133729 757762fd188b50f74ecb0c040812737de9a5dadb	no	4
Warnings:					
Information:					
12	Other Reference-Patent/App/Search documents	Declaration_of_JacquelineWarner.pdf	1575244 2702cbb45300ffe6463af70d90a689e53224a56e	no	25
Warnings:					
Information:					
13	Fee Worksheet (SB06)	fee-info.pdf	30339 d28b17fbe446c6b65442889397e243925fdb2f6f	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	8178136	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

27777 7590 06/02/2014

BERNARD F. PLANTZ
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1621	

DATE MAILED: 06/02/2014

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR TREATING CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$960	$0	$0	$960	09/02/2014

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

27777 7590 06/02/2014
BERNARD F. PLANTZ
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR TREATING CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$960	$0	$0	$960	09/02/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
HUI, SAN MING R	1621	514-170000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
❑ Issue Fee
❑ Publication Fee (No small entity discount permitted)
❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
❑ A check is enclosed.
❑ Payment by credit card. Form PTO-2038 is attached.
❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
❑ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
❑ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
❑ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 06/02/2014

BERNARD F. PLANTZ
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1621	

DATE MAILED: 06/02/2014

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 13/034,340	Applicant(s) AUERBACH ET AL.	
	Examiner SAN-MING HUI	Art Unit 1621	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *5/9/2014*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *37-56*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☒ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/SAN-MING HUI/
Primary Examiner, Art Unit 1621

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 5/9/2014 has been entered.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: the herein claimed method of treating prostate cancer is essentially the same as the notice of allowance mailed 2/11/2014. The commercial success of the combination of prednisone and abiraterone to treat prostate cancer obviate the rejection under 35 USC 103(a).

Claims 37-56 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAN-MING HUI whose telephone number is (571)272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Melenie McCormick can be reached on (571) 272-8037. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1621

/SAN-MING HUI/
Primary Examiner, Art Unit 1621

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	Art Unit
	SAN-MING HUI	1628

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
514	170, 182	1/27/11	SH
514	170, 182	9/5/12	SH
514	170, 182	2/25/13	SH
514	170, 182	6/28/13	SH
514	170, 182	10/21/13	SH
514	170, 182	1/29/14	SH
514	170, 182	5/19/14	SH

SEARCH NOTES		
Search Notes	Date	Examiner
EAST search and inventor search in PALM	1/27/11	SH
EAST search and inventor search in PALM	9/5/12	SH
EAST search and inventor search in PALM	2/25/13	SH
EAST search and inventor search in PALM	6/28/2013	SH
EAST search and inventor search in PALM	10/21/13	SH
EAST search and inventor search in PALM	1/29/14	SH
EAST search and inventor search in PALM	5/19/14	SH

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

INTERFERENCE SEARCH			
US Class/ CPC Symbol	**US Subclass / CPC Group**	**Date**	**Examiner**
514	170, 182	6/28/13	SH
514	170, 182	10/21/13	SH
514	170, 182	1/29/14	SH
514	170, 182	5/19/2014	SH

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L5	2624	abiraterone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L6	3	prdnisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L7	35549	prednisone	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L8	155540	prostate	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L9	2183	L5 and L8	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L10	170	L5 same L8	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L11	1342	514/170.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L12	2924	514/182.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L13	528262	cancer	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L14	2571	L5 and L13	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L15	1345	L5 same L13	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L16	0	"9320097".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L17	2	"9509178".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40
L18	0	"9509178".pn. and L13	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2014/05/19 13:40

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2392	514/182.ccls.	US-PGPUB; USPAT	OR	ON	2014/05/19 13:40
L2	1081	514/170.ccls.	US-PGPUB; USPAT	OR	ON	2014/05/19 13:40
L3	2392	514/182.ccls.	US-PGPUB; USPAT	OR	ON	2014/05/19 13:40
L4	1081	514/170.ccls.	US-PGPUB; USPAT	OR	ON	2014/05/19 13:40
L19	2392	514/182.ccls.	US-PGPUB; USPAT	OR	ON	2014/05/19 13:40
L20	1081	514/170.ccls.	US-PGPUB; USPAT	OR	ON	2014/05/19 13:40
L21	2392	514/182.ccls.	US-PGPUB; USPAT	OR	ON	2014/05/19 13:40
L22	1081	514/170.ccls.	US-PGPUB; USPAT	OR	ON	2014/05/19 13:40

5/19/2014 1:42:17 PM
C:\Users\shui\Documents\EAST\Workspaces\13-034340.wsp

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13034340
Filing Date	2011-02-24
First Named Inventor	Alan H. Auerbach
Art Unit	1621
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20060030608	A1	2006-02-09	Nelson, et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2478907	EP		2012-07-25	Cougar Biotechnology, Inc.		☐
	2	2006027266	WO		2006-03-16	Nitec Pharma AG		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

NON-PATENT LITERATURE DOCUMENTS

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13034340
Filing Date	2011-02-24
First Named Inventor	Alan H. Auerbach
Art Unit	1621
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Assessment Report for Zytiga (abiraterone) published 2011 by the CHMP of the EMA	☐
	2	AUCHUS, R.J., "The genetics, pathophysiology, and the management of human deficiencies of P450c17", Endocrinol Metab Clin North Am (2001), 30, p.101-119	☐
	3	AYUB, M., "Inhibition of testicular 17a-hydroxylase and 17,20-lyase but not 3B-hydroxysteroid dehydrogenase-isomerase or 17B-hydroxysteroid oxidoreductase by ketoconazole and other imidazole drugs, Journal of Steroid Biochemistry (1987) 28(5), p.521-531	☐
	4	Campbell-Walsh Urology, Ninth Edition, Saunders, Vol. 3, Chapters 104 and 105 2007	☐
	5	Cecil Textbook of Medicine, Wyngaarden & Smith 18th edition; Chapter on "Glucocorticosteroid Therapy", Wyngaarden & Smith 18th edition, (1988) p.128-131	☐
	6	Cougar Biotechnology Inc. with the U.S. Securities and Exchange Commission, Form 10-QSB 2013	☐
	7	CZOCK, et al., "Pharmacokinetics and Pharmacodynamics of Systemically Administered Glucocorticoids", Pharmacokinet (2005), 44(1), p.61-98	☐
	8	ERGUN-LONGMIRE, Berrin, et al., "Two Novel Mutations Found in a Patient with 17a-Hydroxylase Enzyme Deficiency", The Journal of Clinical Endocrinology & Metabolism (2006), 91(10), p.4179-4182	☐
	9	FAKIH, et al., Urology (2002) 60, p.553-561	☐
	10	FRIEL, Patrick N., et al., "Suppression of adrenal function by low-dose prednisone: assessment with 24-hour urinary steroid hormone profiles-A review of five cases", Alternative Medicine Review (2006), 11(1)	☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	Alan H. Auerbach
	Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	11	Internet article: http://clinicaltrials.gov/archive/NCT00485303/2007_06_11	☐
	12	Information concerning Zytiga (abiraterone acetate) from http://www.kompendium.ch/prod/pnr/1183238/de?Platform=Desktop as of March 25, 2014	☐
	13	Internet article: http://clinicaltrials.gov/ct2/show/study/NCT00485303?sec=X501 2014	☐
	14	MOSTAGHEL, E.A., "Abiraterone in the treatment of metastatic castration-resistant prostate cancer", Cancer Management Res. (2014) 6, p.39-51	☐
	15	OSABA, D., et al., "Health-Related Quality of Life in Men with Metastatic Prostate Cancer Treated with Prednisone alone or Mitoxantrone and Prednisone", J. Clin. Oncol. (1999), 17(6), p.1654-1663	☐
	16	PETRYLAK, D.P., "New Paradigms for Advanced Prostate Cancer", Rev. Urol. (2007), 9, Suppl. 2, S3-S12	☐
	17	Prostate Cancer Principles and Practice, Taylor & Francis (2006) Chapter 93	☐
	18	REID, A., et al., "Annals of Oncology", Educational and Abstract Book of the ESMO Conference Lugano (ECLU), (2007), 18(Supplement 9), ix173-ix174. Abstract 50PD	☐
	19	REMINGTON, "The Science and Practice of Pharmacy, 20th Edition (2000), p.1363-1370	☐
	20	RUNGE, Marschall S., et al., "Principles of Molecular Medicine; Second edition; (2006) Humana Press Inc. ISBN: 1-58829-202-9. pgs.365-376 and 482-484	☐
	21	SILLS, Irene N., et al., "17a-hydroxylase deficiency in a genetic male and female sibling pair", Int. J. Gynaecol. Obstet., (1981), 19, p.473-479	☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	Alan H. Auerbach
	Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	22	Summary of Product Characteristics for Zytiga 250mg tablets (16Jan2014)	☐
	23	TANNOCK., et al., "Docetaxel Plus Prednisone or Mitoxantrone Plus Prednisone for Advanced Prostate Cancer", Journal of Urology (2005), 173(2), p.456	☐
	24	The reply of applicant (i.e. the Proprietor of herein opposed patent) dated June 4, 2013 in relation to the corresponding US2011/0144016A1 US proceedings.	☐
	25	WANG, C., et al., "Hypertension due to 17a-Hydroxylase deficiency", Australian and New Zealand Journal of Medicine (1978), 8(3), p.295-299	☐
	26	YANO, A., et al., "Glucocorticoids Suppress Tumor Angiogensis and In vivo Growth of Prostate Cancer Cells", Clin. Cancer Res., (2006) 12, 3003-3009	☐
	27		☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature	/San Ming Hui/	Date Considered	05/19/2014

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

SUBMISSION UNDER MPEP 609.06 Page 1 of 1		
	Confirmation Number	1597
	Application Number	13/034340
	Filing Date	02-24-2014
	First Named Inventor	Alan H. Auerbach
	Group Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	U.S. Patent Document Number	Kind Code[2] (if known)	Pages, Columns, Lines, where relevant passages or relevant figures appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	Foreign Patent Document Office[3]	Number[4]	KindCode[5]	Pages, Columns, Lines, where relevant passages or relevant figures appear	T[6]

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner 's Initials*	Cite No.[1]	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Statement of Opposition, Actavis Group PTC ehf 2014	
		Statement of Opposition, Alfred E. Tiefenbacher 2014	
		Statement of Opposition, Alison Gallafent 2014	
		Statement of Opposition, Arnold Siedsma 2014	
		Statement of Opposition, Cabinet Lavoix 2014	
		Statement of Opposition, Galenicum Health, S.L. 2014	
		Statement of Opposition, Generics Ltd. 2014	
		Statement of Opposition, Helm AG 2014	
		Statement of Opposition, Hetero Drugs 2014	
		Statement of Opposition, Isenbruck Bosl Horschler LLP 2014	
		Statement of Opposition, Laboratorios Leon Farma, S.A. 2014	
		Statement of Opposition, Maiwald Patentanwalts GmbH 2014	
		Statement of Opposition, Stada Arzneimittel 2014	
		Statement of Opposition, Synthon B.V. 2014	
		Statement of Opposition, Teva Pharmaceutical Industries, Ltd. 2014	
		Statement of Opposition, Zentiva k.s. 2014	

Examiner Signature	/San Ming Hui/	Date Considered	05/28/2014

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

CPC						
Symbol					**Type**	**Version**
A61K		31	/	58	F	2013-01-01
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			

CPC Combination Sets							
Symbol					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	20	
/SAN-MING HUI/ Primary Examiner.Art Unit 1621	05/19/2014	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	1

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
514	170	A	6	1	K	31 / 56 (2006.0)						

CROSS REFERENCE(S)					
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)				
514	180				

NONE	Total Claims Allowed:
(Assistant Examiner) (Date)	20

/SAN-MING HUI/ Primary Examiner.Art Unit 1621	05/19/2014	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	1

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13034340	AUERBACH ET AL.
	Examiner	**Art Unit**
	SAN-MING HUI	1629

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 20	
/SAN-MING HUI/ Primary Examiner.Art Unit 1621 (Primary Examiner)	05/19/2014 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 1

SUPPLEMENTAL SUBMISSION UNDER MPEP 609.06 Page 1 of 1		
	Confirmation Number	1597
	Application Number	13/034340
	Filing Date	02-24-2011
	First Named Inventor	Alan H. Auerbach
	Group Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	U.S. Patent Document Number	Kind Code[2] (if known)	Pages, Columns, Lines, where relevant passages or relevant figures appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	Foreign Patent Document Office[3]	Number[4]	KindCode[5]	Pages, Columns, Lines, where relevant passages or relevant figures appear	T[6]

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Statement of Opposition, Actavis Group PTC ehf	
		Statement of Opposition, Alfred E. Tiefenbacher (translated in English)	
		Statement of Opposition, Arnold Siedsma (Synthon B.V.)	
		Statement of Opposition, Cabinet Lavoix	
		Statement of Opposition, Galenicum Health, S.L.	
		Statement of Opposition, Generics Ltd.	
		Statement of Opposition, Helm AG (translated in English)	
		Statement of Opposition, Hetero Drugs	
		Statement of Opposition, Laboratorios Leon Farma, S.A.	
		Statement of Opposition, Maiwald Patentanwalts GmbH	
		Statement of Opposition, Stada Arzneimittel AG (translated in English)	
		Statement of Opposition, Teva Pharmaceutical Industries, Ltd.	

Examiner Signature		Date Considered	

Electronic Acknowledgement Receipt

EFS ID:	19282963
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	12-JUN-2014
Filing Date:	24-FEB-2011
Time Stamp:	11:11:00
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	CGR5001USCNT1_SuppMPEP609_12Jun14.pdf	204621 69ece94da8c78f79d0d28e786715a4b0ed70bc7d	no	1

Warnings:	
Information:	

This is not an USPTO supplied IDS fillable form					
2	Foreign Reference	Opponent_ActavisGrp.pdf	628073 450d2cbf2529b30ff6a2decf0939beaab9ef7cad	no	18
Warnings:					
Information:					
3	Foreign Reference	Opponent_AlfredTiefenbacher.pdf	2055954 a6a8437651fee4e3722ea3db9626b1cdd19694a6	no	17
Warnings:					
Information:					
4	Foreign Reference	Opponent_AlfredETiefenbacher_EnglishVer.pdf	404067 0477fc11b036a6124d1fcc8acb885e7126185dcc	no	16
Warnings:					
Information:					
5	Foreign Reference	Opponent_CabinetLavoix.pdf	1403294 3b15069783beda31a11838add32756032738bbda	no	24
Warnings:					
Information:					
6	Foreign Reference	Opponent_GalenicumHealth.pdf	2994233 2ba4774e306c363544bb55e432c3c3f27fce9d38	no	14
Warnings:					
Information:					
7	Foreign Reference	Opponent_GenericsLtd.pdf	2398633 7d6a944cfef9bbf95733e92a3ef5dc57a0296de3	no	20
Warnings:					
Information:					
8	Foreign Reference	Opponent_HelmAG.pdf	2027216 09e77974dd44743005626 48d7ec0eeec7570bc49	no	17
Warnings:					
Information:					
9	Foreign Reference	Opponent_HelmAG_EnglishVer.pdf	417841 64529152861573dbd9dc2fedb72a888f76d0e8ea	no	13
Warnings:					
Information:					
10	Foreign Reference	Opponent_HeteroDrugs.pdf	2467365 06fd61e5d83f1fe32e7f9ee4044c34da2b00a3bb	no	28

Warnings:					
Information:					
11	Foreign Reference	Opponent_LaboratoriosLeon.pdf	730485 3fcffe0c4dc3d1db601704bf7fb8e494f82d3eb3	no	15
Warnings:					
Information:					
12	Foreign Reference	Opponent_ArnoldSiedsma_Synthon.pdf	1413143 05a2dac9a03a61f458b03e3233025f2095061a6d	no	19
Warnings:					
Information:					
13	Foreign Reference	Opponent_Maiwald.pdf	1941899 0ad2f5f632d07126061177fa084a8468a26b7f52	no	17
Warnings:					
Information:					
14	Foreign Reference	Opponent_StadaArzneimittelAG_EnglishVer.pdf	581088 2e6b4ba0fb3dec3fe11d959a9649baa474522bcc	no	16
Warnings:					
Information:					
15	Foreign Reference	Opponent_Teva.pdf	1269630 1f985319ddca2ef1bfb1e4ff1212b12750e6fb7e	no	27
Warnings:					
Information:					
		Total Files Size (in bytes):	20937542		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Electronic Patent Application Fee Transmittal

Application Number:	13034340
Filing Date:	24-Feb-2011
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
		Total in USD ($)		**180**

Electronic Acknowledgement Receipt

EFS ID:	19287470
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	12-JUN-2014
Filing Date:	24-FEB-2011
Time Stamp:	14:49:44
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$180
RAM confirmation Number	1854
Deposit Account	100750
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Fee Worksheet (SB06)	fee-info.pdf	30339 52568bbc1c12bc3cb650fd1fc09d94d64545807e	no	2

Warnings:

Information:

Total Files Size (in bytes):	30339

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 06/16/2014

BERNARD F. PLANTZ
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1621	

NOTIFICATION DATE	DELIVERY MODE
06/16/2014	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jnjuspatent@corus.jnj.com
lhowd@its.jnj.com
pair_jnj@firsttofile.com

UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office
Address : COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
13/034,340	24 February, 2011	AUERBACH ET AL.	CGR5001USCNT1

BERNARD F. PLANTZ
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
SAN-MING HUI	
ART UNIT	PAPER
1621	20140610

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

The information disclosure statement (IDS) submitted on 5/30/2014 was filed after thefiling of the Request for Continued Examination on 5/9/2014. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAN-MING HUI whose telephone number is (571)272-0626. The examiner can normally be reached on Mon - Fri from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Melenie McCormick can be reached on (571) 272-8037. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAN-MING HUI/
Primary Examiner, Art Unit 1621

PTO-90C (Rev.04-03)

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13034340
Filing Date	2011-02-24
First Named Inventor	Alan H. Auerbach
Art Unit	1621
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐
	2							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

NON-PATENT LITERATURE DOCUMENTS

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13034340
Filing Date	2011-02-24
First Named Inventor	Alan H. Auerbach
Art Unit	1621
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Carducci, M.A., "What is more exciting? The Activity of Docetaxel in Early Prostate Cancer or the Successful Collaboration between Urologists and Medical Oncologists to complete a study in early Prostate Cancer?", Journal of Clinical Oncology (2005), Vol. 23, No. 15, pg. 3304-3307	☐
	2	Sahu, B., et al., "FoxA1 Specifies Unique Androgen and Glucocorticoid Receptor Binding Events in Prostate Cancer Cells", Cancer Research (2013), Vol. 73, pg. 1570-1580	☐
	3	Storlie, J.A., et al., "Prostate Specific Antigen Levels and Clinical Response to Low Dose Dexamethasone for Hormone-Refractory Metastatic Prostate Carcinoma", Cancer (1995) Vol. 76, No. 1, pg. 96-100	☐
	4	Tanagho, E.A., et al., "The Leading Single-Volume Resource in Urology", Smith's General Urology, 16th Edition, (2004), Chapter 19, pgs. 321-323; Chapter 22, pgs. 380-385	☐
	5	Tomic, R., et al., "Hormonal Effects of High Dose Medroxyprogesterone Acetate Treatment in Males with Renal or Prostatic Adenocarcinoma", (1988), Vol. 22 (1), Abstract	☐
	6	Venkitaraman, R., et al., "Efficacy of Low-Dose Dexamethasone in Castration-Refractory Prostate Cancer", BJU Int (2008), 101, pgs 1756-1764	☐
	7	Vogelzang, N.J., Curriculum Vitae, 15 pages	☐
	8	Yano, A., et al., "Glucocorticoids Suppress Tumor Lymphangiogenesis of Prostate Cancer Cells", Clin Cancer Res (2006), Vol. 12, pgs. 6012-6017	☐
	9		☐
	10		☐

EFS Web 2.1.17

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13034340
Filing Date	2011-02-24
First Named Inventor	Alan H. Auerbach
Art Unit	1621
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

	11		☐
	12		☐
	13		☐
	14		☐
	15		☐
	16		☐
	17		☐
	18		☐
	19		☐
	20		☐
	21		☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13034340
	Filing Date	2011-02-24
	First Named Inventor	Alan H. Auerbach
	Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

	22		☐
	23		☐
	24		☐
	25		☐
	26		☐
	27		☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature	/San Ming Hui/	Date Considered	06/10/2014

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

SUBMISSION UNDER MPEP 609.06 Page 1 of 1		
	Confirmation Number	1597
	Application Number	13/034340
	Filing Date	02-24-2014
	First Named Inventor	Alan H. Auerbach
	Group Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	U.S. Patent Document Number	Kind Code[2] (if known)	Pages, Columns, Lines, where relevant passages or relevant figures appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	Foreign Patent Document Office[3]	Number[4]	KindCode[5]	Pages, Columns, Lines, where relevant passages or relevant figures appear	T[6]

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Declaration by Dr. Jacqueline Anne Warner in the matter of Opposition by Northern Rivers Pty Ltd., 25 pages 2004	
		Declaration by Helen Grimes in the matter of Opposition by Northern Rivers Pty Ltd., 43 pages 2004	

Examiner Signature	/San Ming Hui/	Date Considered	06/10/2014

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

7590 06/17/2014

BERNARD F. PLANTZ
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1621	

NOTIFICATION DATE	DELIVERY MODE
06/17/2014	ELECTRONIC

NOTICE OF NON-COMPLIANT INFORMATION DISCLOSURE STATEMENT

An Information Disclosure Statement (IDS) filed 6-12-14 in the above-identified application fails to meet the requirements of 37 CFR 1.97(d) for the reason(s) specified below. Accordingly, the IDS will be placed in the file, but the information referred to therein has not been considered.

The IDS is not compliant with 37 CFR 1.97(d) because:

☑ The IDS lacks a statement as specified in 37 CFR 1.97(e).

☐ The IDS lacks the fee set forth in 37 CFR 1.17(p).

☐ The IDS was filed after the issue fee was paid. Applicant may wish to consider filing a petition to withdraw the application from issue under 37 CFR 1.313(c) to have the IDS considered. See MPEP 1308.

571-272-4200 or 1-888-786-0101
Application Assistance Unit
Office of Data Management

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Alan H. Auerbach, et al.

Serial No. : 13/034,340 Art Unit: 1621

Filed : February 24, 2011 Examiner: San Ming R. Hui

For : METHODS AND COMPOSITIONS FOR TREATING CANCER

CERTIFICATE OF EFS TRANSMISSION I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted to the United States Patent and Trademark Office on the date shown below via the "Electronic Filing System" in accordance with 37 C.F.R. § 1.6(a)(4).		
Denise Mattos-Bosque	/Denise Mattos-Bosque/	June 24, 2014
Type or print name	Signature	Date

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT UNDER 37 C.F.R. §1.97(e)

In accordance with 37 C.F.R. §1.97(e), certification is hereby made that:

☒ Each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the Information Disclosure Statement; or

☐ No item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the undersigned after making reasonable inquiry, no item of information contained in this Information Disclosure Statement, was known to any individual designated in §1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

/Timothy E. Tracy/
Timothy E. Tracy
Reg. No. 39,401
Attorney for Applicants

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-6586
DATED: June 24, 2014

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Sheet 1 of 1

Confirmation Number	1597
Application Number	13/034,340
Filing Date	February 24, 2011
First Named Inventor	Alan H. Auerbach, et al.
Group Art Unit	1621
Examiner Name	San Ming R. Hui
Attorney Docket Number	CGR5001USCNT1

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement (See 37 CFR 1.97(e)(1)), or before the mailing date of a first Office Action on the merits of the above-identified application, or before the mailing date of a first Office Action after the filing of a request for continued examination under §1.114, no additional fee is required.

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ In accordance with §1.97(c), this Information Disclosure Statement is being filed after the period set forth in §1.97(b) above but before the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311, or an action that otherwise closes prosecution and that it is accompanied by one of:

Statement in Accordance with §1.97(e) (attached); or

Please charge Deposit Account No. 10-0750/ / the fee of $180.00 as set forth in §1.17(p).

☒ In accordance with §1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under under §1.113 or a Notice of Allowance under §1.311 but before the payment of the Issue Fee. Applicant(s) hereby petition(s) for consideration of this Information Disclosure Statement. Included are: Statement in Accordance with §1.97(e) as set forth herein.

☒ Any fee set forth in 37 CFR 1.17 (p) has been submitted with the filing of an MPEP 609.06 submission, filed on June 12, 2014. The Commissioner is hereby authorized to charge any additional fees which may be required in connection with the filing of this communication, or credit any overpayment, to Account No. 10-0750.

☐ Attached are copies of the statement(s) from any corresponding document(s), which are listed on the attached Submission Under MPEP 609.06.

☐ The relevance of those listed references which are not in the English language is as follows:

☒ Copies of copyrighted material were made and delivered to the government under license from Copyright Clearance Center, Inc. No further reproduction is permitted.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Timothy E. Tracy/	Date (YYYY-MM-DD)	June 24, 2014
Name/Print	Timothy E. Tracy	Registration Number	39,401

CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being electronically filed via EFS-Web to the Commissioner for Patents with the U.S. Patent and Trademark Office on: June 24, 2014

Name (print/type)	Denise Mattos-Bosque		
Signature	/Denise Mattos-Bosque/	Date	June 24, 2014

Electronic Acknowledgement Receipt

EFS ID:	19398192
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	24-JUN-2014
Filing Date:	24-FEB-2011
Time Stamp:	16:56:50
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	IDS_Stmtunder197e_24Jun14.pdf	270564 f51eecb8e6aab63fe5e049da23c87dbf8982e23c	no	1

Warnings:	
Information:	

This is not an USPTO supplied IDS fillable form					
2	Other Reference-Patent/App/Search documents	CGR5001USCNT1_MPEPCERT_24Jun14.pdf	246046 2c9c8e93b21390d3327f111349572d80e1b1cc26	no	1
Warnings:					
Information:					
			Total Files Size (in bytes):	516610	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

27777 7590 07/17/2014

BERNARD F. PLANTZ
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUI, SAN MING R	
ART UNIT	PAPER NUMBER
1621	

NOTIFICATION DATE	DELIVERY MODE
07/17/2014	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jnjuspatent@corus.jnj.com
lhowd@its.jnj.com
pair_jnj@firsttofile.com

UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office
Address : COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
13/034,340	24 February, 2011	AUERBACH ET AL.	CGR5001USCNT1

BERNARD F. PLANTZ
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
SAN-MING HUI	
ART UNIT	PAPER
1621	20140711

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

The information disclosure statement (IDS) submitted on 6/12/2014 was filed after the mailing date of the Notice of allowance on 6/2/2014. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

/SAN-MING HUI/
Primary Examiner, Art Unit 1621

PTO-90C (Rev.04-03)

SUPPLEMENTAL SUBMISSION UNDER MPEP 609.06 Page 1 of 1		
	Confirmation Number	1597
	Application Number	13/034340
	Filing Date	02-24-2011
	First Named Inventor	Alan H. Auerbach
	Group Art Unit	1621
	Examiner Name	San Ming R. Hui
	Attorney Docket Number	CGR5001USCNT1

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	U.S. Patent Document Number	Kind Code[2] (if known)	Pages, Columns, Lines, where relevant passages or relevant figures appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.[1]	Name of Patentee or Applicant of Cited Document	Foreign Patent Document Office[3]	Number[4]	KindCode[5]	Pages, Columns, Lines, where relevant passages or relevant figures appear	T[6]

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Statement of Opposition, Actavis Group PTC ehf	
		Statement of Opposition, Alfred E. Tiefenbacher (translated in English)	
		Statement of Opposition, Arnold Siedsma (Synthon B.V.)	
		Statement of Opposition, Cabinet Lavoix	
		Statement of Opposition, Galenicum Health, S.L.	
		Statement of Opposition, Generics Ltd.	
		Statement of Opposition, Helm AG (translated in English)	
		Statement of Opposition, Hetero Drugs	
		Statement of Opposition, Laboratorios Leon Farma, S.A.	
		Statement of Opposition, Maiwald Patentanwalts GmbH	
		Statement of Opposition, Stada Arzneimittel AG (translated in English)	
		Statement of Opposition, Teva Pharmaceutical Industries, Ltd.	

Examiner Signature	/San Ming Hui/	Date Considered	07/11/2014

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H./

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

27777 7590 02/11/2014
PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	02/24/2011	Alan H. Auerbach	CGR5001USCNT1	1597

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR TREATING CANCER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$960	$0	$0	$960	05/12/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
HUI, SAN MING R	1621	514-170000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: JANSSEN ONCOLOGY, INC.
(B) RESIDENCE: (CITY and STATE OR COUNTRY): LOS ANGELES, CA

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
- ☒ Issue Fee
- ☒ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number 10-0750 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ☐ Applicant certifying micro entity status. See 37 CFR 1.29
- ☐ Applicant asserting small entity status. See 37 CFR 1.27
- ☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Timothy E. Tracy/ Date July 28, 2014

Typed or printed name Timothy E. Tracy Registration No. 39,401

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Electronic Patent Application Fee Transmittal

Application Number:	13034340
Filing Date:	24-Feb-2011
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Utility Appl Issue Fee	1501	1	960	960
Publ. Fee- Early, Voluntary, or Normal	1504	1	0	0

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**960**

Electronic Acknowledgement Receipt

EFS ID:	19698682
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	28-JUL-2014
Filing Date:	24-FEB-2011
Time Stamp:	13:57:05
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$960
RAM confirmation Number	184
Deposit Account	100750
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Issue Fee Payment (PTO-85B)	USCNT1_Fee_Transm_28JUL14.pdf	99829 001626da778d9275c24b265cc7cd3a39d6aeaee3	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	31978 9ad3f1997a4bd31f5885c56e663a0979532612c0	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	131807	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/034,340	09/02/2014	8822438	CGR5001USCNT1	1597

27777 7590 08/13/2014

BERNARD F. PLANTZ
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Alan H. Auerbach, Hermosa Beach, CA;
Arie S. Belldegrum, Los Angeles, CA;

AO 120 (Rev. 08/10)

TO:	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
Mail Stop 8 **Director of the U.S. Patent and Trademark Office** **P.O. Box 1450** **Alexandria, VA 22313-1450**	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court Southern District of Florida on the following

☐ Trademarks or ☑ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
15-cv-81076-DMM	8/4/2015	Southern District of Florida

PLAINTIFF	DEFENDANT
BTG International Limited et al	Actavis Laboratories FL, Inc. et al

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	5.604.213	2/18/1997	See Attachment
2	8.822.438 B2	9/2/2014	See Attachment
3			
4			
5			

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1		
2		
3		
4		
5		

In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE
Steven M. Larimore	s/ Landys Rodriguez	8/4/2015

Copy 1—Upon initiation of action, mail this copy to Director Copy 3—Upon termination of action, mail this copy to Director
Copy 2—Upon filing document adding patent(s), mail this copy to Director Copy 4—Case file copy

US005604213A

United States Patent [19]

Barrie et al.

[11] **Patent Number: 5,604,213**

[45] **Date of Patent: Feb. 18, 1997**

[54] **17-SUBSTITUTED STEROIDS USEFUL IN CANCER TREATMENT**

[75] Inventors: **Susan E. Barrie**, Kent; **Michael Jarman**, London; **Gerard A. Potter**, Cheshire; **Ian R. Hardcastle**, Sutton, all of Great Britain

[73] Assignee: **British Technology Group Limited**, London, England

[21] Appl. No.: **315,882**

[22] Filed: **Sep. 30, 1994**

Related U.S. Application Data

[63] Continuation-in-part of PCT/GB93/00531 May. 15, 1993.

[30] **Foreign Application Priority Data**

Mar. 31, 1992	[GB]	United Kingdom	9207057
Nov. 27, 1992	[GB]	United Kingdom	9224880
Sep. 30, 1993	[GB]	United Kingdom	9320132
Jul. 14, 1994	[GB]	United Kingdom	9414192

[51] **Int. Cl.**[6] **A61K 31/58**; C07J 43/00

[52] **U.S. Cl.** **514/176**; 540/95

[58] **Field of Search** 540/95; 514/176

[56] **References Cited**

FOREIGN PATENT DOCUMENTS

288053 10/1988 European Pat. Off. .
413270 2/1991 European Pat. Off. .

OTHER PUBLICATIONS

M-J. Shiao, "New synthesis of Azabufalin from C-17 Steroidal Ketones", J. Org. Chem. 47, 5189-5191 (1982).

B. F. Hoffman, "The pharmacology of cardiac glycosides" in Cardiac therapy, ed. M. R. Rosen and B. F. Hoffman, Martinus Nijhoff Publishers (1983), Chapter 11, pp. 387-412.

R. Thomas et al., "Synthesis and Biological Activity of Semisynthetic Digitalis Analogs", J. Pharm. Sci. 63, 1649-1683 (1974).

T. Shigei and S. Mineshita, "Cardiotonic activities of four new compounds . . . ", Experientia 24, 466-467 (1968).

T. Shigei et al., "Structure-Activity Relationship of the Cardenolide . . . ", Experientia 29, 449-450 (1973).

M. Okada and Y. Saito, "Synthesis of 3 β-Hydroxy-5α-card-20 (22) enolide (14-Deoxy-14β-uzarigenin)", Chem. Pharm. Bull. 16, 2223-2227 (1968).

B. K. Naidoo et al., "Cardiotonic Steroids I: Importance of 14β-Hydroxy Group in Digitoxigenin" J. Pharm. Sci. 63, 1391-1394 (1974).

W. Schönfeld and K. R. H. Repke, "A Free-Wilson Analysis of 5β, 14β-Androstane Derivatives Inhibiting the Na/K-ATPase from Human Heart", Quant. Struct.—Act. Relat. 7, 160-165 (1988).

T. Hashimoto et al., "Studies on Digitalis Glycosides XXXV . . . ", Chem. Pharm. Bull. 27, 2975-2979 (1979).

K-O. Haustein et al., "Structure-Activity Relationships of Natural and Semi-Synthetic Genins and Glycosides . . . ", Pharmacology 10, 65-75 (1973).

Th. W. Güntert and H. H. A. Linde, "Cardiac glycosides: Prerequisites for the development of new cardiotonic compounds", Experientia, 33, 698-703 (1977).

J. Wicha et al. 'Synthesis of 17.beta.-Pyridyl-and 17.beta-Pyridyl-androstane Derivatives'. Heterocycles. vol. 16, No. 4, 1981, pp. 521-524.

J. Wicha et al. 'Synthesis and Molecular Biological Activity of the Pyridine Analog of Cardiotonic Steroids'. Heterocycles. vol. 20, No. 2, 1983, pp. 231-234.

G. A. Potter et al., "Discovery of Highly Potent and Selective Enzyme Inhibitors . . . " Poster presented at the SmithKline Beecham Research Symposium, Robinson College, Cambridge, England, 25-26 Mar. 1993.

S. E. Barrie et al., "Highly Potent Inhibitors of Human Cytochrome P-450 (17α) . . . " Poster presented at the British Association for Cancer Research meeting in Sheffield, England, 28-31 Mar. 1993.

G. A. Potter et al., "Highly Potent Inhibitors of Human Cytrochrome P-450 (17α) . . . ", Poster presented at the third Drug Discovery and Development Symposium, San Diego, California, USA, 22-24 Jul. 1993.

B. Schweder et al., "Synthesis des Δ^{16}, 17-Iodids Und—Triflats von Androsta-4-en-3, 17-dion . . . ", J. Prakt. Chem. 335, 201-204 (1993).

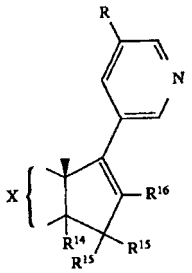
D. H. R. Barton et al., "An Improved Preparation of Vinyl Iodides", Tetrahedron letters 24, 1605-1608 (1983).

(List continued on next page.)

Primary Examiner—Mukund J. Shah
Assistant Examiner—Anthony Bottino
Attorney, Agent, or Firm—Nixon & Vanderhye

[57] **ABSTRACT**

Compounds of the general formula (1)



(1)

wherein X represents the residue of the A, B and C rings of a steroid, R represents a hydrogen atom or an alkyl group of 1 to 4 carbon atoms, R^{14} represents a hydrogen atom and R^{15} represents a hydrogen atom or an alkyl or alkoxy group of 1-4 carbon atoms, or a hydroxy or alkylcarbonyloxy group of 2 to 5 carbon atoms or R^{14} and R^{15} together represent a double bond, and R^{16} represents a hydrogen atom or an alkyl group of 1 to 4 carbon atoms, in the form of the free bases or phannaceutically acceptable acid addition salts, are useful for treatment of androgen-dependent disorders, especially prostatic cancer, and also oestrogen-dependent disorders such as breast cancer.

22 Claims, No Drawings

US008822438B2

(12) **United States Patent**
Auerbach et al.

(10) **Patent No.: US 8,822,438 B2**
(45) **Date of Patent: Sep. 2, 2014**

(54) **METHODS AND COMPOSITIONS FOR TREATING CANCER**

(75) Inventors: **Alan H. Auerbach**, Hermosa Beach, CA (US); **Arie S. Belldegrun**, Los Angeles, CA (US)

(73) Assignee: **Janssen Oncology, Inc.**, Los Angeles, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **13/034,340**

(22) Filed: **Feb. 24, 2011**

(65) **Prior Publication Data**

US 2011/0144016 A1 Jun. 16, 2011

Related U.S. Application Data

(63) Continuation of application No. 11/844,440, filed on Aug. 24, 2007, now abandoned.

(60) Provisional application No. 60/921,506, filed on Aug. 25, 2006.

(51) **Int. Cl.**
A61K 31/56 (2006.01)
A61K 31/58 (2006.01)

(52) **U.S. Cl.**
CPC ***A61K 31/58*** (2013.01)
USPC **514/170**; 514/180

(58) **Field of Classification Search**
USPC 514/170, 182
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2006/0030608 A1 2/2006 Nelson et al.

FOREIGN PATENT DOCUMENTS

EP	2478907	7/2012
WO	2006027266	3/2006

OTHER PUBLICATIONS

O'Donnell et al., British Journal of Cancer, 2004;90:2317-2325.*
Tannock et al., J. Clin. Oncol., 1996;14:1 756-1764.*
ASCO Cancer Foundation, Poster Session F: Hormone Refractory, ASCO. 2005.
Bruno et al, Targeting cytochrome P450 enzymes: A new approach in anti-cancer drug development, Elsevier, 2007, pp. 5047-5060, vol. 15.
Cannell, 100th Annual Meeting of the American Association for Cancer Research, Los Angeles, CA, USA;, http://oncology.thelancet.com, 2007, pp. 471, vol. 8.
Collins, et al. "A Systematic Review of the effectiveness of Docetaxel and Mitoxantrone for the Treatement of Metastatic Hormone-Refractory Prostate Cancer", British J. of Cancer, 95, pp. 457-462 (2006).
Cougar Biotechnology, Cougar Biotechnology Announces Initiation of Phase I/II Trial for CB7630 (Arbiraterone Acetate), Cougar Biotechnology, Dec. 14, 2004.
Cougar Biotechnology, Cougar Biotechnology Announces Presentation of Positive CB7630 Clinical Data at AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, Cougar Biotechnology, Oct. 2007.
Cougar Biotechnology, Cougar Biotechnology Announces Presentation of Positive CB7630 Clinical Data at ESMO Conference, Drugs.com, Jul. 2007.
Cougar Biotechnology, Cougar Biotechnology announces presentation of positive phase I and phase II data at ASCO Prostate Cancer Symposium, Cougar Biotechnology, Feb. 23, 2007.
Cougar Biotechnology, Cougar Biotechnology presents CB7630 Phase I clinical data at the 2005 Prostate Cancer Symposium, AllBusiness, 2005.
Cougar Biotechnology, Cougar Biotechnology presents positive CB7630 Clinical Data at AACR Annual Meeting Late-Breaking Clinical Trials Session, Cougar Biotechnology, Apr. 17, 2007.
Cougar Biotechnology, Cougar Technology Announces Presentation of Positive CB7630 Clinical Data at ASCO Annual Meeting, The Free Library, Jun. 4, 2007.
De Bono et al, Inhibition of CYP450c17 by abiraterone administered once daily to castrate patients with prostate cancer resistant to LHRH analogues, anti-androgens and steriod therapy is well tolerated . . . , The institute of Cancer Research, 2007.
De Coster, et al., Effects of High-Dose Ketoconazole and Dexamethason on ACTH-Stimulated Adrenal Steriodogenesis in Orchiectomized Prostatic Cancer Patients, ACTA Endocrinologica (Copenh), 1987, pp. 265-271, vol. 115.
Duc et al, In Vitro and in vivo models for the evaluation of potent inhibitors of male rat 17 -hydroxylase/C-lyase, Pergamon, 2003, pp. 537-542, vol. 84.
Endocrinology, Inhibition of Androgen Synthesis in Human Testicular and Prostatic Microsomes and in Male Rats by Novel Steroidal Compounds, Endocrinology, 1999, pp. 2891-2897, vol. 140 No. 6.
Fossa, et al., Weekly Docetaxel and Prednisone Versus Prednisolone Alone in Androgen-Independent Prostate Cancer: A Randomized Phase II Study, European Urology, 2007, pp. 1691-1699, vol. 52.
Gerber, et al., Prostate Specific Antigen for Assessing Response to Ketoconazole and Prednisone in Patients with Hormone Refractory Metastatic Prostate Cancer, The Journal of Urology, 1990, pp. 1177-1179, vol. 1444, No. 5.
Hakki et al, CYP17- and CYP11B-dependent steriod hydroxylases as drug development targets, Elsevier, 2006, pp. 27-52, vol. 11.
Harris, et al., Low Dose Ketoconazole with Replacement Doses of Hydrocortisone in Patients with Progressive Androgen Independent Prostate Cancer, The Journal of Urology, 2002, pp. 542-545, vol. 168.
Moreira et al, Synthesis and evaluation of novel 17-indazole androstene derivatives designed as CYP17 inhibitors, Elsevier, 2007, pp. 939-948, vol. 72.
Newell et al, The Cancer Research UK experience of pre-clinical toxicology studies to support early clinical trials with novel cancer therapies, Elsevier, 2004, pp. 899-906, vol. 40.

(Continued)

Primary Examiner — San-Ming Hui

(57) **ABSTRACT**

Methods and compositions for treating cancer are described herein. More particularly, the methods for treating cancer comprise administering a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, such as abiraterone acetate (i.e., 3β-acetoxy-17-(3-pyridyl)androsta-5,16-diene), in combination with at least one additional therapeutic agent such as an anti-cancer agent or a steroid. Furthermore, disclosed are compositions comprising a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor, and at least one additional therapeutic agent, such as an anti-cancer agent or a steroid.

20 Claims, No Drawings

Trials@uspto.gov
571-272-7822

Paper 14
Entered: May 31, 2016

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AMERIGEN PHARMACEUTICALS LIMITED,
Petitioner,

v.

JANSSEN ONCOLOGY, INC.,
Patent Owner.

IPR2016-00286
Patent 8,822,438 B2

Before LORA M. GREEN, RAMA G. ELLURU, and KRISTINA M. KALAN, *Administrative Patent Judges.*

KALAN, *Administrative Patent Judge.*

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Amerigen Pharmaceuticals Limited ("Petitioner") filed a Petition (Paper 1, "Pet.") to institute an *inter partes* review of claims 1–20 of U.S. Patent No. 8,822,438 B2 (Ex. 1001, "the '438 patent") pursuant to 35 U.S.C. §§ 311–319. Janssen Oncology, Inc. ("Patent Owner") filed a Preliminary Response (Paper 12, "Prelim. Resp."). Applying the standard set forth in 35 U.S.C. § 314(a), which requires demonstration of a reasonable likelihood that Petitioner would prevail with respect to at least one challenged claim, we institute an *inter partes* review as to claims 1–20 as discussed below.

Our findings of fact and conclusions of law, including those relating to the broadest reasonable construction of the patent claim terms, are based on the record developed thus far, prior to Patent Owner's Response. This is not a final decision as to the patentability of any challenged claim. Our final decision will be based on the full record developed during trial.

II. BACKGROUND

A. Related Matters

The parties indicate that the '438 patent is being asserted in a number of District Court proceedings, some of which have been terminated. Pet. 1–2; Paper 6, 2–3. Patent Owner represents that the following proceedings have not been terminated: *BTG Int'l Ltd., et al. v. Actavis Labs. FL, Inc., et al.*, C.A. No. 2:15-cv-05909-KM-JBC (D. N.J.); and *Janssen Biotech, Inc., et al. v. Mylan Pharm. Inc., et al.*, C.A. No. 1:15-cv-00130-IMK (N.D. W. Va.). Paper 13, 2–3. Patent Owner also states that the '438 patent is "the subject of *ex parte* reexamination request No. 90/020,096, which has been assigned to an Office examiner for determination." *Id.* at 2.

B. The '438 Patent

The '438 patent, titled "Methods and Compositions for Treating Cancer," describes methods that comprise "administering a 17α-hydroxylase/$C_{17, 20}$-lyase inhibitor, such as abiraterone acetate (i.e., 3β-acetoxy-17-(3-pyridyl)androsta-5,16-diene), in combination with at least one additional therapeutic agent such as an anti-cancer agent or a steroid." Ex. 1001, Title, Abstract. As described in the '438 patent, it is believed that testosterone and dihydrotestosterone promote the growth of prostate cancer. *Id.* at 1:49–51. Hormone therapy can be used to suppress the production or block the effects of hormones such as testosterone. *Id.* at 1:43–51. The enzyme 17α-hydroxylase/$C_{17, 20}$-lyase ("CYP17") is involved in testosterone synthesis. *Id.* at 3:66–4:1. CYP17 inhibitors have been shown to be useful in the treatment of cancer, specifically, androgen-dependent disorders like prostate cancer. *Id.* at 5:23–27. Abiraterone acetate, a prodrug of abiraterone, is a CYP17 inhibitor. *Id.* at 2:10–12. The '438 patent describes administration of an effective amount of a CYP17 inhibitor, such as abiraterone acetate, with a steroid such as prednisone or dexamethasone. *Id.* at 2:9–3:20.

C. Claims

Claim 1 of the '438 patent is reproduced below:

> 1. A method for the treatment of a prostate cancer in a human comprising administering to said human a therapeutically effective amount of abiraterone acetate or a pharmaceutically acceptable salt thereof and a therapeutically effective amount of prednisone.

Ex. 1001, 16:16–20. Dependent claims 2–20 of the '438 patent describe additional limitations of the method, including the amount of abiraterone

acetate and the amount of prednisone used, and the type of prostate cancer being treated. *Id.* at 16:21–17:14.

D. The Prior Art

Petitioner relies on the following prior art:

1. O'Donnell, A. et al., *Hormonal impact of the 17α-hydroxylase/ $C_{17,20}$-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer*, British Journal of Cancer 90:2317–2325 (2004) ("O'Donnell") (Ex. 1003);
2. Gerber, G.S. & Chodak, G.W., *Prostate specific antigen for assessing response to ketoconazole and prednisone in patients with hormone refractory metastatic cancer*, J. Urol. 144:1177–79 (1990) ("Gerber") (Ex. 1004); and
3. U.S. Patent No. 5,604,213 to Barrie, issued February 18, 1997 ("Barrie") (Ex. 1005).

Petitioner also relies on the declarations of Scott R. Serels, M.D. (Ex. 1002, the "Serels Declaration") and DeForest McDuff, Ph.D. (Ex. 1017, the "McDuff Declaration") in support of its arguments.

E. The Asserted Grounds

Petitioner challenges claims 1–20 of the '438 patent on the following grounds:

References	**Basis**	**Claims Challenged**
O'Donnell and Gerber	§ 103	1–20
Barrie and Gerber	§ 103	1–4 and 6–11

III. ANALYSIS

We turn now to Petitioner's asserted grounds of unpatentability, Patent Owner's arguments in the Preliminary Response, and the supporting evidence

to determine whether Petitioner has met the threshold standard of 35 U.S.C. § 314(a).

A. Claim Interpretation

The Board interprets claims in an unexpired patent using the "broadest reasonable construction in light of the specification of the patent in which [they] appear[]." 37 C.F.R. § 42.100(b); *see In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1275–79 (Fed. Cir. 2015), *cert. granted sub nom. Cuozzo Speed Techs. LLC v. Lee*, 136 S. Ct. 890 (mem.) (2016). Under the broadest reasonable interpretation standard, claim terms are given their ordinary and customary meaning in view of the specification, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

Petitioner proposes that we construe the claim terms "treat," "treating," "treatment," "anti-cancer agent," and "refractory cancer." Pet. 17–19. Patent Owner accepts Petitioner's definitions of those terms. Prelim. Resp. 18. These claim terms are discussed and defined explicitly in the specification of the '438 patent, as noted by Petitioner. Pet. 18. Accordingly, we construe those terms as set forth in the specification and below:

Claim term(s)	**Construction**
"treat," "treating," and "treatment	include the eradication, removal, modification, management or control of a tumor or primary, regional, or metastatic cancer cells or tissue and the minimization or delay of the spread of cancer Ex. 1001, 3:46–50
"anti-cancer agent"	any therapeutic agent that directly or indirectly kills cancer cells or directly or

	indirectly prohibits, stops or reduces the proliferation of cancer cells Ex. 1001, 4:8–16
"refractory cancer"	cancer that is not responding to an anti-cancer treatment or cancer that is not responding sufficiently to an anti-cancer treatment Ex. 1001, 4:23–27.

Patent Owner proposes that we construe the phrase "therapeutically effective amount of prednisone" to mean "an amount of prednisone effective for treating cancer." Prelim. Resp. 19. In support of its proposed construction, Patent Owner points to the definition in the specification, which provides: "As used herein, and unless otherwise defined, the phrase 'therapeutically effective amount' when used in connection with a 17α-hydroxylase/$C_{17,20}$-lyase inhibitor or therapeutic agent means *an amount of the 17α-hydroxylase/ $C_{17,20}$-lyase inhibitor* or *therapeutic agent effective for treating a disease or disorder disclosed herein, such as cancer*." *Id.* at 18–19 (quoting Ex. 1001, 4:17–22) (emphasis by Patent Owner). The specification's definition of "therapeutically effective amount," applies to a therapeutic agent. Ex. 1001, 4:17–22. The specification provides examples of a "therapeutic agent" such as "an anti-cancer agent or a steroid, e.g., a corticosteroid or, more specifically, a glucocorticoid." *Id.* at 1:14–16. Thus, the definition of "therapeutically effective amount" in the specification would apply to prednisone, a glucocorticoid. *Id.* at 3:10–11. Furthermore, claim 1 is directed to "A method for the treatment of a prostate cancer in a human." Ex. 1001, 16:16–17. Based on the definition and discussion the specification, and the manner in which the term is used in the claims, we construe

"therapeutically effective amount of prednisone" as "an amount of prednisone effective for treating prostate cancer."

B. Grounds Asserted by Petitioner

1. Ground Based on O'Donnell and Gerber

Petitioner challenges claims 1–20 as obvious under 35 U.S.C. § 103 over O'Donnell and Gerber. Pet. 36–48. Patent Owner disputes Petitioner's contentions. Prelim. Resp. 32–44.

O'Donnell, which is titled "Hormonal impact of the 17α-hydroxylase/C17-20-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer," discloses that treatment of prostate cancer with abiraterone acetate, at a dose of 500–800 mg, can successfully suppress testosterone levels. Ex. 1003, Abstract. O'Donnell also discloses that ketoconazole, another CYP17 inhibitor, has been evaluated as a possible agent with which to achieve decreased production of adrenal steroids, but that abiraterone acetate was developed as a more selective inhibitor. *Id.* at 2318. O'Donnell further discloses that adrenocortical suppression may require administration of replacement glucocorticoid. *Id.* at Abstract, 2323. O'Donnell states that "some impact on adrenal reserve was predictable from the steroid synthesis pathway." *Id.* at 2323. Regarding administration of ketoconazole, O'Donnell states that "it is common practice to administer supplementary hydrocortisone" and that this may prove necessary with abiraterone acetate. *Id.* On the basis of the clinical evidence, O'Donnell reports that the need for concomitant therapy of abiraterone acetate with a glucocorticoid needs to be further investigated. *Id.*

Gerber, which is titled "Prostate Specific Antigen for Assessing Response to Ketoconazole and Prednisone in Patients with Hormone

Refractory Metastatic Prostate Cancer," discloses use of ketoconazole, a known CYP17 enzyme inhibitor and inhibitor of gonadal and adrenocortical steroid synthesis, with prednisone to treat patients with progressive prostate cancer. Ex. 1004, 1177. Gerber provides that patients exhibiting progressively increasing prostate specific antigen ("PSA") levels, when treated with ketoconazole and prednisone, experienced a decrease in PSA levels. *Id.* at 1178–79.

Regarding claim 1, Petitioner argues that although O'Donnell does not disclose administration of abiraterone acetate with prednisone, "O'Donnell teaches that concomitant hormone replacement therapy with a glucocorticoid may be needed for continuous use of abiraterone acetate in treating a prostate cancer in a human patient." Pet. 38. Gerber, Petitioner argues, teaches that "the combination of ketoconazole and prednisone is safe and effective in treating human patients with hormone-refractory advanced prostate cancer." *Id.* Thus, Petitioner reasons, the "motivation to add prednisone to a method of treating prostate cancer in a human patient that includes abiraterone acetate is clearly seen in Gerber," which "teaches that the administration of ketoconazole, a CYP17 inhibitor, in combination with 5 mg prednisone twice daily, is safe and effective in treating human patients with hormone-refractory prostate cancer." *Id.* Regarding dependent claims 2–20, Petitioner argues that the additional limitations found in the dependent claims also are obvious over O'Donnell and Gerber. *Id.* at 40. Patent Owner does not separately address Petitioner's arguments directed to the dependent claims.

On this record, we are persuaded by Petitioner's arguments and presentation of the evidence. O'Donnell suggests that co-administration of a glucocorticoid, of which prednisone is one, may be needed in connection

with use of abiraterone acetate. Ex. 1003, 2323. Gerber discloses co-administration of a glucocorticoid, prednisone, with ketoconazole for the safe and effective treatment of prostate cancer. Ex. 1004, 1179. Ketoconazole and abiraterone acetate are both characterized as CYP17 inhibitors. Ex. 1003, 2318; Ex. 1002 ¶¶ 36, 45; *see also* Prelim. Resp. 42, Figs. 1, 2. We are persuaded, on this record, that the relative success of administration of ketoconazole together with prednisone to treat prostate cancer would lead one of ordinary skill in the art to expect that the "addition of 10 mg of prednisone daily according to Gerber to the treatment regimen of O'Donnell would be safe and effective in treating a prostate cancer, including prostate cancer refractory to anticancer therapy, including hormone and anti-androgen therapy." Pet. 39.

Patent Owner argues that Petitioner's challenges to the claims based on O'Donnell and Gerber fail for a number of reasons. First, Patent Owner argues that the prior art does not teach the problem of mineralocorticoid excess. Prelim. Resp. 32. Patent Owner also challenges Petitioner's and Dr. Serels's assertion that administration of abiraterone acetate or ketoconazole causes mineralocorticoid excess. *Id.* at 32–33. Dr. Serels's opinion that one of ordinary skill in the art would have expected that CYP17 inhibition would result in mineralocorticoid excess, according to Patent Owner, is erroneously based on "the experience of individuals with specific and rare forms of complete congenital CYP17 deficiency." *Id.* at 34.

Notwithstanding Patent Owner's arguments that Dr. Serels's reasoning is flawed, we are not persuaded that Dr. Serels's analysis and reliance on certain resources is in error. We can accord appropriate weight to an expert's testimony, taking into account the expert's understanding of the level of skill

in the art at the time of the invention, and the references relied upon in support thereof. *See, e.g.*, *Yorkey v. Diab*, 601 F.3d 1279, 1284 (Fed. Cir. 2010) (holding the Board has discretion to give more weight to one item of evidence over another "unless no reasonable trier of fact could have done so"). Our review of Dr. Serels's declaration and supporting evidence leads us to credit his testimony that "one of skill in the art would have expected that the co-administration of prednisone with abiraterone would improve the safety and tolerability of administering abiraterone by reducing the potential for side effects associated with the administration of a CYP17 inhibitor." Pet. 27–28 (citing Ex. 1002 ¶ 34).

Next, Patent Owner argues that Petitioner fails to establish a motivation to combine the references, because both abiraterone acetate and ketoconazole can be safely administered alone. *Id.* at 37. Only with hindsight, Patent Owner argues, could Petitioner argue that prednisone should be administered with abiraterone acetate. *Id.* at 39. Patent Owner also argues that the prior art teaches away from concomitant administration of abiraterone acetate and prednisone. *Id.* at 44. As discussed above, we are persuaded that Petitioner has articulated a reason to combine the references that, on this record, demonstrates a reasonable likelihood that Petitioner would prevail on its arguments in this regard. We are unpersuaded, on this record, that Petitioner's reasoning demonstrates impermissible hindsight; Petitioner's reasoning incorporates and relies on the knowledge of those of ordinary skill in the art at the time of the invention. *See, e.g.*, *In re McLaughlin*, 443 F.2d 1392, 1395 (CCPA 1971) ("Any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning, but so long as it takes into account only knowledge which was

within the level of ordinary skill at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper."). Nor are we persuaded that that the teachings of the references rise to the level of teaching away from Petitioner's proposed combination – they do not criticize, discredit, or otherwise discourage the solution claimed, but rather, as Petitioner argues, encourage exploration of such a combination. *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004) (explaining "[t]he prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed"). We are persuaded on the record thus far that Petitioner has demonstrated a reasonable likelihood of prevailing on its obviousness challenge to claim 1.

Claims 2–20 each depend directly or indirectly from claim 1. Petitioner contends these claims are also unpatentable under 35 U.S.C. § 103 based on O'Donnell and Gerber. Pet. 40–48. Concerning these claims, we determine that the supporting evidence demonstrates a reasonable likelihood that Petitioner would prevail in its showing, the substance of which has not been addressed specifically by Patent Owner. In view of the Petition, the Preliminary Response, and the evidence before us, we are persuaded that Petitioner has demonstrated a reasonable likelihood of prevailing on its assertion that claims 1–20 are obvious over O'Donnell and Gerber.

2. Ground Based on Barrie and Gerber

Petitioner challenges claims 1–4 and 6–11 as obvious under 35 U.S.C. § 103 over Barrie and Gerber. Pet. 36–45. Patent Owner disputes Petitioner's contentions. Prelim. Resp. 44–46.

Barrie, which is titled "17-Substituted Steroids Useful in Cancer Treatment," is directed to a class of 17-substituted steroids and their use in the treatment of androgen-dependent and estrogen-dependent disorders. Ex. 1005, 1:11–14. Specifically, Barrie discloses abiraterone, acid addition salts and 3-esters of abiraterone, and abiraterone acetate. *Id.* at 5:21–26, 7:23–26, 11:39–55. Barrie discloses that abiraterone acetate may be administered in a method of treating disorders, including prostate cancer, as a pharmaceutical composition comprising a therapeutically effective amount of abiraterone acetate. *Id.* at 10:27–57. Barrie compares the inhibition levels of hormone production by abiraterone acetate with ketoconazole, concluding that the decrease in testosterone levels resulting from administration of abiraterone acetate was much more marked than for ketoconazole. *Id.* at 26:32–38.

Regarding claim 1, Petitioner argues that although Barrie does not disclose co-administering abiraterone acetate with prednisone, it teaches "that abiraterone acetate is a CYP17 inhibitor that is more effective in suppressing testosterone levels in a mammal in vivo than ketoconazole, a CYP17 inhibitor known in the art." Pet. 39. Gerber, Petitioner argues, teaches that "the combination of ketoconazole and prednisone is safe and effective in treating human patients with hormone-refractory advanced prostate cancer." *Id.* Thus, Petitioner reasons, the "motivation to add prednisone to the method of treating prostate cancer of [Barrie] is clearly seen in Gerber," which "teaches that the administration of ketoconazole, a CYP17 inhibitor, in

combination with 5 mg prednisone twice daily, is safe and effective in treating human patients with hormone-refractory prostate cancer." *Id.* Regarding dependent claims 2–4 and 6–11, Petitioner argues that the additional limitations found in the dependent claims also are obvious over Barrie and Gerber. *Id.* at 40–46. Patent Owner does not separately address Petitioner's arguments directed to the dependent claims.

We are persuaded, at this stage of the proceeding, by Petitioner's arguments and presentation of the evidence. Barrie discloses use of abiraterone acetate for the treatment of prostate cancer. Ex. 1005, 1:11–13. Barrie contrasts the performance of ketoconazole with the performance of its disclosed compounds, including abiraterone acetate, in determining the relative activity of the tested compounds. *Id.* at 25:13–26:39, Table 3. Gerber discloses co-administration of a glucocorticoid, prednisone, with ketoconazole for the safe and effective treatment of prostate cancer. Ex. 1004, 1179. Ketoconazole and abiraterone acetate are both characterized as CYP17 inhibitors. Ex. 1002 ¶¶ 36, 45; *see also* Prelim. Resp. 42, Figs. 1, 2. We are persuaded, on this record, that the relative success of administration of ketoconazole together with prednisone to treat prostate cancer would lead one of ordinary skill in the art to expect that the "addition of 5 mg twice daily prednisone to the treatment regimen of [Barrie] also would be safe and effective in treating a prostate cancer, including prostate cancer refractory to anti-cancer therapy, including hormone and anti-androgen therapy." Pet. 39. Notwithstanding Patent Owner's arguments that Dr. Serels's reasoning is flawed, our review of Dr. Serels's declaration and supporting evidence leads us to credit his testimony that "one of skill in the art would have expected that the co-administration of prednisone with abiraterone would improve the

safety and tolerability of administering abiraterone by reducing the potential for side effects associated with the administration of a CYP17 inhibitor." Pet. 27–28 (citing Ex. 1002 ¶ 34).

Patent Owner argues that Petitioner's challenges to the claims based on Barrie and Gerber fail for "all of the same reasons discussed above with respect to the combination of" O'Donnell and Gerber. Prelim. Resp. 44. For the reasons articulated with respect to the combination of O'Donnell and Gerber, above, we are not persuaded by Patent Owner's arguments. Patent Owner also argues that Barrie states that abiraterone acetate did not inhibit corticosterone biosynthesis in rodents, leading one of skill in the art to understand "that abiraterone acetate did not inhibit glucocorticoid production." *Id.* at 45 (citing Ex. 1005, 25:45–48). Patent Owner also states that Barrie does not include clinical trial results, does not mention glucocorticoid replacement, and does not teach that abiraterone acetate could give rise to any side effects, let alone mineralocorticoid excess. *Id.* at 45–46.

The portion of Barrie on which Patent Owner relies states that the compounds of the invention had no significant effect on adrenal weight, "suggesting that they did not inhibit corticosterone biosynthesis." Ex, 1005, 25:45–48. Although this suggestion is present in Barrie, it is insufficiently conclusive to unseat Petitioner's arguments at this stage of the proceeding. The additional alleged shortcomings of Barrie noted by Patent Owner similarly do not unseat Petitioner's arguments, which rely on sources other than Barrie, such as Gerber and the Serels Declaration, to demonstrate the presence of those elements. We are persuaded on the record thus far that Petitioner has demonstrated a reasonable likelihood of prevailing on its obviousness challenge to claim 1.

Claims 2–4 and 6–11 each depend directly or indirectly from claim 1. Petitioner contends these claims are also unpatentable under 35 U.S.C. § 103 based on Barrie and Gerber. Pet. 40–45. Concerning these claims, we determine that the supporting evidence demonstrates a reasonable likelihood that Petitioner would prevail in its showing, the substance of which has not been addressed specifically by Patent Owner. In view of the Petition, the Preliminary Response, and the evidence before us, we are persuaded that Petitioner has demonstrated a reasonable likelihood of prevailing on its assertion that claims 1–4 and 6–11 are obvious over Barrie and Gerber.

3. Objective Indicia of Non-Obviousness

Petitioner contends that the Patent Owner may try to rely on secondary considerations of non-obviousness. Pet. 48–59. Patent Owner presents arguments directed to objective indicia of nonobviousness. Prelim. Resp. 46–52. Specifically, Petitioner pre-emptively raises arguments and evidence relating to commercial success, unexpected benefits, long-felt need, the existence of a blocking patent, and copying. Pet. 48–59. Patent Owner presents arguments related to unexpected results, long-felt need, and commercial success. Prelim. Resp. 46–52.

The issue of secondary considerations is highly fact-specific. At this stage of the proceeding, the record regarding such secondary considerations is incomplete. Based on the record before us, we determine that Patent Owner's evidence of secondary considerations is insufficient to preclude trial. Such evidence of secondary considerations should be more fully evaluated in the context of a trial when the ultimate determination of obviousness is made. We conclude that the information presented in the

Petition establishes a reasonable likelihood that the Petitioner will prevail in challenges to claims 1–20 of the '438 patent.

4. Patent Owner's Additional Arguments

Patent Owner makes several additional arguments in its Preliminary Response, namely: (A) Petitioner fails to meet the requirements of 35 U.S.C. § 311(b), which requires that an IPR challenge can be brought "only on the basis of prior art consisting of patents and printed publications,"; (B) Petitioner's obviousness arguments are redundant; (C) the Petition should be rejected under 35 U.S.C. § 325(d), which allows the Board to take into account whether the same or substantially the same prior art or arguments previously were presented to the Office; and (D) the Petition is an improper use of the IPR proceeding and/or an abuse of process under 35 U.S.C. §§ 316(a)(6) & 316(b), in that Petitioner is seeking to short circuit the Hatch Waxman process and deprive companies who have complied with ANDA procedure from obtaining the 180 day exclusivity period to which they will be entitled if their court challenges are successful. Prelim. Resp. 52–55. We address these arguments in turn.

(A) 35 U.S.C. § 311(b)

A conference call was held to discuss a similar issue on February 16, 2016, and a subsequent Order issued on February 22, 2016. Paper 11. Patent Owner sought to file a motion to exclude the declaration of Petitioner's expert and related arguments addressing commercial success. *Id.* As we stated in the Order of February 22, 2016: "There is no authority for excluding Petitioner's arguments and evidence addressing commercial success at the petition stage. Moreover, as Petitioner notes, the petition is the

first and last chance for a petitioner to present its case." *Id.* at 3. We maintain the position articulated in the Order for purposes of this Decision.

(B) Redundancy

Our governing statute requires the Director of the Patent and Trademark Office to "prescribe regulations . . . setting forth the standards for the showing of sufficient grounds to institute a review under section 314(a)," and requires the Director to "consider the effect of any such regulation on the economy, the integrity of the patent system, the efficient administration of the Office, and the ability of the Office to timely complete proceedings instituted under this chapter." 35 U.S.C. § 316(a)(2), (b). In view of the considerations listed in 35 U.S.C. § 316(b), the Director prescribed 37 C.F.R. § 42.108, which provides: (1) "the Board may authorize the review to proceed on all or some of the challenged claims and on all or some of the grounds of unpatentability asserted for each claim," and (2) "the Board may deny some or all grounds of unpatentability for some or all of the challenged claims." 37 C.F.R. § 42.108(a), (b). Based on our analysis of the information before us at this point, we decline to exercise our discretion to deny institution based on redundancy.

(C) 35 U.S.C. § 325(d)

Patent Owner requests that the Board exercise its discretion under 35 U.S.C. § 325(d) and decline to initiate *inter partes* review of the '438 patent because substantially the same prior art and arguments were before the Examiner during prosecution of the '438 patent. Prelim. Resp. 54–55. Specifically, Patent Owner contends: "Obviousness based on the teachings of O'Donnell (2004) was one of the primary grounds that the Examiner relied on during the prosecution of the '438 Patent" and the argument now

advanced by Petitioner in the context of Gerber "was specifically considered by the Examiner in the context of O'Donnell (2004)." *Id.* at 54.

The permissive language of § 325(d) does not prohibit instituting *inter partes* review based on arguments previously presented to the Office. *See* 35 U.S.C. § 325(d) ("In determining whether to institute or order a proceeding under this chapter, chapter 30, or chapter 31, the Director *may take into account* whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.") (emphasis added). We are mindful of the burden on Patent Owner and the Office to rehear the same or substantially the same prior art or arguments that were considered previously by the Office. For the reasons discussed herein, however, we are persuaded that Petitioner's arguments with respect to the combinations of O'Donnell and Gerber, and Barrie and Gerber, are supported by the evidence of record at this stage of the proceeding. Therefore, we do not exercise our authority to decline an *inter partes* review of the '438 patent under 35 U.S.C. § 325(d).

(D) 35 U.S.C. § 316(a)(6) and § 316(b)

Regarding Patent Owner's argument that the Petition is an improper use of the IPR proceeding and/or an abuse of process, we are mindful of the policy argument advanced by Patent Owner. Notwithstanding its citations to portions of our statute concerning abuse of process and the Director's considerations in prescribing regulations (35 U.S.C. § 316(a)(6) and § 316(b)), however, Patent Owner has demonstrated no statutory basis for a Hatch-Waxman carve-out in the arguments presented. Absent such authority, we decline to find abuse of process in Petitioner's filing of its Petition in this case.

C. Conclusion

We conclude that Petitioner has demonstrated a reasonable likelihood of prevailing with respect to its challenge of claims 1–20 of the '438 patent. We have not made, however, a final determination under 35 U.S.C. § 318(a) with respect to the patentability of the challenged claims.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that *inter partes* review is instituted on the following grounds of unpatentability asserted in the Petition:

Claims 1–20 as obvious under 35 U.S.C. § 103 over O'Donnell and Gerber;

Claims 1–4 and 6–11 as obvious under 35 U.S.C. § 103 over Barrie and Gerber; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(a), *inter partes* review of the '438 patent is hereby instituted commencing on the entry date of this decision, and pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial; and

FURTHER ORDERED that the trial is limited to the grounds identified above, and no other ground set forth in the Petition as to any challenged claim is authorized.

FOR PETITIONER:

William Hare
Gabriela Materassi
McNEELEY HARE & WAR LLP
bill@miplaw.com
materassi@miplaw.com

FOR PATENT OWNER:

Dianne B Elderkin
Barbara L. Mullin
Ruben H. Munoz
AKIN GUMP STRAUSS HAUER & FELD LLP
delderkin@akingump.com
bmullin@akingump.com
rmunoz@akingump.com

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re of : A. Auerbach, et al. **Confirmation No.: 6850**

Patent No.: 8,822,438 **Issued: September 2, 2014**

Serial No. : 13/034,340 **Filed: February 24, 2011**

Title : METHODS AND COMPOSITIONS FOR TREATING CANCER

CERTIFICATE OF EFS TRANSMISSION		
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted to the United States Patent and Trademark Office on the date shown below via the "Electronic Filing System" in accordance with 37 C.F.R. § 1.6(a)(4).		
Denise Mattos-Bosque	/Denise Mattos-Bosque/	06-08-2016
Type or print name	Signature	Date

Commissioner for Patents
Office of Data Management
Attention: Certificates of Correction Branch
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION OF PATENT PURSUANT TO 37 CFR § 1.322(a)

Dear Sir:

It is respectfully requested that a Certificate of Correction be issued for the above-identified patent. Applicant would like to correct the Assignee's full mailing address with the Patent and Trademark Office.

Enclosed herewith please find a completed Certificate of Correction form and a recently submitted Corrective Assignment reflecting the same.

The Commissioner is hereby authorized to charge any deficiency or credit any overpayment of the fees associated with this communication to Deposit Account No. 10-0750/CGR5001USCNT1.

Respectfully submitted,

/Timothy E. Tracy, Reg. No. 39,401/
Timothy E. Tracy
Reg. No. 39,401

One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-6586
Dated: June 7, 2016

PTO/SB/44 (09-07)
Approved for use through 08/31/2013. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 8,822,438

APPLICATION NO.: 13/034,340

ISSUE DATE : 09/02/2014

INVENTOR(S) : A. Auerbach, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Applicant would like to correct the Assignee's mailing address

from:
10990 Wilshire Boulevard
Suite 1200
Los Angeles, CA 90024

to:
10990 Wilshire Boulevard
Suite 300
Los Angeles, CA 90024

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Timothy E. Tracy
Johnson & Johnson
One Johnson & Johnson Plaza

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PATENT ASSIGNMENT

Electronic Version v1.1
Stylesheet Version v1.1

SUBMISSION TYPE:	NEW ASSIGNMENT
NATURE OF CONVEYANCE:	CHANGE OF NAME

CONVEYING PARTY DATA

Name	Execution Date
Cougar Biotechnology, Inc.	04/30/2012

RECEIVING PARTY DATA

Name:	Janssen Oncology, Inc.
Street Address:	10990 Wilshire Blvd.
Internal Address:	Suite 1200
City:	Los Angeles
State/Country:	CALIFORNIA
Postal Code:	90024

PROPERTY NUMBERS Total: 1

Property Type	Number
Application Number:	11844440

CH $40.00 11844440

CORRESPONDENCE DATA

Fax Number: 7325242808
Correspondence will be sent via US Mail when the fax attempt is unsuccessful.
Phone: 7325243967
Email: jnjuspatent@corus.jnj.com
Correspondent Name: Johnson & Johnson
Address Line 1: One Johnson & Johnson Plaza
Address Line 4: New Brunswick, NEW JERSEY 08933

ATTORNEY DOCKET NUMBER:	CGR5001
NAME OF SUBMITTER:	Laurie A. Phillips

Total Attachments: 2
source=Name_change_Cougar_Biotechnology_to_Janssen_Oncoloy#page1.tif
source=Name_change_Cougar_Biotechnology_to_Janssen_Oncoloy#page2.tif

United States Patent and Trademark Office

Electronic Patent Assignment System

Confirmation Receipt

Your assignment has been received by the USPTO.
The coversheet of the assignment is displayed below:

PATENT ASSIGNMENT COVER SHEET

Electronic Version v1.1
Stylesheet Version v1.2

SUBMISSION TYPE:	CORRECTIVE ASSIGNMENT
NATURE OF CONVEYANCE:	Corrective Assignment to correct the ASSIGNEE'S ADDRESS previously recorded on Reel 029001 Frame 0251. Assignor(s) hereby confirms the CORRECTED ASSIGNEE ADDRESS IS:10990 WILSHIRE BLVD.SUITE 300LOS ANGELES, CA 90024.

CONVEYING PARTY DATA

Name	Execution Date
COUGAR BIOTECHNOLOGY, INC.	04/30/2012

RECEIVING PARTY DATA

Name:	JANSSEN ONCOLOGY, INC.
Street Address:	10990 WILSHIRE BOULEVARD
Internal Address:	SUITE 300
City:	LOS ANGELES
State/Country:	CALIFORNIA
Postal Code:	90024

PROPERTY NUMBERS Total: 1

Property Type	Number
Patent Number:	8822438

CORRESPONDENCE DATA

Fax Number: (732)524-2808
Phone: 7325242771
Email: JNJUSPATENT@CORUS.JNJ.COM
Correspondence will be sent to the e-mail address first; if that is unsuccessful, it will be sent using a fax number, if provided; if that is unsuccessful, it will be sent via US Mail.
Correspondent Name: JOSEPH F. SHIRTZ
Address Line 1: ONE JOHNSON & JOHNSON PLAZA
Address Line 4: NEW BRUNSWICK, NEW JERSEY 08933

ATTORNEY DOCKET NUMBER:	CGR5001USCNT1
NAME OF SUBMITTER:	DENISE MATTOS-BOSQUE
Signature:	/Denise Mattos-Bosque/
Date:	06/07/2016

Total Attachments: 1
source=AssnCoversht#page1.tif

RECEIPT INFORMATION

EPAS ID: PAT3906202
Receipt Date: 06/07/2016

Return to home page

| HOME | INDEX| SEARCH | eBUSINESS | CONTACT US | PRIVACY STATEMENT

Electronic Patent Application Fee Transmittal

Application Number:	13034340
Filing Date:	24-Feb-2011
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Attorney Docket Number:	CGR5001USCNT1

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Certificate of Correction	1811	1	100	100

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**100**

Electronic Acknowledgement Receipt

EFS ID:	25999036
Application Number:	13034340
International Application Number:	
Confirmation Number:	1597
Title of Invention:	METHODS AND COMPOSITIONS FOR TREATING CANCER
First Named Inventor/Applicant Name:	Alan H. Auerbach
Customer Number:	27777
Filer:	Timothy E. Tracy/Denise Mattos-Bosque
Filer Authorized By:	Timothy E. Tracy
Attorney Docket Number:	CGR5001USCNT1
Receipt Date:	08-JUN-2016
Filing Date:	24-FEB-2011
Time Stamp:	09:34:31
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$100
RAM confirmation Number	7119
Deposit Account	100750
Authorized User	TRACY, TIMOTHY E.

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 CFR 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 CFR 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 CFR 1.19 (Document supply fees)

Charge any Additional Fees required under 37 CFR 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Certificate of Correction	CGR5001USCNT1_ReqForCOC_08Jun16.pdf	237985 323582c2c56c4ddbe1f8653a81e6026bb231f9b2	no	2
Warnings:					
Information:					
2	Change of Address	CertifofCorr_07Jun16.pdf	153684 d09774916636a3e7f872393155caf3dcd9b11eff	no	2
Warnings:					
Information:					
3	Change of Address	CorrectiveAssn_08Jun16.pdf	336667 4101cb62b7ced5a331c3aa3ed4ae846f634c8ae5	no	3
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	30340 b4b7188f96cef9f4e24aadc07dd254abec1ba18c	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	758676		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

<u>New International Application Filed with the USPTO as a Receiving Office</u>
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

AO 120 (Rev. 08/10)

TO:	**Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313–1450**	**REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK**

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the **U.S. District Court for the District of New Jersey** on the following:
____ Trademarks or **X** Patents. (____ the patent action involves 35 U.S.C. § 292.)

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
2:16–cv–02449–KM–JBC	5/2/2016	NEWARK, NJ
PLAINTIFF BTG INTERNATIONAL LIMITED		DEFENDANT AMERIGEN PHARMACEUTICALS, INC.

PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1 See Attached Complaint & Exhibit		
2		
3		
4		
5		

In the above––entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ___ Amendment ___ Answer ___ Cross Bill ___ Other Pleading

PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1		
2		
3		
4		
5		

In the above––entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE
William T. Walsh	s/ Shea Smith	5/2/2016

Copy 1––Upon initiation of action, mail this copy to Director Copy 3––Upon termination of action, mail this copy to Director
Copy 2––Upon filing document adding patent(s), mail this copy to Director Copy 4––Case file copy