UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE PATENT TRIAL AND APPEAL BOARD MILTENYI BIOMEDICINE GmbH and MILTENYI BIOTEC INC. Petitioner v. THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA Patent Owner IPR Trial No. IPR2022 -U.S. Patent No. 9,540,445 Issue Date: January 10, 2017

PETITION FOR INTER PARTES REVIEW OF U.S. PATENT NO. 9,540,445

Title: Compositions and Methods for Treatment of Cancer



Table of Contents

I.	INTRODUCTION				
II.	MANDATORY NOTICES				
	A.	Notice of Real Party-In-Interest (37 C.F.R. § 42.8(b)(1))	11		
	B.	Notice of Related Matters (37 C.F.R. § 42.8(b)(2))	11		
	C.	Designation of Lead and Back-Counsel (37 C.F.R. § 42.8(b)(3)).	11		
	D.	Service Information (37 C.F.R. § 42.8(b)(4))	12		
	E.	Power of Attorney			
III.	PAY	MENT OF FEES (37 C.F.R. § 42.103)	12		
IV.	REQUIREMENTS UNDER §§ 42.104 AND 42.108				
	A.	Grounds for Standing (§ 42.104(a))1			
	B.	Grounds of Challenge (§ 42.104(b))	13		
	C.	Requirements for IPR (§ 42.108(c))	13		
V.	PRIC	PRIORITY DATE			
VI.	TECHNOLOGY BACKGROUND				
	A.	T Cells	15		
	B.	CAR T Cells	15		
	C.	Engineering CAR T Cells	16		
VII.	PERS	SON OF ORDINARY SKILL IN THE ART	18		
VIII.	THE	E '445 PATENT			
IX.	CLAIM CONSTRUCTION		19		
	A.	"Anti-tumor effective amount"	19		
X.	PRIOR ART				
	A.	Campana	21		
	B.	Sequence Art	23		
	C.	Milone	24		
	D.	CART-19 ClinicalTrials.gov	25		
	E.	Porter	26		
	F.	Select Art Teaching Pharmaceutical Compositions of T-Cell Therapy			
		1 1101 ap J			



		1.	Hons	sik	27	
		2.	Ridd	ell	27	
XI.	GROUND 1: INDEPENDENT CLAIM 1 AND DEPENDENT CLAIMS 2, 4, 6, 8-9, 11, 16, 21-22, AND 27-30 ARE RENDERED OBVIOUS BY CAMPANA IN VIEW OF NICHOLSON, HONSIK, AND CART-19 CLINICALTRIALS.GOV					
	A.	Indep	enden	nt Claim 1	28	
		1.		m Limitations Directed to the Structure of the med CAR T Cell	30	
			a.	"[c] wherein T cells comprise a nucleic acid sequence encoding a chimeric antigen receptor (CAR)"	30	
			b.	"[d] wherein the CAR comprises a CD19 antigen binding domain comprising, from the amino to the carboxy terminus, a light chain variable region and a heavy chain variable region of SEQ ID NO: 20"	31	
			c.	"[e] wherein the CAR further comprises a transmembrane domain, a 4-1BB costimulatory signaling region, and a CD3 zeta signaling domain"	35	
			d.	"[f] wherein the T cells are from a human having cancer"	36	
		2.	Com	n Limitations Directed to a Pharmaceutical position Compromising an Anti-tumor Effective unt	37	
			a.	Preamble of "[a] pharmaceutical composition"	37	
			b.	"anti-tumor effective amount"	38	
	В.	Dependent Claims				
		1.	10^9 c	n 2: "anti-tumor effective amount of T cells is 10^4 to tells per kg body weight of a human in need of such "	46	
		2.		n 4: "wherein said antigen binding fragment is a	46	
		3.		m 6: "wherein the transmembrane domain is CD8α	46	



		4.	Claims 8 and 9: "wherein the CAR further comprises a hinge domain" and "wherein the hinge domain is a CD8α hinge domain"	46
		5.	Claims 11 and 16: "wherein the 4-1BB costimulatory signaling region comprises the amino acid sequence of SEQ ID NO: 23" and "wherein the 4-1BB costimulatory signaling region comprises the nucleic acid sequence of SEQ ID NO: 17"	47
		6.	Claims 21 and 22: "wherein the T cells are T cells of a human having a cancer" and "wherein the cancer is a hematological cancer"	47
		7.	Claims 27, 28, and 29: "wherein the pharmaceutical composition further comprises a pharmaceutically acceptable carrier, diluent or excipient," "wherein the pharmaceutical composition comprises a buffer," or "wherein the buffer is a neutral buffer saline or phosphate	40
XII.	CLA) OBV	IMS 2. IOUS	buffered saline"	
	A.	Indep	oendent Claim 1	49
		1.	([a]) "A pharmaceutical composition comprising"	49
		2.	([b]) "an anti-tumor effective amount of a population of human T cells,"	49
		3.	([c]) "wherein the T cells comprise a nucleic acid sequence encoding a chimeric antigen receptor (CAR),"	50
		4.	([d]) "wherein the CAR comprises a CD19 antigen binding domain comprising, from the amino to the carboxy terminus, a light chain variable region and a heavy chain variable region of SEQ ID NO:20"	51
		5.	([e]) "wherein the CAR further comprises a transmembrane domain, a 4-1BB costimulatory signaling region, and a CD3 zeta signaling domain,"	53



	В.	Dependent Claim 3: an "anti-tumor effective amount of T cells is 10 ⁵ to 10 ⁶ cells per kg body weight of a human in need of such cells"			
	C.	Dependent Claims 5 and 13: "wherein the scFv comprises the amino acid sequence of SEQ ID NO: 20" and "wherein the CD19 antigen binding domain is encoded by a nucleic acid sequence comprising SEQ ID NO: 14"			
	D.	Depe	ndent Claims 2, 4, 6, 8-9, 11, 16, 21-22, 27-29	57	
XIII.	GROUND 3: ALL CHALLENGED CLAIMS ARE RENDERED OBVIOUS BY CAMPANA IN VIEW OF MILONE, CART-19 CLINICALTRIALS.GOV, SEQUENCE ART (NICHOLSON, JENSEN, LITTMAN, SADELAIN), HONSIK, AND RIDDELL				
	A.	Claim 1			
	B.	Dependent Sequence Claims			
		1.	Claims 7 and 14: "wherein the CD8\alpha transmembrane domain comprises the amino acid sequence of SEQ ID NO: 22" and "wherein the CD8\alpha transmembrane domain comprises the nucleic acid sequence of SEQ ID NO: 16," respectively	60	
		2.	Claim 10 and 15: "wherein the CD8α hinge comprises the amino acid sequence of SEQ ID NO: 21" or "wherein the CD8α hinge comprises the nucleic acid sequence of SEQ ID NO: 15"	62	
		3.	Claims 12 and 17: "wherein the CD3 zeta signaling domain comprises the amino acid sequence of SEQ ID NO: 24" or "wherein the CD3 zeta signaling domain comprises the nucleic acid sequence of SEQ ID NO: 18"	64	
		4.	Claims 18 and 19: "wherein the CAR comprises amino acid sequence of SEQ ID NO: 12" or "wherein the CAR comprises nucleic acid sequence of SEQ ID NO: 8"	66	
	C.	C. Dependent Vector/Promoter Claims			
		1.	Claims 23 and 24: "wherein the T cells comprise a vector that comprises the nucleic acid sequence" or "wherein the vector is a lentiviral vector"	67	



DOCKET A L A R M

Explore Litigation Insights



Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time** alerts and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.

