

Discontinued drugs in 2007: oncology drugs

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Expert Opinion

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Oncologic

Discontinued drugs in 2007: oncology drugs

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This perspective is part of an annual series of papers discussing drugs dropped from clinical development in the previous year. Specifically, this paper focuses on the 28 oncology drugs discontinued in 2007. Information for this perspective was derived from a search of the Pharmaprojects database for drugs discontinued after reaching Phase I – III clinical trials.

Keywords: ABJ-789, Advant, AG-24322, AG-858, ATRA, AZD-5896, CAT-3888, CAT-5001, CE-245677, CEP-7055, CP-868596, Epothilone-D, Ethynylcytidine, Exisulind, GMK, Ibotectadecin, Neovastat, NS-9, OSI-461, Siplizumab, Talotrexin, Telatinib, VX-667

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1. Background

The article titled 'Discontinued drugs in 2006: oncology drugs' [1] in 2007 reported lack of efficacy as the principal reason for failure of drug candidates in clinical development for cancer. High attrition rates in clinical development are a critical problem for the pharmaceutical and biotechnology industries and recent data suggest that in the oncology area candidate failure rates are increasing with a paltry 3.2% of drugs entering Phase I actually reaching the market [2]. This snapshot report documents those candidates for which development was reported to have been terminated in 2007 and provides a brief analysis of the reported data.

2. Discontinued drugs

2.1 General overview

According to the analysis contained in Table 1, 28 drugs were dropped from the oncology development pipeline in 2007. However, 2 of these molecules were supportive therapies (HE-2100 and CB-001) and 3 were discontinued for failure in clinical trials outside of the oncology area (Incyclinide, Semapimod and Visilizumab). These drugs have not been considered further in this analysis. Of the remaining 23 drugs 9 were dropped in Phase I, 10 in Phase II and 4 in Phase III. In keeping with the 2006 analysis a broad range of therapeutic modalities is represented in terminated candidates from both large pharma and biotech pipelines. Table 2 details the reasons for candidate termination from both the 2006 and 2007 data sets.

2.2 Failures in Phase I

Termination of development was reported for nine compounds in Phase I development. Of these drugs five were protein kinase inhibitors (AG-24322, CE-245677, CEP-7055, CP-868596 and VX-667). The Aurora kinase inhibitor VX-667 failed to meet pharmacokinetic objectives whereas the VEGF receptor kinase inhibitor CEP-7055 was reported as not showing activity. Reasons for discontinuation of development of AG-24322 (cyclin-dependent kinase or CDK inhibitor), CE-245677 (Tie-2 and TRK/B inhibitor) and CP-868596 (platelet-derived growth factor or PDGF receptor kinase inhibitor) were not disclosed. Reasons for

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Table 1. Discontinued drugs in 2007: oncologic drugs.

Drug name	Originator (Licensee)	Indications	Pharmacology description	Target	Development Phase reached	Reason	Notes
ABI-789	Novartis	Cancer	Tubulin antagonist TUBE-1 Microtubule stimulant Apoptosis agonist Mitotic inhibitor Cell cycle inhibitor	Tubulin, beta	I	Unspecified	Novartis has discontinued development of ABI-789, a semi-synthetic derivative of epothilone B, for the treatment of cancer (R&D Day, Novartis, 17 May 2006, Form 20-F, Novartis, 2006)
Ovarian cancer therapy, Advant	Advantagene	Cancer, ovarian	Thymidine kinase stimulant DNA-directed DNA polymerase inhibitor Immunostimulant Angiogenesis inhibitor	Polymerase (DNA-directed), alpha 1	I	Financial	Advantagene has discontinued development of a GMCI system for the treatment of ovarian cancer owing to limited resources. The system involved local injection of an adenoviral vector (Adv-tk) encoding herpes simplex virus TK, followed by an oral prodrug, which was then activated by TK to kill tumour cells and inhibit angiogenesis. The GMCI system also induced a complete systemic antitumour immune response, exposing tumour-associated antigens, promoting antigen presentation and amplifying tumour-specific T-cells

Source: Pharmaprojects, copyright (c) Informa UK Ltd. 2009 [4].

AMD: Age-related macular degeneration; ARS: Acute radiation syndrome; CML: Chronic myelogenous leukaemia; CTCL: Cutaneous T-cell lymphoma; EF2: Elongation factor 2; FAP: Familial adenomatous polyposis; GMCI: Gene-mediated cytotoxic immunotherapy; GvHD: Graft-versus-host disease; HCL: Hairy cell leukaemia; HRPc: Hormone-refractory prostate cancer; IBD: Inflammatory bowel disease; MMP: Metalloproteinase; OA: Osteoarthritis; PDGF: Platelet-derived growth factor; PTCL: Peripheral T-cell lymphoma; RA: Rheumatoid arthritis; RCC: Renal cell carcinoma; rhIL-18: Recombinant human interleukin-18; SAAND: Selective apoptotic antineoplastic drug; TK: Thymidine Kinase; UC: Ulcerative colitis; VEGFR: Vascular endothelial growth factor receptor.

Table 1. Discontinued drugs in 2007: oncologic drugs (continued).

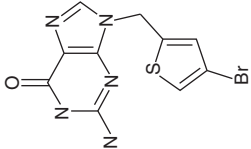
Drug name	Originator (Licensee)	Indications	Pharmacology description	Target	Development Phase reached	Reason	Notes
AG-24322	Pfizer	Unspecified	Cell cycle inhibitor	Unspecified	I	Unspecified	Pfizer has discontinued development of AG-24322 for the treatment of cancer (Company pipeline, Pfizer, 31 July 2007)
AG-858	Antigenics	Cancer and leukaemia	Immunostimulant	Unspecified	II	Strategic	Antigenics has discontinued development of AG-858, a personalised vaccine made from individual patient cancerous cells and based on a complex of heat shock protein-70 and antigen for the treatment of CML to focus on the development of other products (Form 10-K, Antigenics, 2006). The antigens are derived from human cell lines infected by the relevant bacterium or virus. The products were disease-specific rather than patient-specific. Pathogen-derived HSPPC-96 and patient-specific HSPPC-96 (Oncophage; both q.v.), were also under development by Antigenics (Company Web Pages, Antigenics, 10 May 2001 & 21 February 2005)

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Discontinued drugs in 2007: oncology drugs

Table 1. Discontinued drugs in 2007: oncologic drugs (continued).

Drug name	Originator (Licensee)	Indications	Pharmacology description	Target	Development Phase reached	Reason	Notes
4-Bromotherylguanine 	AstraZeneca	Melanoma and colorectal cancer	O6-alkylguanine-DNA alkyltransferase inhibitor	O-6-methylguanine-DNA methyltransferase	II	Unspecified	KuDOS (AstraZeneca) has discontinued development of 4-bromotherylguanine (Patrin; AZD-5896), an orally active pseudosubstrate and inhibitor of the DNA repair enzyme O6-alkylguanine DNA alkyltransferase (ATase), for the treatment of solid tumours (Company pipeline, AstraZeneca, 26 July 2007). It was being developed under license from Cancer Research Technology (Cancer Research Ventures before the merger) as a chemosensitiser to alkylating agents such as temozolomide (q.v.) (11th NCJ-EORTC-AACR Symp New Drugs Cancer Ther., Amsterdam, 2000, Abs 538; 4th ERBI Conf., Cambridge), 2002)

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