Drug pipeline 3Q13

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US Food and Drug Administration approvals continue to lag behind the European Medicine Agency (EMA), particularly with the US government shutdown; 2013 is shaping up as a very poor year for first-in-class drug approvals. EMA approved the first biosimilar monoclonal antibody; Biogen, Pharmacyclics, Clinuvel, Actelion and Celgene all await final regulatory decisions.

Notable clinical trial results (Q3 2013)

Drug/company	Indication	Summary
Relaxin/Novartis	Acute decompensated heart failure	9/2/2013. Recombinant relaxin peptide met one of two endpoints in phase 3 trial (Journal abstract: *Eur. Heart J.* (2013) doi:10.1093/eurheartj/eht371, European Society of Cardiology, 2 September 2013)
Vedolizumab/Takeda	Crohn's disease	8/22/2013. Phase 3 trial of monoclonal antibody (mAb) against gut-specific alpha-4 beta-7 integrin showed patients more likely to be in remission at 6 weeks (*N. Engl. J. Med.* **369**, 711–712, 2013)
Obinutuzumab/Roche	Large diffuse cell carcinoma/ mantle cell lymphoma	7/8/2013. Phase 2 trial of glycoengineered CD20 mAb showed clinical activity (*J. Clin. Oncol.* **31**, 2912–2919, 2013)
Cerepro/WKD Holding	Brain cancer	7/12/2013. Adenovirus-mediated thymidine kinase delivered by multiple injections increased time to death for ganciclovir-treated patients in phase 3 trial (*Lancet Oncol.* **14**, 823–833, 2013)
AD04/Adial Pharmaceuticals	Alcohol dependence	8/27/2013. In phase 2b trial, patients with five markers responded to ultra low dose of 5-hydroxytryptamine 3 receptor agonist (*Am. J. Psychiatry* doi:10.1176/appi.ajp.2013.12091163, 30 July 2013)
MM-398/Merrimack Pharmaceuticals	Pancreatic cancer	8/22/2013. 75% of subjects in a phase 2 trial of nanoliposomal (distearoylphosphatidylcholine/cholesterol/methoxypoly(ethylene) glycol-derivatized distearoylphosphatidylethanolamine in sucrose octasulfate) irinotecan showed 3 month's survival (*Br. J. Cancer* doi:10.1038/bjc.2013.408, 23 July 2013)
Brincidofovir/Chimerix	Cytomegalovirus (CMV) infection	9/26/2013. In phase 2 trial, lipid-conjugated prodrug form of cidofovir met primary endpoint of reduced CMV viremia (*N. Engl. J. Med.* doi:10.1056/NEJMoa1303688, 26 September 2013)
ALN-TTR02/Alnylam	Transthyretin-related hereditary amyloidosis	8/28/2013. Knockdown of serum transthyretin by RNA interference achieved in phase 1 (*N. Engl. J. Med.* doi:10.1056/NEJMoa1208760, 29 August 2013)
Pacritinib/Cell Therapeutics	Myelofibrosis	7/3/2013. In two phase 2 trials, JAK/FLT-3 inhibitor showed disease response and symptom reduction (*Drugs Future* **38**, 375, 2013)

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/).

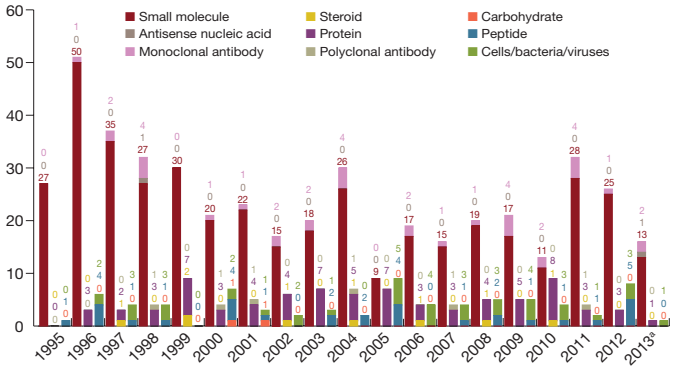
Notable upcoming regulatory decisions (Q1 2014)

Drug/company	Indication	Upcoming catalyst
Ibrutinib/Pharmacyclics	Mantle cell lymphoma/chronic lymphocytic leukemia	2/28/2014. FDA PDUFA Bruton's tyrosine kinase inhibitor of B-cell maturation
Apremilast/Celgene	Psoriatic arthritis	3/21/2014. FDA PDUFA small-molecule inhibitor of phosphodiesterase 4
Alprolix/Biogen Idec	Hemophilia B	1/3/2014. FDA PDUFA recombinant factor IX fused to Fc region of IgG
Metreleptin/BMS	Lipodystrophy	2/24/2014. FDA PDUFA recombinant human leptin
Vimizim (elosulfase alfa)/ BioMarin	Mucopolysaccharidosis IV	2/28/2014. FDA PDUFA recombinant human N-acetylgalactosamine-6-sulfate sulfatase
Eloctate/Biogen Idec	Hemophilia A	3/12/2014. FDA PDUFA recombinant factor VIII fused to Fc region of IgG
Scenesse (afamelanotide)/ Clinuvel	Porphyria	2/28/2014. EMA synthetic peptide analog of alpha melanocyte-stimulating hormone
Opsumit (macetentan)/Actelion	Pulmonary arterial hypertension	4/30/2014. EMA tissue-targeting small molecule endothelial receptor antagonist
Vintafolide/Merck	Ovarian cancer	4/30/2014. EMA folate-targeting vinca alkaloid
Albiglutide/GSK	Diabetes mellitus, type II	2/1/2014. EMA recombinant glucagon-like peptide fused to recombinant human albumin
Bemfola/FINOX Biotech	Reproductive disorder	4/30/2014. EMA recombinant biosimilar to recombinant follicle-stimulating hormone
Ataluren (PCT124)/PTC Therapeutics	Muscular dystrophy	5/31/2014. EMA exon-skipping molecule for bypassing nonsense mutation

FDA, US Food and Drug Administration; PDUFA, prescription drug user fee act; EMA, European Medicines Agency.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/).

FDA approvals by drug molecule type



[a]Partial year to October 10. Source: US Food and Drug Administration; BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/).

Notable regulatory approvals (Q3 2013)

Drug/company	Indication	Drug information
Gilotrif (afatinib)/ Boehringer Ingleheim	Non–small cell lung carcinoma	7/12/2012, FDA. Irreversible binder of EGFR, HER2 (ERB2), ERBB3, ERBB4 tyrosine kinases
Imvamune/Bavarian Nordic	Smallpox	7/31/2013, EMA. Modified vaccinia Ankara virus vaccine
Declage (LBO3002)/LG Life Sciences	Short stature	8/5/2013, EMA. Sustained release of human growth hormone encapsulated in microparticles of hyaluronic acid
Lonquez (lipegfilgrastim)/Teva	Neutropenia/ leukopenia	8/8/2013, EMA. Long-acting pegylated granulocyte stimulating factor
Tivicay (dolutegravir)/ GlaxoSmithKline	HIV/AIDS	8/12/2013, FDA. HIV integrase inhibitor
Herceptin-rHuPH20/ Roche	Breast cancer	9/2/2013, EMA. Subcutaneous formulation oftrastuzumab with recombinant hyaluronidase
Remsima (infliximab)/ Celltrion	Inflammatory conditions	9/10/2013, EMA. Rituxan biosimilar targeting TNF-alpha
Cobicistat (GS9350)/ Gilead	HIV/AIDS	9/25/2013, EMA. CYP3A inhibitor, which acts as a pharmacokinetic enhancer when used with other drugs

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/).

FDA, US Food and Drug Administration; EGFR, epidermal growth factor receptor; EMA, European Medicines Agency.

Notable regulatory setbacks (Q3 2013)

Drug/company	Indication	Drug information
Delamanid/Otsuka	Tuberculosis	7/25/2013. EMA gave a negative opinion of mycolic acid synthesis inhibitor due to insufficiency of efficacy data
Sovaprevir/Achillon	Hepatitis C	7/1/2013. FDA issued a clinical hold on this noncovalent, reversible protease inhibitor based on elevated liver enzymes
VX-135/Vertex	Hepatitis C	7/25/2013. FDA put a clinical hold on phase 2 trial based on elevated liver enzymes with this HCV polymerase inhibitor
ISIS-CRPRx/Isis	Rheumatoid arthritis	8/5/2012. Company suspended development of antisense against C-reactive protein after lack of efficacy over placebo
Allovectin (velimogene aliplasmid)/ Vical	Melanoma	8/12/2013. Company suspended development of lipid complex/ DNA plasmid encoding human leukocyte antigen B7 and beta-2-microglobulin after phase 3 trial showed no improvement over first-line chemotherapy
R343/Rigel	Asthma	8/26/2013. Company suspended phase 2 trial of inhaler-delivered, small-molecule Syk kinase inhibitor after failure to meet primary/ secondary endpoints
Tivantinib/Arqule	Non–small cell lung carcinoma	9/30/2013. Company announced results of phase 3 trial with Avastin in which addition of c-Met inhibitor failed to meet primary endpoint

EMA, European Medicines Agency; FDA, US Food and Drug Administration; HCV, hepatitis C virus.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/)

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