Drug pipeline: Q111

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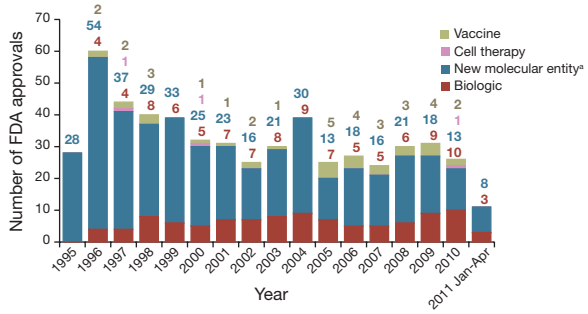
Drug approvals picked up speed in the US and Europe in Q1. Registrations included Bristol-Myers Squibb's Yervoy (ipilimumab) for melanoma and Human Genome Sciences' Benlysta (belimumab) for lupus. However, MannKind's inhaled insulin (Afrezza), Abbott Laboratories' ABT-874 (briakinumab) and Protalix BioTherapeutics' Uplyso (taliglucerase) suffered setbacks. Efficacy data are in for several new cell and gene therapies and Baxter's vero cell–derived flu vaccine showed promise in a key US phase 3 trial.

US regulatory approvals by drug class



[a]New molecular entity (NME) class includes mainly small-molecule drugs, but also steroid, synthetic peptide and mixed compounds. [b]Partial year to April 7. Source: US Food and Drug Administration (FDA) (http://www.fda.gov/), excluding non-NME drugs or new formulation.

Notable regulatory approvals (Q1 2011)

Drug/company	Indication	Drug information
Esbriet (pirfenidone)/ InterMune	Idiopathic pulmonary fibrosis	2/28/11 EMA The p38 kinase inhibitor approved in the EU and Japan; undergoing phase 3 trial in the US after regulatory setback in May 2010.
Benlysta (belimumab)/ Human Genome Sciences	Systemic lupus erythema-tosus	3/10/11 FDA Fully human mAb against B-lymphocyte stimulator also awaiting approval from EMA in H2 2011. Latest phase 3 trial met efficacy and safety primary end-points (*Lancet* **377**, 721–731, 2011).
Halaven (eribulin mesylate)/ Eisai	Breast cancer	3/23/11 EMA Synthetic nontaxane tubulin inhibitor derived from marine sponge halichondrin B. The phase 3 trial results increased overall survival primary endpoint (*Lancet* **377**, 914–923, 2011).
Yervoy (ipili-mumab)/Bristol-Myers Squibb	Melanoma	3/25/11 FDA The fully human IgG1k mAb against cytotoxic T-lymphocyte antigen-4 is also expecting approval from EMA in H2 2011.
Zictifa (vandetanib)/ AstraZeneca	Thyroid cancer	4/7/11 FDA Small-molecule, vascular endothelial growth factor receptor 2 inhibitor (also targets EGF and RET receptors) indicated for thyroid cancer.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). FDA, US Food and Drug Administration; EMA, European Medicines Agency; PDUFA, Prescription Drug User Fee Act; mAb, monoclonal antibody.

Notable regulatory setbacks (Q1 2011)

Drug/company	Indication	Setback summary
ABT-874 (briakinumab)/ Abbott Laboratories	Psoriasis	1/13/11 Company withdrew both BLA and MAA after regulatory agencies suggesting that additional data and analysis required for approval. Briakinumab is a fully human IL-12/23 monoclonal antibody.
Afrezza (inhaled insulin)/ MannKind	Type 2 diabetes	1/19/11 FDA issued complete response letter regarding the inhaled insulin powder requesting additional trials to demonstrate similar dosing efficiencies of the two types of inhalers used throughout development.
Iniparib/ Sanofi-aventis	Breast cancer	1/27/11 Company press release reported poly-ADP-ribose polymerase inhibitor missed co-primary endpoints in phase 3.
Uplyso (taliglu-cerase)/Protalix BioTherapeutics & Pfizer	Gaucher's disease	2/25/11 FDA issued complete response letter regarding the recombinant human glucocerebrosidase expressed from plant cells. Additional data from clinical trials and manufacturing data are requested.
Juvista (avotermin)/ Renovo	Wound healing	3/3/11 Company suspended further development of the recombinant human transforming growth factor beta for wound healing after phase 3 trial failed to meet primary endpoint.
Otelixizumab/ Tolerx & GlaxoSmithKline	Type 1 diabetes	3/11/11 Company announced that phase 3 trial results of the humanized anti-CD3 monoclonal antibody failed to meet primary endpoint.
RGN-352 (human thymosin beta 4 peptide)/RegeneRx	Acute myocardial infarction	3/16/2011 FDA put phase 2 trial of the peptide with wide-range cardiovascular actions on hold citing manufac-turing noncompliance.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). BLA, biologic license application; MAA, market authorization application; HPV, human papiloma virus.

Notable upcoming regulatory decisions (Q2 2011)

Drug/company	Indication	Expected regulatory decision
Telaprevir/ Vertex Pharmaceuticals	HCV infection	5/23/11 PDUFA. Telaprevir is a HCV NS3 protease inhibitor.
Victrelis (boceprevir)/ Merck	HCV infection	05/11-06/11 PDUFA. Phase 3 trial of bocepre-vir, a HCV NS3 protease inhibitor, met primary endpoint (*N. Engl. J. Med.* **364**, 1207–1217, 2011).
Dificid (fidaxomicin)/ Optimer Pharmaceuticals	*Clostridium difficile* infection	5/30/11 PDUFA. Phase 3 trial of antibiotic selectively targeting *C. difficile* RNA polymerase showed efficacy similar to vancomycin and reduced recurrence rate (*N. Engl. J. Med.* **364**, 422–431, 2011).
Belatacept/ Bristol-Myers Squibb	Kidney transplant rejection	6/13/11 PDUFA. 2-amino acid mutant of CD80/ CD86 costimulatory signal blocker abatacept, which is recombinant fusion of cytotoxic T-lymphocyte antigen 4 and human IgG1 Fc fragment.
Istodax (romidepsin)/ Celgene	Non-Hodgkin's lymphoma	6/17/11 PDUFA. Histone deacetylase inhibitor indicated for non-Hodgkin's lymphoma.
Abiraterone/ Johnson & Johnson	Prostate cancer	6/20/11 PDUFA. A selective inhibitor of cyto-chrome p450 complex and testosterone produc-tion; the first inhibitor of androgen production rather than signaling.
LaViv (azficel-T)/ Fibrocell Science	Skin wrinkles	6/22/11 PDUFA. Cell therapy using autologous fibroblasts (obtained from skin behind the ear) expanded *in vitro* and re-injected to 'regenerate skin' and reduce wrinkles.
LBH 589 (panobinostat)/Novartis	Hodgkin's lymphoma	6/30/11 PDUFA. Histone deacetylase inhibitor indicated for Hodgkin's lymphoma.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). HCV, hepatitis C virus. Bydureon (exanatide, long-acting release) from Amylin Pharmaceutical is expecting H1 2011 market authorization application approval (see *Nat. Biotechnol.* **29**, 101, 2011 for details). PDUFA, Prescription Drug User Fee Act.

Notable trial results (Q1 2011)

Drug/company	Indication	Result summary
SL-701/ Stemline Therapeutics	Glioma	Phase 2 trial of the dendritic cell vaccine loaded with glioma-associated antigen in 22 patients supported safety and immunogenicity against tumor antigen (*J. Clin. Oncol.* **29**, 330–336, 2011).
PreFluCel/ Baxter	Influenza prevention	Phase 3 trial of the Vero cell–derived influenza vaccine demonstrated comparable protective efficacy to egg-derived vaccines (*Lancet* **377**, 751–759, 2011).
Excellarate (GMA 501)/ Cardium Therapeutics	Diabetic foot ulcer	Phase 2b trial of the collagen gel loaded with adeno-viral vector encoding human platelet-derived growth factor B demonstrated safety and tolerance (*Wound Repair Regen.* published online, doi:10.1111/j.1524-475X.2011.00669.x (3 March 2011).
Degludec/ Novo Nordisk	Type 1 & 2 diabetes	Phase 2 study of ultralong-acting insulin containing ThrB30 deletion with addition of 16-carbon fatty diacid attached to LysB29 via a glutamic acid spacer demon-strated comparable primary endpoint of glycemic control efficacy (*Lancet* **377**, 924–931, 2011).
NLX-P101 (AAV2-GAD)/Neurologix	Parkinson's disease	Phase 2 study of intracerebral gene therapy using adeno-associated virus 2 to deliver glutamic acid decar-boxylase with a Medtronic catheter system met primary endpoint in improving motor function and overall Parkinson disease rating (*Lancet Neurol.* **10**, 309–319, 2011).
PRO051 (GSK2402968)/ GlaxoSmithKline	Duchenne's muscular dystrophy	Phase 2 study of dystrophin pre-mRNA antisense therapy demonstrated safety, pharmacokinetic, and modest clinical effects (*N. Engl. J. Med.* **364**, 1513-1522, 2011).

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

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