Drug pipeline: Q310

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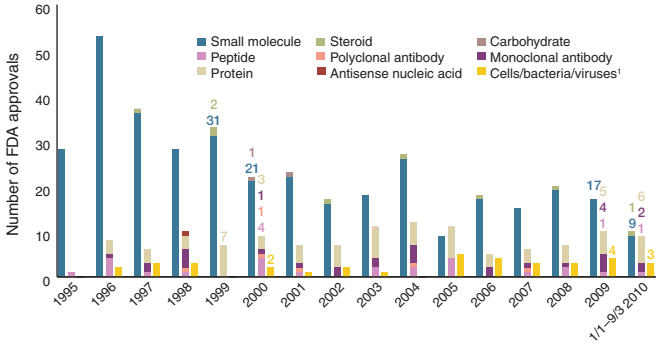
The number of small-molecule approvals declined more sharply than that of biologics over the past decade. However, new targets, such as atrium-specific K^+ channel, phosphodiesterase-4 and renal Na^+-glucose co-transporter, continue to open up new opportunities. Such novel targets are not without risk, as Eli Lilly found this quarter when its gamma-secretase inhibitor failed to meet its endpoints in Alzheimer's. Meanwhile, MannKind's inhaled insulin, Afrezza, demonstrated both efficacy and safety in a key trial. Approvals are also expected for Benlysta (belimumab), ipilimumab and Bydureon (exenatide LAR).

FDA approvals by drug molecule type

Fewer small molecules are being approved than before.



Source: US Food and Drug Administration and BioMedTracker, a service of Sagient Research (http://biomedtracker.com/). Includes vaccines approved by the FDA.

Notable regulatory approvals (June–September 2010)

Company/drug name	Indication	Approvals	Drug description
Genentech-Roche/ Lucentis (ranibizumab)	Retinal venous occlusion	FDA, 6/22/10 (sBLA)	Humanized anti-VEGF monoclonal antibody Fab fragment
Forest Lab/Daxas (roflumilast)	Chronic obstructive pulmonary disease	EMA, 7/6/10	The first selective phosphodiesterase-4 inhibitor
Shire/Vpriv (velaglucerase alfa)	Gaucher's disease	EMA, 8/26/10; FDA, 2/26/10	Gene-activated human glucocerebrosidase
Cardiome Pharma/ Kynapid (vernakalant)	Atrial fibrillation	EMA, 9/1/10	Small-molecule blocker for atrium-specific potassium channel Kv1.5
Savient/Krystexxa (pegloticase)	Gout	FDA, 9/14/10	PEG-conjugated recombinant human uricase

Source: FDA and EMA. FDA, US Food and Drug Administration. EMA, European Medicines Agency. sBLA, supplemental Biologic License Application. VEGF, vascular endothelial growth factor.

Notable development setbacks (June-September 2010)

Company/drug name	Indication	Setback summary
MedImmune-AstraZeneca/ Numax (motavizumab)	Respiratory syncytial virus (RSV) infection	On 6/2/10, an FDA panel voted against approval. On 8/30/10, the FDA issued Complete Response Letter requesting additional trials to support the risk-benefit profile. Motavizumab is a humanized monoclonal antibody against the fusion (F) protein of RSV.
Merck/Peg-Intron (peg-interferon alpha-2b)	Melanoma	Phase 3 trial did not meet either primary or secondary endpoints; treatment is no better than conventional low-dose interferon treatment. (American Society of Clinical Oncology Annual Meeting, 6/05/10, Abstract LBA8506)
Human Genome Sciences (mapatumumab)	Multiple myeloma	Phase 2 study showed that treatment did not significantly improve disease response or progression-free survival. (Company press release, 06/09/10) Mapatumumab is a human monoclonal antibody agonist to TRAIL receptor-1.
Eli Lilly/ Semagacestat (LY450139)	Alzheimer's disease	Company discontinued development of the gamma-secretase inhibitor after interim analysis of phase 3 trial data showed that treatment resulted in worse outcomes than placebo. (Company press release, 8/17/10)
Roche (taspoglutide)	Type 2 diabetes	On 9/10/10, company announced suspension of phase 3 trials for the long-acting glucagon-like peptide-1 analog because serious side effects led too many patients to drop out of the trial.

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

Notable trial results (June–September 2010)

Company/drug name	Indication	Result summary
Bristol-Myers Squibb and AstraZeneca/dapagliflozin	Type 2 diabetes	Phase 3 study met primary and secondary endpoints after 24 weeks of treatment with this small-molecule inhibitor of the renal sodium glucose co-transporter 2 (SGLT-2). (*Diabetes Care*, doi: 10.2337/dc10-0612)
Morphoteck-Eisai/ farletuzumab	Ovarian cancer	Phase 2 study met primary endpoints and demonstrated benefits of this humanized monoclonal antibody against folate receptor alpha compared with conventional carboplatin+taxane treatment. (American Society of Clinical Oncology Annual Meeting, 7/07/10, Abstract 5001)
Jerini-Shire/Firazyr (icatibant)	Hereditary angioedema	Phase 3 study showed significant benefit of this selective peptide antagonist of bradykinin B2 receptor. (*N. Engl. J. Med.* **363**, 532–541)
ThromboGenetics/ ocriplasmin (recombinant microplasmin)	Vitreomacular adhesion	Phase 2 study showed significantly increased non-surgical resolution of vitreomacular adhesion by intravitreal injection of the recombinant human protein (*Retina* **30**, 1122–1127). Preliminary phase 3 data also met primary endpoint. (American Society of Retina Specialists Annual Meeting, 8/31/10)

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

Notable upcoming approvals (Q4 2010)

Company/ drug name	Indication	Approval decision
Amylin Pharmaceuticals/ Bydureon (exenatide LAR)	Type 2 diabetes	10/22/10 PDUFA date. Phase 3 trial met primary and secondary endpoints and showed significant superiority over comparators (American Diabetes Association Annual Meeting, 6/25–29/2010). This controlled release form of Byetta (exenatide, a 39-amino-acid peptide agonist of glucagon-like peptide-1, GLP-1) uses the Medisorb technology (microspheres made of polylactide co-glycolide polymer).
Human Genome Sciences/ Benlysta (belimumab)	Systemic lupus erythematosus	12/09/10 PDUFA date, priority review. MMA approval expected in H2 2011. Two phase 3 trials showed significant improvement in patient response after 52 weeks of treatment of this human monoclonal antibody against B-lymphocyte stimulator (BLyS). (European League Against Rheumatism Annual Congress, 6/17/10)
Medarex-Bristol-Myers Squibb (ipilimumab)	Metastatic melanoma	12/25/10 PDUFA date. Priority review granted on 8/18/10. Ipilimumab is a fully human antibody against cytotoxic T-lymphocyte antigen-4 (CTLA-4). Phase 3 study met primary and secondary endpoints (*N. Engl. J. Med.* **363**, 711–723, 2010)
MannKind/ Afrezza (inhaled insulin, dry powder)	Diabetes, types 1 and 2	12/29/10 PDUFA date. In phase 3 trial, inhaled insulin was statistically noninferior to injected insulin. Over 52 weeks, there was no difference in pulmonary function between groups. Inhaled insulin was as effective and well tolerated. (*The Lancet* **375**, 2244–2253, 2010)
LG Life Sciences/ LB03002 (SR-rHGH)	Growth hormone deficiency	09/10/10 - 01/03/11 PDUFA date range. MMA approval expected in H2 2010. LB03002 is the sustained release form of recombinant human growth hormone and requires once-weekly injection versus current daily treatment. Phase 3 study results showed significant superiority over placebo in adult patients after 26 weeks of treatment. (Endocrine Society Annual Meeting, 6/11/09, Abstract P2-746)

Other expected approvals in Q4 include Theratechnologies' Egrifta (tesamorelin) and Novartis' Gilenia (fingolimod). See *Nat. Biotechnol.* **28**, 640, 2010, for details.
Source: BioMedTracker, a service of Sagient Research (http://biomedtracker.com/). PDUFA, Prescription Drug User Fee Act. MAA, market authorization application. LAR, long-acting release. SR, sustained release.

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