Drug pipeline: Q311

Wayne Peng

The US Food and Drug Administration continued to approve drugs at a faster pace than during the same time last year. Small molecules were particularly prominent, including Roche's B-RAF V600E mutation-specific Zelboraf (vemurafenib), which was approved for melanoma treatment just 99 days after filing. Seattle Genetics's antibody-drug conjugate, Adcetris (brentuximab vedotin), was also approved for lymphoma. Several biologics and novel therapeutics made progress in early stages, including AVI BioPharma's exon-skipping-inducer, eteplirsen, for muscular dystrophy, Baxter's autologous stem cell therapy for cardiovascular diseases and Novavax's influenza vaccine comprising virus-like particles. Several companies announced yet to be published late-stage results: Roche/Genentech's pertuzumab met its endpoints in breast cancer, Sanofi's alemtuzumab showed efficacy in the new indication of multiple sclerosis and Dynavax's hepatitis B virus vaccine Heplisav was protective. Regulatory decisions on JAK-STAT pathway inhibitor INCB 18424 (ruxolitinib) for treating myeloproliferative disorders and myelofibrosis and Bristol-Myers Squibb's dapagliflozin in insulin-independent diabetes are eagerly awaited.

Notable regulatory approvals (Q3 2011)

Drug/company	Indication	Approval and drug information
Zelboraf (vemurafenib; PLX4032)/Roche	Melanoma	8/17/11, FDA. Specific inhibitor for B-RAF V600E mutation.
Adcetris (brentuximab vedotin)/Seattle Genetics	Hodgkin's lymphoma; anaplastic large cell lymphoma	8/19/11, FDA. Antibody-drug conjugate for two lymphoma indications.
Firazyr (icatibant acetate)/ Shire Pharmaceuticals	Hereditary angioedema	8/25/11, FDA. Selective bradykinin B2 antagonistic peptide, which was approved by EMA 3 years ago (7/15/08).
Xalkori (crizotinib)/Pfizer	Non–small cell lung cancer	8/26/11, FDA. Dual-specific inhibitor of hepatocyte growth factor receptor (HGFR/ c-Met) and ALK tyrosine kinases.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). FDA, Federal Drug Administration; EMA, European Medicines Agency.

Notable regulatory setbacks (Q3 2011)

Drug/company	Indication	Setback summary
Macugen (pegaptanib)/Pfizer	Diabetic macular edema	On 7/19/11, company withdrew MAA for new indication owing to unfavorable CHMP review. The RNA aptamer targeting VEGF-165 isoform was approved for wet age-related macular degeneration in the US and EU in 2005.
NicVAX/Nabi Biopharmaceuticals	Smoking cessation	On 7/18/11, company announced that a phase 3 trial of the nicotine conjugate 'vaccine', intended to elicit neutralizing antibodies that block nicotine molecules in circulation from reaching the brain, failed to meet the primary endpoint in boosting abstinence rate.
Laquinimod/Teva Pharmaceuticals	Multiple sclerosis	On 8/1/11, company announced that phase 3 trial of Active Biotech's small-molecule immunosuppressant, which is believed to modulate Th1/Th2 cytokine balance, failed to meet the primary endpoint.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). MAA, market authorization application; CHMP, Committee for Medicinal Products for Human Use.

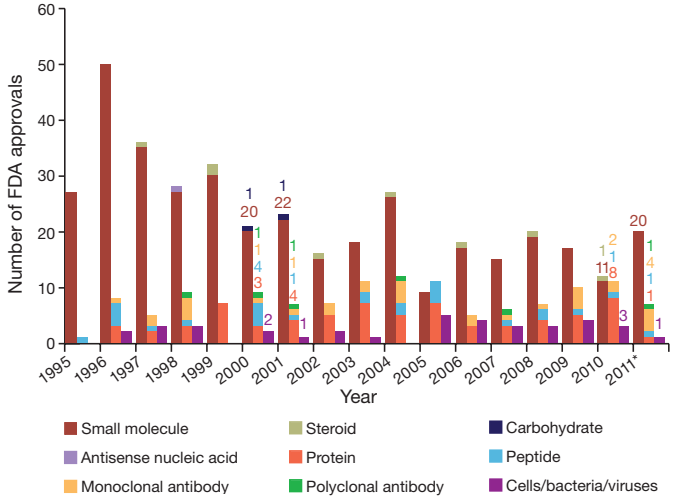
Notable upcoming regulatory decisions (Q4 2011–Q1 2012)

Drug/company	Indication	Expected regulatory decision
SOM 230 (pasireotide)/ Novartis	Cushing's disease	9/21/11–12/31/11, MAA decision. Pasireotide is a somatostatin-based cyclohexapeptide and a somatostatin receptor-1, 2, 3 and 5 agonist.
Uplyso (taliglucerase alfa)/Pfizer	Gaucher's disease	10/01/11–5/31/12, MAA decision. 2/1/12, PDUFA, second review after responding to FDA complete response letter on 8/17/11. Phase 3 trial of the plant cell–expressed recombinant glucocerebrosidase enzyme replacement therapy met both primary and secondary endpoints and demonstrated safety. (*Blood* published online, doi:10.1182/blood-2011-07-366955, 6 September 2011)
Dapagliflozin/ Bristol-Myers Squibb	Type 2 diabetes mellitus	10/28/11, PDUFA; 11/01/11--5/31/12, MAA decision. The sodium glucose cotransporter type 2 (SGLT-2) inhibitor met the primary endpoints for weight loss and blood sugar control in two phase 3 trials in combination with metformin (American Diabetes Association Abstract 0307-OR, 6/27/11). On 7/19/11, however, an FDA advisory panel voted 9–6 against approval based on safety concerns.
Eylea (aflibercept, intravitreal)/ Regeneron	Wet age-related degeneration	11/18/11, PDUFA, 3-month extension. FDA advisory panel voted on 6/23/11 in favor of approval of the selective bradykinin B2 antagonist peptide, which received EU approval in July 2008.
INCB 18424 (ruxolitinib)/Incyte	Myeloproliferative disorders; myelofibrosis	12/3/11, PDUFA. Ruxolitinib is the lead compound of a series of synthetic JAK1/JAK2 kinase inhibitors.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). PDUFA, Prescription Drug User Fee Act.

FDA approvals by drug molecule type

Small-molecule approval picks up speed again in 2011.



Source: FDA; BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). *Partial year 2011 to 9/9/11.

Notable trial results (Q3 2011)

Drug/company	Indication	Results
Autologous CD34+ stem cells/Baxter	Coronary artery disease	Phase 2 trial involving 167 patients met the primary endpoint in reducing angina episodes as well as the secondary endpoint of increasing exercise tolerance time. (*Circ. Res.* published online, doi:10.1161/ CIRCRESAHA.111.245993, 7 July 2011)
AVI 4658 (eteplirsen)/AVI BioPharma	Duchenne muscular dystrophy	Phase 1b/2 trials involving 19 patients demonstrate safety of the phosphorodiamidate morpholino RNA oligomer that induces exon 51 skipping of dystrophin gene. (*Lancet* **378**, 595–605, 2011)
Lebrikizumab/ Roche	Asthma	Phase 2a trial of the humanized anti-IL13 monoclonal antibody met primary and secondary endpoints in improving respiratory function. (*N. Engl. J. Med.* published online, doi:10.1056/NEJMoa1106469, 31 August 2011)
Preos (parathyroid hormone, PTH, 1-84)/NPS Pharmaceuticals	Hypoparathyroidism	Phase 2 trial showed that the recombinant human parathyroid hormone fragment (1-84) reduces the requirement for calcium and vitamin D supplements in hypoparathyroid patients. The drug was approved for osteoporosis treatment in the EU in 2006 under a different trade name (Preotact). (*J. Bone Mineral Res.* published online, doi:10.1002/jbmr.470, 19 July 2011)
VLP influenza vaccine/Novavax	Influenza	Phase 1/2 trials of the trivalent virus-like particle vaccine against influenza infection demonstrated safety, immunogenicity and cross-reactivity. (*J. Virol.* published online, doi:10.1128/JVI.05406-11, 24 August 2011; *Vaccine* published online, doi:10.1016/j.vaccine.2011.07.099, 4 August 2011)

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

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