Drug pipeline: Q411

H Craig Mak

Despite several big pharmas leaving neurology, the drug pipeline is the second largest after oncology. The FDA approved Hemacord, the first off-the-shelf human cord blood cell product. Positive efficacy was also obtained for cell therapies in congestive heart failure (MyoCell) and limb ischemia (Imyelocel-T). Panaclar and ocrelizumab met their end points in multiple sclerosis as did DiaPep277 in type I diabetes. The oncolytic treatment Reolysin showed positive phase 2 results in head and neck cancer. On the downside, Sangamo Biosciences' lead zinc-finger program was discontinued.

Notable regulatory approvals (Q4 2011)

Drug/company	Indication	Approval information
Hemacord/New York Blood Center	Bone marrow transplant; stem cell transplant	11/10/2011, FDA. Hematopoietic progenitor cells from human cord blood.
Jakafi (ruxolitinib; INCB18424)/Incyte	Myelofibrosis; myelopro-liferative disorders	11/16/2011, FDA. Janus-associated kinase 1/2 inhibitor.
Capreisa (vande-tanib)/AstraZeneca	Thyroid cancer	11/17/2011, EMA. MAA tyrosine kinase inhibitor that blocks vascular endothelial growth factor receptor 2.
Tafamidis meglumine/Pfizer	Amyloidosis	11/17/2011, EMA. MAA small molecule that stabilizes transthyretin.
Erwinaze (asparagi-nase *Erwinia chrysanthemi*)/EUSA	Acute lymphocytic leukemia	11/18/2011, FDA. Asparaginase enzyme purified from *Erwinia chrysanthemi*.
Eylea (aflibercept)/ Regeneron	Wet age-related macular degeneration	11/18/2011, FDA. Soluble VEGF receptor fusion protein.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/). FDA, U.S. Food and Drug Administration; EMA, European Medicines Agency; MAA, Market Authorization Application.

Notable regulatory setbacks (Q4 2011)

Drug/company	Indication	Setback summary
SB-509/Sangamo Biosciences	Diabetic peripheral neuropathy	10/3/2011. In phase 2b trial, plasmid DNA encoding a vascular endothelial growth factor A–inducing zinc finger did not meet its primary or secondary clinical end points.
CVAC-301/ Bavarian Nordic	Pancreatic cancer	10/6/2011. In phase 3 trial, the prime-boost vaccine targeting tumor-associated antigens did not meet the primary end point of overall survival.
Oral salmon calcitonin/Novartis	Osteoarthritis	10/13/2011. Preliminary analysis of a phase 3 trial showed recombinant hormone did not meet either co-primary or secondary end points.
Actemra (tocilizumab)/ Roche	Ankylosing spondylitis	10/17/2011. Phase 3 trial of the humanized anti-IL-6 receptor monoclonal antibody did not meet primary end point.
AMG 827/Amgen	Crohn's disease	10/25/2011. Interim data from phase 2 study suggest fully human anti-interleukin 17 monoclonal antibody unlikely to benefit patients.
ALX-0081/Ablynx	Percutaneous coronary interventions; stable angina	11/10/2011. In phase 2 study, bivalent anti–von Willebrand factor nanobody did not perform better than ReoPro.
Vorapaxar (SCH 530348)/Merck	Acute coronary syndrome	11/14/2011. In phase 2 study, thrombin receptor antagonist did not meet the primary end point. (*NEJM* published online, doi:10.1056/NEJMoa1109719 (13 November 2011))
Avastin (bevacizumab)/ Roche	Breast cancer	11/18/2011. FDA revoked approval for metastatic breast cancer.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/); FDA, U.S. Food and Drug Administration.

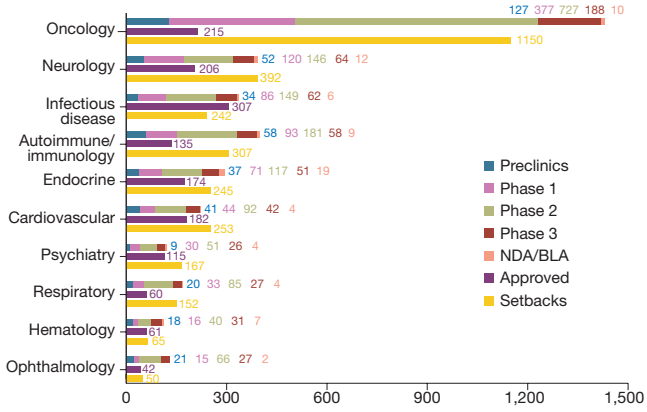
Notable upcoming regulatory decisions (Q1–Q2 2012)

Drug/company	Indication	Expected regulatory decision
NN1841/Novo Nordisk	Factor XIII deficiency	12/23/11, PDUFA. NN1841 is a recombinant factor XIII that stabilizes blood clots.
Voraxaze (glucarpidase)/BTG	Drug toxicity	1/18/12, PDUFA, priority review. Glucarpidase is a recombinant bacterial enzyme that rapidly hydrolyzes the chemotherapy methotrexate.
Surfaxin (lucinac-tant)/Discovery Laboratories	Respiratory distress syndrome	3/6/12, PDUFA, fifth review. A 21-residue synthetic sinapultide peptide that mimics the human surfactant protein, SP-B.
Vismodegib/Roche	Basal cell carcinoma	3/8/12, PDUFA. FDA priority review status for the small-molecule hedgehog antagonist.
Hematide (pegine-satide)/Affymax	Anemia due to chronic renal failure, dialysis-dependent	3/27/2012, PDUFA. Hematide is a PEGylated synthetic peptidomimetic of erythropoietin.
Carfilzomib/Onyx	Multiple myeloma	3/28/12, estimated PDUFA date if priority review is granted for the tetrapeptide epoxyketone proteasome inhibitor.
HyQ (Gammagard Subcutaneous with Enhanze)/Baxter	Primary immunodeficiencies	4/1/12–4/30/12, PDUFA. Antibody formulated with recombinant human hyaluronidase to facilitate subcutaneous delivery.
Kalydeco (ivacaftor)/Vertex	Cystic fibrosis	4/19/12, estimated PDUFA date if priority review is granted for the cystic fibrosis transmembrane conductance regulator protein.
Gattex (teduglutide)/NPS	Short bowel syndrome	6/1/12, estimated PDUFA date if priority review is granted for glucagon-like peptide-2 analog.

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

Top ten diseases grouped by pipeline size

Oncology continues to dominate. Attrition is highest in neurology, cardiovascular and psychiatry.



Notable trial results (Q4 2011)

Drug/company	Indication	Result summary
MyoCell (autologous skeletal myoblasts)/ Bioheart	Congestive heart failure	Phase 2/3 trial showed that intramyocardial injection of myoblasts in heart failure patients improves functional capacity (walking distance over time). (*American Heart Journal* published online, doi:10.1016/j.ahj.2011.07.020 (12 September 2011))
Panaclar (BG-12; dimethyl fumarate)/ Biogen IDEC	Multiple sclerosis	Phase 3 trial of the second-generation fumarate derivative in 1,430 patients shows a significantly reduced annualized relapse rate.
Ocrelizumab/Roche	Multiple sclerosis	Phase 2b trial of the fully humanized anti-CD20 monoclonal antibody met primary end point of reducing gadolinium-enhancing lesions. (*The Lancet* published online, doi:10.1016/S0140-6736(11)61649-8 (1 November 2011))
Ixmyelocel-T/ Aastrom	Peripheral arterial disease	Phase 2b trial showed that the mixture of adult bone marrow stem and progenitor cells reduces the risk of disease progression in critical limb ischemia patients with no revascularization options.
Reolysin/Oncolytics	Head and neck cancer	Phase 2 trial of respiratory enteric orphan virus administered with paclitaxel and carboplatin showed significant activity in patients with platinum-refractory head and neck cancer.
DiaPep277/Teva	Diabetes mellitus, type I	Phase 3 trial of 457 patients with the synthetic peptide of human heat shock protein 60 met its primary and secondary end points.

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

H. Craig Mak is Associate Editor of Nature Biotechnology