Drug pipeline: 1Q13

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US Food and Drug Administration approvals continued at breakneck pace with 12 new molecular and biological entities. These included Roche's long-anticipated antibody-drug conjugate Kadcyla and Janssen's

first-in-class sodium glucose type 2 transporter Invokana. The quarter was not without disappointment, however; in particular, Affymax recalled its recently approved erythropoietin mimetic Omontys.

Historic US regulatory approvals by drug class

*New molecular entity class includes mainly small-molecule drugs, but also steroid, synthetic peptide and mixed compounds. *Partial year to March 29.
Source: U.S. Food and Drug Administration (FDA) (<http://www.fda.gov>), excluding non-NME drugs or new formulation.

Notable regulatory setbacks (Q1 2013)

Drug/company	Indication	Setback summary
Metreleptin (r-metHuLeptin)/BMS	Lipodystrophy	1/31/13. Amylin announced plans to resubmit BLA for this recombinant human leptin
Ampligen (rintatolimod)/Hemispherx	Chronic fatigue syndrome	2/4/13. FDA sent complete response letter for polyI/polyC dsRNA immune activator, requesting further studies on safety and efficacy
Ryzodeg (degludecplus)/Novo Nordisk	Diabetes	2/8/13. FDA sent a complete response letter for this fixed combination of long-acting and fast-acting insulins requesting additional cardiovascular data
Tresiba (insulin degludec)/Novo Nordisk	Diabetes	2/8/13. FDA sent a complete response letter for this long-acting insulin requesting additional cardiovascular data
Omontys (peginesatide)/Affymax	Kidney dialysis	2/22/13. FDA recall due to several cases of anaphylaxis, three leading to death
Heplisav/Dynavax	Hepatitis vaccine	2/25/13. FDA sent complete response letter requesting further evaluation of safety in broad patient range (18–70 years)
Kynamro/Sanofi Isis	Dyslipidemia/hypercholesterolemia	3/21/13. European CHMP panel confirmed negative opinion after appeal by company
CRLX101/Cerulean	Non-small-cell lung cancer	3/22/13. Company announced that phase 2b study of camptothecin-polymer conjugate failed to meet endpoint of overall survival
Zymafos (palifosfamide)/Ziopharm Oncology	Sarcoma	3/26/13. Company suspended development of bifunctional DNA alkylator after phase 3 trial failed to meet primary endpoint of progression-free survival
Ixmyelocel-T/Aastrom	Critical limb ischemia	3/27/13. Company suspended phase 3 trial because of recruitment problems. Phase 2b trial for dilated cardiac myopathy will continue.
Elacetytarabine/Clavis Pharma	AML	4/1/13. Company reported that phase 3 trial of its lipid-conjugated form of cytarabine failed to improve overall survival over control arm.

Source: BioMedTracker, a service of Sagient Research (<http://www.biomedtracker.com/>). FDA, US Food and Drug Administration; EMA, European Medicines Agency; BMS, Bristol-Myers Squibb; AML, acute myeloid leukemia; CHMP, Committee for Medicinal Products for Human Use (EMA).

Notable upcoming regulatory decisions (Q3 2013)

Drug/company	Indication	Expected regulatory decision
Afatinib/Boehringer	Non-small-cell lung cancer	7/15/13, FDA PDUFA. Novel irreversible binder of EGFR and HER2
Suvorexant/Merck	Insomnia	5/20–5/21/13, FDA PDUFA. Orexin A and B antagonist
[18F]Flutemetamol/GE	Alzheimer's disease	6/25–7/25/13, FDA PDUFA. PET imaging agent for beta amyloid plaques
Tivopath (tivozanib)/AVEO, Astellas	Renal cell carcinoma	7/26/13, FDA PDUFA. Small-molecule inhibitor of VEGF receptors 1,2,3
Alpharadin (radium 223 chloride)/Bayer, Algeta	Prostate cancer	8/14/13, FDA PDUFA. Bone-targeting radium 223 isotope
Florbetaben/Piramal Health	Alzheimer's disease	9/3/13–10/3/13, PDUFA. F18-tagged sugar molecule for detecting beta amyloid plaques

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.

Notable clinical trial results (Q1 2013)

Drug/company	Indication	Result summary
MEK162/Novartis	Melanoma	2/13/13. Phase 2 open-label, non-randomized clinical trial showed efficacy on patients with <i>NRAS</i> -mutated or Val600 <i>BRAF</i> mutations (<i>Lancet Oncol.</i> 14 , 249–256)
Treanda (bendamustine)/TEVA	Mantle cell lymphoma, non-Hodgkin lymphoma	2/20/13. In a randomized open-label phase 3 trial, this novel DNA alkylating agent with Rituxan/MabThera (rituximab) showed increased progression-free survival and fewer side effects than the standard of care (<i>Lancet</i> 381 , 1203–1210)
Pradaxa (dabigatran etexilate)/Boehringer Ingelheim	Venous thromboembolism	2/20/13. Two double-blind randomized phase 3 trials show that this direct thrombin inhibitor reduces the risk of recurrent embolisms (<i>N. Engl. J. Med.</i> 368 , 709–718)
Enobosarm/Gtx	Cachexia/weight loss	3/14/13. In phase 2b trial, patients showed significant increase in body mass and stair climbing power. (<i>Lancet Oncol.</i> 14 , 335–345, 2013, doi:10.1016/S1470-2045(13)70055-X)

Source: BioMedTracker, a service of Sagient Research (<http://www.biomedtracker.com/>). FDA, US Food and Drug Administration; EMA, European Medicines Agency; NRAS, neuroblastoma rat sarcoma.

Notable regulatory approvals (Q1 2013)

Drug/company	Indication	Drug information
Pomalyst (pomalidomide)/Celgene	Multiple myeloma	2/8/13, FDA. Cell signaling molecule via cereblon (CBRN) with immunomodulatory and anti-angiogenesis properties
Kadcyla (trastuzumab DM-1)/Roche	Breast cancer	2/22/13, FDA. Antibody-drug conjugate against HER2
Stivarga (regorafenib)/Bayer	Gastrointestinal stromal tumors	2/25/13, FDA. Multi-kinase inhibitor against various RAF kinases and VEGF receptor family (already approved in colon cancer)
TOBI (tobramycin) Podhaler/Novartis	Cystic fibrosis	3/22/13, FDA. First inhaled powder aminoglycoside antibiotic
Tecfidera (dimethyl fumarate)/Biogen	Multiple sclerosis	3/27/13, FDA. Oral neuroprotective anti-inflammatory molecule targeting NF-KappaB
Invokana (canaglifloxin)/Janssen (J&J)	Type 2 diabetes	3/29/13, FDA. First-in-class sodium-glucose co-transporter inhibitor

Source: BioMedTracker, a service of Sagient Research (<http://www.biomedtracker.com/>). FDA, US Food and Drug Administration; EMA, European Medicines Agency; J&J, Johnson & Johnson.

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