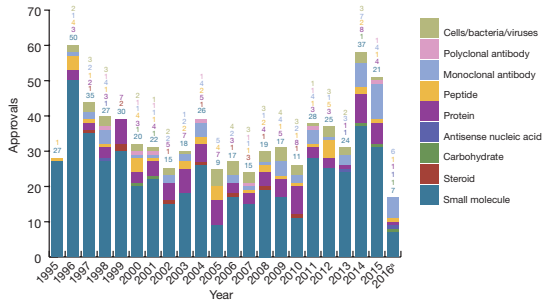
# Drug pipeline: 3Q16

Laura DeFrancesco

The controversial approval of an antisense drug for muscular dystrophy dominated news this quarter, with overall approvals down compared with recent years. Two biosimilars made it over the finish line at the US Food and Drug Administration (FDA), and the European Medicines Agency (EMA) approved a genetically modified allogeneic T-cell therapy for use in bone marrow/stem cell transplants. A slew of breakthrough designations included two gene therapies; December looks to be a busy month at the FDA.

### Historic FDA approvals by drug type

The trend for fewer drug approvals continues in 2016.




[a]2016 partial year ending Sept. 30.

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

### Notable setbacks (3Q16)

| Drug/company | Indication | Summary |
|---|---|---|
| Rociletinib/Clovis Oncology | Non-small cell lung cancer | 6/30/2016 FDA issued a complete response letter for this epidermal growth factor receptor inhibitor for patients with EGFR T70-M mutation owing to inconsistent results in phase 2 trial |
| ChondroCelect/TiGenix | Cartilage and joint repair | 7/05/2016 Company withdrew autologous chondrocyte therapy from market for commercial reasons |
| Biosimilar Pegfilgrastim (Sandoz)/Novartis | Neutropenia/ leukopenia | 7/19/2016 FDA issued a complete response letter for this Neulasta biosimilar |
| Andexxa (andexanet alfa)/Portola | Drug toxicity | 8/17/2016 FDA issued a complete response letter owing to manufacturing issues of this recombinant Factor IX antidote |
| Parsabiv/Amgen | Hyperparathyroidism (secondary) | 8/24/2016 FDA issued a complete response letter for this peptide protein kinase C epsilon inhibitor |
| RG-101/Regulus | Hepatitis C | 6/27/2016 FDA put a clinical hold on this GalNAc-conjugated, small interfering RNA antagonist, which targets microRNA-122 after a second jaundice adverse event |
| Krystexxa (pegloticase)/ Horizon Pharma | Gout | 7/4/2016 Company withdrew recombinant polyethylene glycol conjugate of uricase from European market |
| NY-ESO-1(C259)/ Adaptimmune | Ovarian cancer | 8/3/2016 The company announced an amendment to its protocol for its TCR targeting testis antigen2B due to lack of objective clinical response in ph 1/2 trial |

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

### Notable clinical trial results (3Q16)

| Drug/company | Indication | Summary |
|---|---|---|
| Dalcetrapib/ DalCor | Dyslipidemia/ hypercholesterolemia | 7/14/2016 Randomized, placebo-controlled phase 3 trial of cholesterylester transfer protein inhibitor in which patients showed adenylate cyclase 9 polymorphism-dependent effects on inflammation and cholesterol efflux. (*Circ. Cardiovasc. Genet.* **9**, 340–348, 2016) |
| Veliparib/ AbbVie | Breast cancer | 7/7/2016 Adaptive trial of poly ADP-ribose polymerase inhibitor with standard chemo on patients grouped by eight biomarker subtypes outperformed complete response rates compared with standard therapy alone, especially triple negative cancers. (*N. Engl. J. Med.* **375**, 23–34, 2016) |
| Neratinib/Puma Biotechnology | Breast cancer | 7/7/2016 Adaptive trial of small molecule, an irreversible pan-HER (Erbb1, ErbB2 and ErbB4) tyrosine kinase inhibitor, added to standard of care with women tested with MammaPrint showed complete response of 48% compared with 29% in control arm. (*N. Eng. J. Med.* **375**, 11–22, 2016) |
| Romosozumab/ Amgen | Osteoporosis/ osteopenia | 9/18/2016 Phase 3 random, placebo-controlled trial of a humanized anti-sclerostin mAb of post-menopausal women showed 73% reduction in new vertebral fractures. (*N. Engl. J. Med.* **375**, 1532–1543, 2016) |
| Cx601/TiGenix | Crohn's disease | 7/28/2016 In randomized, placebo-controlled phase 3 trial of allogenic-expanded adipose-derived stem cells, 50% of patients achieved remission compared to 34% in controls. (*Lancet* **388**, 1281–1290, 2016) |
| Aducanumab/ Biogen | Alzheimer's disease | 8/31/2016 In phase 1b study of anti-beta-amyloid human mAb, prodermal or mild Alzheimer's patients had dose-dependent reduction in plaques and slowing in clinical decline. (*Nature* **537**, 50–56, 2016) |

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

### Notable regulatory approvals (3Q16)

| Drug/company | Indication | Drug Information |
|---|---|---|
| Zalmoxis (TK-DLI)/ MolMed | Bone marrow transplant and stem cell transplant | 8/18/2016 EMA approved allogeneic T cells engineered with a retroviral vector encoding truncated human low affinity nerve growth factor receptor and herpes simplex I virus thymidine kinase suicide gene to combat infection and graft-versus-host disease |
| Adlyxin (lixisenatide)/Sanofi | Diabetes mellitus II | 7/28/2016 FDA approved glucagon-like peptide 1 receptor (exendin-4(1-39)) modified C-terminally with six additional lysine residues for longer half-life |
| Erelzi (etanercept)/ Novartis | Psoriasis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, juvenile rheumatoid arthritis | 8/30/2016 FDA approved Enbrel biosimilar (fusion protein of Fc portion of human antibody grafted to ligand binding portion of TNF) |
| Amjevita (adalimumab)/Amgen | Juvenile rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulceritis colitis, psoriasis | 8/30/2016 FDA approved Humira biosimilar (recombinant human IgG1 against TNF) |
| Exondys 51 (eteplirsen)/ Sarepta | Muscular dystrophy | 9/19/2016 FDA approved phosphorodiamidate morpholino oligomer that promotes exon 51 skipping in dystropin gene |
| Xiidra (lifitegrast)/ Shire | Dry eye | 7/11/2016 FDA approved small-molecule binder of integrin lymphocyte function-associated antigen-1 |
| **Breakthrough therapy designation** | | |
| LOXO-101/Loxo Oncology | Solid tumors | 7/13/2016 Small-molecule inhibitor selective for ATP binding site of tropomyosin-related kinase (Trk) family fusions |
| AVXS-101/AveXis | Spinal muscular atrophy | 7/20/2016 Adeno-associated virus serotype 9 (AAV9)-delivered human survival motor neuron gene |
| PF-06838435/ Pfizer | Hemophilia B | 7/21/2016 AAV2-delivered human coagulation factor IX gene |
| Darzalex (daratumumab)/Johnson & Johnson | Multiple myeloma | 7/26/2016 Fully human IgG1 kappa mAb targeting CD38 |
| Pracinostat/ Helsinn Healthcare | Acute myelogenous leukemia | 8/01/2016 Small-molecule biaryl-linked hydroxamate deacetylase inhibitor |
| LEE011 (ribociclib)/Novartis | Breast cancer | 8/03/2016 Small-molecule selective inhibitor of cyclin D1/cyclin-dependent kinase 4/6 inhibitor |
| Esketamine/ Johnson & Johnson | Major depressive disorder | 8/16/2016 S-enantiomer of ketamine, an N-methyl-D-aspartate receptor antagonist |
| SL-401/Stemline therapeutics | Blastic plasmacytoid dendritic cell neoplasm | 8/23/2016 Recombinant fusion protein of human IL-3 conjugated to diphtheria toxin |
| SAGE-547 (allopregnanolone)/ Sage Therapeutics | Major depressive disorder | 9/06/2016 Small-molecule positive gamma amino butyric acid-A receptor allosteric modulator |

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

### Notable upcoming catalysts (4Q16)

| Drug/company | Indication | Drug information |
|---|---|---|
| Sarilumab/Regeneron | Rheumatoid arthritis | 10/28/2016 FDA PDUFA date for fully human anti-IL-6 alpha receptor (IL-6R) mAb |
| Siliq (brodalumab)/ Valeant | Psoriasis | 11/16/2016 FDA PDUFA date for fully human IgG2 mAb against IL-17A receptor |
| Olaratumab/Eli Lilly | Sarcoma | 11/30/2016 FDA PDUFA date for IgG1 mAb against platelet-derived growth factor receptor alpha |
| Ocrevus/(ocrelizumab)/Roche | Multiple sclerosis | 12/28/2016 FDA PDUFA date for second-generation fully humanized anti-CD20 mAb |
| Tenofovir alafenamide fumarate/Gilead | Hepatitis B | 11/11/2016 FDA PDUFA date for prodrug of tenofir, a nucleoside analog of AMP |
| Solithera (solithromycin)/Cempra | Community-acquired pneumonia | 12/27/2016 FDA PDUFA for next-generation macrolide, the first fluoroketolide |
| Lutathera/Advanced Accelerator Applications | Neuroendocrine tumors | 12/28/2016 FDA PDUFA for 177-lutetium-radiolabeled somatostatin receptor-targeted peptide |

PDUFA, The Prescription Drug User Fee Act; IL, interleukin; mAb, monoclonal antibody. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com/)

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