OPTUMRx®

RxOutlook®

4th Quarter 2016

Pending drug approvals

Drug name	Manufacturer	Indication/use	Expected FDA decision date
abaloparatide	Radius Health/Ipsen/ Novartis/Teijin Pharma	Osteoporosis	3/2017
baricitinib	Eli Lilly/Incyte	Rheumatoid arthritis	1/19/2017
crisaborole	Pfizer	Atopic dermatitis	1/7/2017
deflazacort	Marathon	Duchenne muscular dystrophy	2/14/2017
dupilumab (Dupixent™)	Regeneron/Sanofi	Atopic dermatitis	3/29/2017
empagliflozin/metformin ER	Boehringer Ingelheim	Type 2 diabetes mellitus	11/2016–2/2017
house dust mite immunotherapy (Mitizax®)	ALK-Abello/Abbott/Torii	House dust mite allergic rhinitis	2/2017
naldemedine	Shionogi	Opioid-induced constipation	3/23/2017
plecanatide (Guanilib™)	Synergy/Ironwood	Chronic idiopathic constipation	1/29/2017
rucaparib	Clovis Oncology/Pfizer	Ovarian cancer	2/23/2017

abaloparatide

Manufacturers: Radius Health/Ipsen/ Novartis/Teijin Pharma

Therapeutic use
Abaloparatide is in development for the treatment of postmenopausal women with severe osteoporosis.

- Treatment of osteoporosis in postmenopausal women

Clinical profile
Abaloparatide is an analog of parathyroid hormone-related protein (PTHrP). PTHrP is structurally related to parathyroid hormone (PTH), and therefore, binds to the same receptor. PTHrP is synthesized in many normal cells and affects bone development.

In a pivotal trial involving postmenopausal women at high risk of fracture due to severe osteoporosis, fewer vertebral fractures occurred with abaloparatide vs. placebo (0.58% vs. 4.22%, $p < 0.001$). Similarly, fewer non-vertebral fractures occurred with abaloparatide vs. placebo (2.7% vs. 4.7%, $p = 0.049$).

The rate of non-vertebral fractures was not statistically significant for abaloparatide compared to Forteo® (teriparatide) (2.7% vs. 3.3%, $p = 0.44$), and the statistical analysis comparing the risk for vertebral fractures with abaloparatide vs. Forteo was not reported.

The common adverse events reported in trials with abaloparatide included hypercalcemia, dizziness, nausea, headache, hypertension, infection, and palpitations. However, the rate of hypercalcemia was lower with abaloparatide vs. Forteo (3.4% vs. 6.4%). In addition, the rates of neoplasm were no worse than placebo and lower compared to Forteo (2.4% vs. 3.5% vs. 3.8%, respectively).

Based on the pivotal trial, abaloparatide is given subcutaneously (SC) once daily.

- PTHrP analog
- SC formulation
- Fewer vertebral and non-vertebral fractures vs. placebo
- Non-vertebral fracture risk was not statistically significant compared to Forteo
- Common adverse events: hypercalcemia, dizziness, nausea, headache, hypertension, infection, and palpitations
- Lower rate of hypercalcemia vs. Forteo

Competitive environment
Currently, Forteo is the only anabolic agent approved for use in osteoporosis. If approved, abaloparatide would offer another anabolic treatment option for patients.

Furthermore, there was a lower risk for hypercalcemia and neoplasms with abaloparatide vs. Forteo.

However, Forteo is a similar available product and abaloparatide has not demonstrated clinical superiority to Forteo in reducing fracture risk.

The projected U.S. annual sales for abaloparatide are $306 million by 2021.

- Advantages: limited anabolic agents available for osteoporosis, lower risk of hypercalcemia and neoplasms vs. Forteo
- Disadvantages: similar product is available (ie, Forteo), no evidence of lower fracture risk vs. Forteo
- Projected U.S. sales are $306 million by 2021

Expected FDA decision date
An FDA decision regarding the approval of abaloparatide is expected by March 2017.

- PDUFA: 3/2017

baricitinib

Manufacturers: Eli Lilly/Incyte

Therapeutic use

Baricitinib is an oral drug in development for the treatment of moderate to severe rheumatoid arthritis (RA).

- Treatment of moderate to severe RA

Clinical profile

Baricitinib is a janus-associated kinase 1 and 2 (JAK 1/2) inhibitor.

In placebo-controlled trials, baricitinib demonstrated greater improvements in the signs and symptoms of RA vs. placebo by week 12.

Moreover, in a trial comparing baricitinib to Humira, greater improvements in the signs and symptoms of RA were observed with baricitinib vs. Humira at week 12 (70% vs. 61%, $p \leq 0.05$) and at week 24 (74% vs. 66%, $p \leq 0.05$).

In a non-inferiority trial, baricitinib was also compared against oral methotrexate administered once weekly. Baricitinib demonstrated non-inferiority to methotrexate at week 24.

The most common adverse events reported in trials with baricitinib were nasopharyngitis and bronchitis. However, serious safety concerns did occur, including major cardiovascular (CV) events and malignancies. In one of the trials, two deaths occurred in the baricitinib arm — one case of pneumonia and one case of duodenal hemorrhagic ulcer.

Based on trials, baricitinib is administered orally once daily.

- JAK 1/2 inhibitor
- Oral formulation
- Greater improvement in RA signs and symptoms vs. Humira
- Non-inferior to methotrexate
- Safety concerns: CV events and malignancies

Competitive environment

Baricitinib is an oral, once daily JAK inhibitor and was found to be efficacious in patients who had failed on conventional disease modifying anti-rheumatic drugs (DMARDs).

Nonetheless, baricitinib is not the first JAK inhibitor. Currently, Xeljanz and Xeljaz XR are both available and approved for use in RA. In addition, baricitinib has been associated with serious safety concerns (ie, CV events and malignancies).

Despite the safety concerns, the projected U.S. peak annual sales for baricitinib range from $1 billion by 2020 to $2.9 billion by 2025.

- Advantages: oral, once daily dosing, efficacious in patients who failed DMARDs
- Disadvantages: similar products are available (ie, Xeljanz, Xeljanz XR), serious safety concerns
- Projected U.S. peak sales are $1 billion by 2020 to $2.9 billion by 2025

Expected FDA decision date

An FDA decision regarding the approval of baricitinib is expected by January 19, 2017.

- PDUFA: 1/19/2017

crisaborole

Manufacturer: Pfizer

Therapeutic use

Crisaborole is a novel topical agent in development for the treatment of mild to moderate atopic dermatitis (AD) in children and adults.

- Treatment of mild to moderate AD in children and adults

Clinical profile

Crisaborole targets phosphodiesterase-4 (PDE-4), an enzyme that plays an important role in the production of tumor necrosis factor-alpha (TNF-alpha) and other cytokines. Blocking PDE-4 is thought to suppress and reduce the inflammatory process associated with certain diseases, including dermatological conditions.

In two pivotal trials, crisaborole was compared against vehicle. At day 29, a larger proportion of patients were clear or almost clear of their lesions and experienced a two-grade improvement from baseline with crisaborole vs. vehicle (32.8% vs. 25.4%, $p = 0.038$; 31.4% vs. 18%, $p < 0.001$).

The most common treatment-emergent adverse event with crisaborole use was application site pain. Skin infection also occurred in the trial but at a lower rate vs. vehicle (0.1% vs. 1%, $p = 0.017$).

Based on trials, crisaborole is administered topically twice daily.

- PDE-4 inhibitor
- Topical formulation
- Greater improvement in AD signs and symptoms vs. vehicle
- Common adverse event: application site pain

Competitive environment

If approved, crisaborole will be a first in-class, nonsteroidal treatment option for AD and a possible substitute for topical steroids and topical calcineurin inhibitors (eg, Protopic®, Elidel™).

Furthermore, an estimated 18–25 million Americans have AD, the majority of whom have mild to moderate disease.

However, topical steroids are considered the first-line prescription treatment for AD and offer several advantages over crisaborole; topical steroids are generically available, relatively inexpensive, and have varying potencies, which can address different patient severity levels. In contrast, crisaborole is not intended for patients with severe AD.

The projected U.S. peak annual sales for crisaborole are > $2 billion.

- Advantages: first in-class, nonsteroidal treatment option; possible substitute for topical steroids and calcineurin inhibitors
- Disadvantages: not intended for severe AD; topical steroids are inexpensive, generically available, and available in varying potencies
- Projected U.S. peak sales are > $2 billion

Expected FDA decision date

An FDA decision regarding the approval of crisaborole is expected by January 7, 2017.

- PDUFA: 1/7/2017

deflazacort

Manufacturer: Marathon

Therapeutic use
Deflazacort is an oral corticosteroid in development for the treatment of Duchenne muscular dystrophy (DMD).

DMD is a rare genetic disorder caused by a non-functional dystrophin protein. It is characterized by progressive muscle degeneration and weakness. The onset of DMD symptoms typically occurs before the age of 5, and patients are often wheelchair-bound before their teenage years due to declining muscle strength, in particular their hip and leg muscles. Patients rarely survive to their fourth decade of life due to cardiac or respiratory failure.

- Treatment of DMD

Clinical profile
Deflazacort is a glucocorticosteroid prodrug and a derivative of prednisone. Approximately, 1.3 mg of deflazacort is equivalent to 1 mg of prednisone.

In a pivotal trial in patients with DMD, deflazacort was compared to placebo and prednisone. The primary endpoint was improvement in muscle strength after 12 weeks, at which point patients in the placebo arm were randomly transitioned to receive either deflazacort or prednisone. Improvements in muscle strength were comparable between deflazacort and prednisone, and both drugs were superior to placebo.

Common adverse events reported in trials with deflazacort included Cushingoid appearance, erythema, and hirsutism. In other trials, deflazacort had higher rates of growth delays in children vs. prednisone, but the overall rate of adverse events were greater and more severe with prednisone, especially weight gain and psychiatric events, such as aggression and irritability.

Based on trials, deflazacort is given orally and dosed according to body weight.

- Corticosteroid
- Oral formulation
- Greater improvement in muscle strength vs. placebo but comparable with prednisone
- Common adverse events: Cushingoid appearance, erythema, and hirsutism

Continued…

deflazacort (Continued…)

Manufacturer: Marathon

Competitive environment

DMD affects an estimated 1 in 3,500 to 6,000 male births. Thus, deflazacort was granted an orphan drug designation. If approved, deflazacort will be the first FDA approved oral treatment for DMD. Currently, Exondys 51™ (eteplirsen) is the only FDA approved treatment for DMD but requires once weekly intravenous infusions. Moreover, only 13% of DMD patients are amenable to treatment with Exondys 51.

In terms of competitive disadvantages, there are other drugs similar to deflazacort that are available, such as prednisone. Furthermore, chronic, long-term use of systemic steroids poses many safety concerns, including adrenal suppression, weight gain, impairment of wound healing, increased blood glucose levels, cataracts, changes in mental status, and risk of osteoporosis.

- Advantages: orphan drug, no FDA-approved oral treatments for DMD
- Disadvantages: similar drugs are available (eg, prednisone), safety concerns with long-term use of systemic steroids

Expected FDA decision date

Deflazacort is an orphan drug and was granted fast track status and priority review by the FDA.

Two new drug applications (NDAs) were filed with the FDA for deflazacort. One is for a tablet formulation and the other for an oral suspension. An FDA decision regarding the approval of deflazacort is expected by February 14, 2017.

- Orphan drug
- Fast track status
- Priority review
- PDUFA: 2/14/2017

dupilumab (Dupixent)

Manufacturers: Regeneron/Sanofi

Therapeutic use
Dupilumab is a human monoclonal antibody in development for the treatment of moderate to severe AD in adults.

Dupilumab is also being studied for use in adolescent patients with AD.

- Treatment of moderate to severe AD in adults

Clinical profile
Dupilumab targets and antagonizes interleukin-4 (IL-4) and interleukin-13 (IL-13) receptors.

In clinical trials, dupilumab was compared against placebo in adult patients with moderate to severe AD. The primary endpoint was the proportion of patients who were clear or almost clear of their skin lesions and achieved at least a 2 point improvement from baseline as determined by the Investigator's Global Assessment (IGA) score. More patients achieved the endpoint with dupilumab vs. placebo (36% - 39% vs. 8.5%–12%, $p < 0.0001$).

Common adverse events reported in trials with dupilumab included injection site reactions and conjunctivitis; however, the overall rates of serious reactions were not higher than placebo.

Dupilumab has been studied as a once weekly and once every other week SC injection.

- IL-4/IL-13 antagonist
- SC formulation
- Greater improvement in AD signs and symptoms vs. placebo
- Common adverse events: injection site reactions, conjunctivitis

Competitive environment
Currently, there are limited unique treatment options for AD and no FDA-approved systemic treatment options for this condition. Thus, dupilumab could become the first approved systemic treatment for AD.

Though the majority of AD patients have mild to moderate disease, dupilumab will be entering a large market consisting of 18–25 million Americans, of whom 2%–10% are adults.

However, dupilumab will require frequent SC injections. In addition, the long-term safety profile of dupilumab with chronic use is unknown at this time.

Similar to other monoclonal antibodies, the cost for dupilumab is expected to be high.

The projected peak annual U.S. sales for dupilumab vary widely with optimistic analysts expecting sales as high as $2.5 to $5 billion.

- Advantages: limited unique treatment options, first systemic treatment for AD
- Disadvantages: requires SC injection, long-term safety remains unknown, projected high cost
- Projected peak U.S. sales are $2.5–$5 billion

Continued…

dupilumab (Dupixent) (Continued…)

Manufacturers: Regeneron/Sanofi

Expected FDA decision date

Dupilumab was granted breakthrough status by the FDA.

An FDA decision regarding the approval of dupilumab is expected by March 29, 2017.

- Breakthrough status
- PDUFA: 3/29/2017

empagliflozin/metformin ER

Manufacturer: Boehringer Ingelheim

Therapeutic use
Empagliflozin/metformin extended-release (ER) is an oral fixed-dose combination (FDC) product in development as an adjunct to diet and exercise for the treatment of type 2 diabetes mellitus (T2DM).

- Adjunct to diet and exercise for the treatment of T2DM

Clinical profile
This FDC product contains the sodium glucose co-transporter 2 (SGLT-2) inhibitor, empagliflozin, and an extended-release version of the biguanide, metformin.

Trials have been conducted to evaluate the relative bioavailability of empagliflozin/metformin ER to its individual components when administered singularly. Additional trials were performed to examine the free combination of empagliflozin and metformin ER following high fat or high caloric meals. However, results from these various trials are not available at this time.

Empagliflozin/metformin ER is an oral product intended for once daily dosing.

- SGLT-2 inhibitor/ biguanide combination
- Oral formulation
- Supported by bioequivalence studies

Competitive environment
Empagliflozin/metformin ER offers a convenient once daily option for patients currently taking Synjardy® (empagliflozin/metformin) or the individual components separately. Synjardy is dosed twice daily.

In addition, a recent trial comparing empagliflozin to placebo (EMPA REG OUTCOME) demonstrated a 14% reduction in the risk for CV events with empagliflozin. While this data cannot be used to suggest that similar benefits will apply to empagliflozin/metformin ER, the trial may still influence prescribing behaviors and affect the utilization of all empagliflozin-containing products.

However, other related combination products are also available (eg, Synjardy, Invokamet®, Xigduo® XR). In addition, CV outcomes trials are in progress for Invokana® and Farxiga® as well.

- Advantages: offers convenient once daily dosing, empagliflozin has shown reduction in CV risk vs. placebo
- Disadvantages: related products are available (eg, Synjardy, Invokamet, Xigduo XR)

Expected FDA decision date
An FDA decision regarding the approval of empagliflozin/metformin ER is expected between the fourth quarter of 2016 and the first quarter of 2017.

- PDUFA: 4Q2016–1Q2017

house dust mite immunotherapy (Mitizax)

Manufacturers: ALK-Abello/Abbott/Torii

Therapeutic use

Mitizax is a novel drug in development for the treatment of allergic rhinitis associated with house dust mites (HDM).

- Treatment of allergic rhinitis associated with HDM

Clinical profile

Mitizax is a sublingual immunotherapeutic (SLIT) agent.

Mitizax contains biological extracts of HDM allergen, which is used to desensitize patients and reduce or eliminate allergic symptoms associated with dust mites.

- Immunotherapeutic agent
- Sublingual formulation

In two pivotal trials, Mitizax was compared against placebo. The primary endpoint was the Total Combined Rhinitis Score (TCRS), which evaluates patients' daily symptoms and use of allergy medications, such as antihistamines, intranasal steroids, or oral steroids. In both trials, greater improvements in TCRS were observed with Mitizax vs. placebo (17%–22%).

- Greater improvement in allergic rhinitis symptoms vs. placebo

The primary safety concern with SLIT agents is the risk for systemic allergic reactions. There was one treatment-related incident requiring epinephrine therapy.

- Safety concern: systemic allergic reaction

Based on trials, Mitizax is given sublingually once daily.

Competitive environment

If approved, Mitizax will be the first outpatient HDM-specific drug approved by the FDA. Thus, it offers a convenient at-home dosing option for patients.

- Advantages: will be first outpatient drug for HDM, offers convenient at-home dosing

Nonetheless, the primary benefit will be for patients with only HDM allergic rhinitis. Patients with other concurrent allergies may find less benefit with Mitizax since these other allergic conditions will still require separate treatment by an allergist. Moreover, approximately 20% of patients report poor to no effect with allergen-specific immunotherapy.

- Disadvantage: primarily for patients with only HDM allergy, ~20% of patients report poor to no effect with allergen-specific immunotherapy

The projected U.S. annual sales of Mitizax are $110–$236 million by 2020 or 2021.

- Projected U.S. sales are $110–$236 million by 2020 or 2021

Expected FDA decision date

An FDA decision regarding the approval of Mitizax is expected by February 2017.

- PDUFA: 2/2017

naldemedine

Manufacturers: Shionogi

Therapeutic use
Naldemedine is in development for the treatment of opioid induced constipation (OIC) associated with chronic non-cancer pain (NCP) in adults receiving opioid therapy.

- Treatment of OIC in adults with chronic NCP

Clinical profile
Naldemedine is a peripheral opioid antagonist.

In placebo-controlled trials, patients were evaluated for an increase in the frequency of spontaneous bowel movement from baseline. A greater proportion of subjects responded to naldemedine vs. placebo (47.6% vs. 34.6%, $p = 0.002$; 52.5% vs. 33.6%, $p < 0.0001$).

The most common adverse events reported in trials were abdominal pain, diarrhea, and vomiting.

Based on trials, naldemedine is administered orally once daily.

- Peripheral opioid antagonist
- Oral formulation
- Greater proportion of responders with naldemedine vs. placebo
- Common adverse events: abdominal pain, diarrhea, and vomiting

Competitive environment
Naldemedine is touted as a fast acting drug with onset as early as 11 hours in one phase 2b trial. In addition, there was no effect on opioid efficacy or risk for opioid withdrawal with naldemedine.

Currently, there is limited safety data available for naldemedine. Alternative treatments include Amitiza®, Movantik™, and Relistor®. Relistor is available as an oral tablet and as an injectable product.

The projected U.S. annual sales for naldemedine are $219 million by 2020.

- Advantage: fast onset, no effect on opioid efficacy or opioid withdrawal risk
- Disadvantages: limited safety data, alternatives are available (eg, Amitiza, Movantik, Relistor)
- Projected U.S. sales are $219 million by 2020

Expected FDA decision date
An FDA decision regarding the approval of naldemedine is expected by March 23, 2017.

- PDUFA: 3/23/2017

plecanatide (Guanilib)

Manufacturer: Synergy/Ironwood

Therapeutic use
Plecanatide is a novel drug in development for the treatment of chronic idiopathic constipation (CIC).

Plecanatide is also in phase 3 trials for irritable bowel syndrome (IBS).

- Treatment of CIC

Clinical profile
Plecanatide is an oral uroguanylin analog. Uroguanylin is a natural hormone produced by the gastrointestinal (GI) system that helps to regulate intestinal function by activating guanylate cyclase C (GC-C). GC-C promotes fluid and ion transport in the GI tract, leading to looser stools.

In two placebo-controlled trials, a greater proportion of patients experienced spontaneous bowel movements with plecanatide vs. placebo (19.5% vs. 10.2%, $p < 0.001$; 20% vs. 12.8%, $p = 0.004$).

The most common adverse event was diarrhea.

Based on trials, plecanatide is administered orally once daily.

- Uroguanylin analog
- Oral formulation
- Greater proportion of responders with plecanatide vs. placebo
- Common adverse event: diarrhea

Competitive environment
Plecanatide offers a novel, once daily option for patients with CIC. Onset of effect typically occurs within the first week of therapy. In addition, it may provide benefit to patients with constipation predominant IBS.

However, safety data are limited for plecanatide, and various alternatives are available, such as Amitiza, Linzess®, and various over-the-counter (OTC) options.

Assuming both the CIC and IBS indications are approved, the projected U.S. annual sales for plecanatide are $421 million by 2020.

- Advantage: novel mechanism, once daily dosing, fast onset, may benefit constipation predominant IBS patients
- Disadvantages: limited safety data, alternatives are available (eg, Amitiza, Linzess, OTC products)
- Projected U.S. sales are $421 million by 2020 for CIC and IBS indications

Expected FDA decision date
An FDA decision regarding the approval of plecanatide is expected by January 29, 2017.

- PDUFA: 1/29/2017

rucaparib

Manufacturer: Clovis Oncology/Pfizer

Therapeutic use
Rucaparib is a new poly ADP ribose polymerase (PARP) inhibitor in development for the treatment of advanced ovarian cancer in patients with deleterious BRCA-mutated tumors (inclusive of both germline and somatic BRCA mutations) previously treated with ≥ 2 prior therapies.

- Treatment of advanced ovarian cancer in patients with deleterious BRCA-mutated tumors previously treated with ≥ 2 prior therapies

Clinical profile
Rucaparib is a PARP inhibitor.

In a pooled analysis of two single-arm trials, 54% of patients achieved an objective response with rucaparib. Most patients were partial responders. In patients who had received 2 prior chemotherapies, the objective response rate (ORR) was 68% (95% CI: 51.9, 81.9). In patients who received 3 prior platinum-based chemotherapies, the ORR was 65% (95% CI: 51.6, 76.9).

Common adverse events reported in trials were nausea, fatigue, vomiting, anemia, increase liver enzymes, and constipation.

In the two trials, 100% of subjects experienced a treatment-emergent adverse event, and 61% experienced an adverse event of grade 3 or higher. In addition, adverse events requiring dose interruption occurred in 59% of subjects.

Rucaparib is being studied as oral and injectable formulations. The oral formulation has been studied for twice daily administration.

- PARP inhibitor
- Oral formulation
- Also being studied as an injectable formulation
- Pooled ORR = 54%
- Common adverse events: nausea, fatigue, vomiting, anemia, increase liver enzymes, and constipation.

Competitive environment
Rucaparib offers an oral formulation that targets both germline and somatic BRCA mutations in patients with advanced ovarian cancer.

Nonetheless, rucaparib is not intended for first-line therapy.

A related product, Lynparza™ (olaparib), is also a PARP inhibitor with a similar indication in advanced ovarian cancer; however, it is only approved for germline BRCA mutations and is intended for patients who have been treated with ≥ 3 prior lines of chemotherapy.

The projected U.S. annual sales for rucaparib are $304 million by 2020.

- Advantage: oral, targets both germline and somatic BRCA mutations
- Disadvantages: not first-line therapy, related product is available (ie, Lynparza)
- Projected U.S. sales are $304 million by 2020

Expected FDA decision date
Rucaparib was granted an orphan drug designation and breakthrough status by the FDA.

An FDA decision regarding the approval of rucaparib is expected by February 23, 2017.

- Orphan drug
- Breakthrough status
- PDUFA: 2/23/2017

OptumRx brand pipeline forecast

OptumRx closely monitors and evaluates the pipeline landscape for upcoming brand drug approvals, including both traditional and specialty medications. This report provides a summary of developmental drugs that may be approved in the upcoming two years.

Read more

OptumRx generic pipeline forecast

OptumRx closely monitors and evaluates the pipeline landscape for upcoming first-time generics and biosimilars. This report provides a summary of upcoming first-time generic drugs and biosimilars that may be approved in the upcoming two years.

Read more

Getting acquainted with pipeline forecast terms

Clinical trial phases

Phase I trials	Researchers test an experimental drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.
Phase II trials	The experimental study drug or treatment is given to a larger group of people to see if it is effective and to further evaluate its safety.
Phase III trials	The experimental study drug or treatment is given to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.
Phase IV trials	Post marketing studies delineate additional information including the drug's risks, benefits, and optimal use.

Pipeline acronyms

ANDA	Abbreviated New Drug Application
BLA	Biologic License Application
CRL	Complete Response Letter
FDA	Food and Drug Administration
NME	New Molecular Entity
NDA	New Drug Application
sBLA	Supplemental Biologic License Application
sNDA	Supplemental New Drug Application
OTC Drugs	Over-the-Counter Drugs
PDUFA	Prescription Drug User Fee Act
REMS	Risk Evaluation and Mitigation Strategy

References:

ALK-Abello Press Release. ALK-Abello website. ALK announces positive outcome of pivotal Phase III trial with new allergy immunotherapy tablet against house dust mite allergy. https://newsclient.omxgroup.com/cdsPublic/viewDisclosure.action?disclosureId=562244&messageId=694077. June 19, 2013. Accessed on September 12, 2016.

ALK-Abello Press Release. ALK-Abello website. ALK's partner, MSD, submits US license application for investigational house dust mite SLIT-tablet. https://newsclient.omxgroup.com/cdsPublic/viewDisclosure.action?disclosureId=695974&lang=en. February 10, 2016. Accessed on September 12, 2016.

ALK-Abello Press Release. ALK-Abello website. ALK presents Phase III data on house dust mite SLIT-tablet at EAACI Annual Congress in Copenhagen. https://newsclient.omxgroup.com/cdsPublic/viewDisclosure.action?disclosureId=613132&lang=en. June 9, 2014. Accessed on September 12, 2016.

ALK-Abello Press Release. ALK-Abello website. ALK submits registration application for house dust mite SLIT-tablet in Europe. https://newsclient.omxgroup.com/cdsPublic/viewDisclosure.action?disclosureId=633390&lang=en. November 20, 2014. Accessed on September 12, 2016.

Anacor Pharmaceuticals. Anacor Pharmaceuticals website. Crisaborole topical ointment, 2%, a novel non-steroidal topical anti-inflammatory PDE-4 inhibitor, is our lead product development candidate for the potential treatment of mild-to-moderate atopic dermatitis and psoriasis. https://www.anacor.com/R-and-D/crisaborole/. Accessed on September 12, 2016.

Angelini C, Pegoraro E, Turella E, Intino MT, Pini A, and Costa C. Deflazacort in Duchenne dystrophy: study of long-term effect. Muscle Nerve. 1994;17(4):386-91.

Biggar WD, Politano L, Harris VA, et al. Deflazacort in Duchenne muscular dystrophy: a comparison of two different protocols. Neuromuscul Disord. 2004;14(8-9):476-82.

BioMedTracker Drug Intelligence Platform. BioMedTracker website. http://www.biomedtracker.com/.

Bonifati MD, Ruzza G, Bonometto P, et al. A multicenter, double-blind, randomized trial of deflazacort versus prednisone in Duchenne muscular dystrophy. Muscle Nerve. 2000;23(9):1344-7.

BusinessWire News Release. BusinessWire website. Pfizer to acquire Anacor. http://www.businesswire.com/news/home/20160516005711/en/Pfizer-Acquire-Anacor. May 16, 2016. Accessed on September 12, 2016.

Campbell T. The Motley Fool website. Why Clovis Oncology shares are falling 14.5% today. http://www.fool.com/investing/2016/10/07/why-clovis-oncology-shares-are-falling-15-today.aspx. October 7, 2016. Accessed on October 7, 2016.

Clinical Pharmacology database. Clinical Pharmacology website. http://www.clinicalpharmacology-ip.com.

Clovis Oncology News Release. Clovis Oncology website. Clovis Oncology presents efficacy and safety data from new drug application (NDA) population for rucaparib in the treatment of advanced mutant BRCA ovarian cancer at 2016 ESMO Congress. http://phx.corporate-ir.net/phoenix.zhtml?c=247187&p=irol-newsArticle&ID=2210141. October 7, 2016. Accessed on October 7, 2016.

Cortellis database. Thomson Reuters Cortellis website. https://cortellis.thomsonreuterslifesciences.com.

Eli Lilly News Room. Eli Lilly website. Baricitinib demonstrates superiority to adalimumab in improving signs and symptoms of rheumatoid arthritis in pivotal phase 3 study. https://investor.lilly.com/releasedetail.cfm?ReleaseID=936515. October 14, 2015. Accessed on September 8, 2016.

Eli Lilly News Room. Eli Lilly website. Baricitinib superior to methotrexate in reducing signs and symptoms in pivotal phase 3 study in patients with rheumatoid arthritis. https://investor.lilly.com/releasedetail.cfm?ReleaseID=934142. September 29, 2015. Accessed on September 8, 2016.

Eli Lilly News Room. Eli Lilly website. Baricitinib superior to placebo in reducing rheumatoid arthritis disease activity in second phase 3 study. https://investor.lilly.com/releasedetail.cfm?ReleaseID=897566. February 23, 2015. Accessed on September 8, 2016.

Eli Lilly News Room. Eli Lilly website. Detailed results demonstrate baricitinib superiority to adalimumab in improving signs and symptoms of rheumatoid arthritis. https://investor.lilly.com/releasedetail.cfm?ReleaseID=941386. November 8, 2015. Accessed on September 8, 2016.

Eli Lilly News Room. Eli Lilly website. Jardiance (empagliflozin) is the only diabetes medication to show a significant reduction in both cardiovascular risk and cardiovascular death in a dedicated outcome trial. https://investor.lilly.com/releasedetail.cfm?ReleaseID=932154. September 17, 2015. Accessed on September 12, 2016.

Eli Lilly News Room. Eli Lilly website. Lilly and Incyte announce patients treated with baricitinib demonstrated significant improvement in signs and symptoms of rheumatoid arthritis compared with methotrexate. https://investor.lilly.com/releasedetail.cfm?ReleaseID=941381. November 7, 2015. Accessed on September 8, 2016.

Fleischmann R, Takeuchi T, Schlichting DE, et al. [Abstract]. Baricitinib, methotrexate, or baricitinib plus methotrexate in patients with early rheumatoid arthritis who had received limited or no treatment with disease-modifying anti-rheumatic drugs (DMARDs): phase 3 trial results. Arthritis Rheumatol. 2015; 67 (suppl 10). http://acrabstracts.org/abstract/baricitinib-methotrexate-or-baricitinib-plus-methotrexate-in-patients-with-early-rheumatoid-arthritis-who-had-received-limited-or-no-treatment-with-disease-modifying-anti-rheumatic-drugs-dmards-p/. Accessed on September 8, 2016.

Genovese MC, Kremer J, Zamani O, et al. Baricitinib in patients with refractory rheumatoid arthritis. N Engl J Med. 2016;374:1243-1252.

Hendrik N et al. [Abstract]. Efficacy and safety of the SQ-house dust mite sublingual immunotherapy tablet in North American children and adults: findings from a large randomized, placebo-controlled clinical trial. https://aaaai.confex.com/aaaai/2016/webprogram/Paper25771.html. March 6, 2016. Accessed on September 8, 2016.

Houde S, Filiatrault M, Fournier A, et al. Deflazacort use in Duchenne muscular dystrophy: an 8-year follow-up. Pediatr Neurol. 2008 Mar;38(3):200-6. doi: 10.1016/j.pediatrneurol.2007.11.001.

Marathon Press Release. Marathon website. Marathon Pharmaceuticals announces Neurology publication of pivotal phase 3 data for deflazacort for Duchenne muscular dystrophy. http://marathonpharma.com/news/2016/08/marathon-pharmaceuticals-announces-neurology-publication-pivotal-phase-3-data-deflazacort-duchenne-muscular-dystrophy/. August 30, 2016. Accessed on September 12, 2016.

Mesa Le, Dubrovsky AL, Corderi J, Marco P, and Flores D. Steroids in Duchenne muscular dystrophy – deflazacort trial. Neuromuscul Disord. 1991;1(4):261-6.

Miller PD, Hattersley G, Riis BJ, et al. Effect of abaloparatide vs. placebo on new vertebral fractures in postmenopausal women with osteoporosis. JAM. 2016;316(7):722-733.

Paller AS, Tom WL, Lebwohl MG, et al. Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults. J Am Acad Dermatol 2016;75(3):494-503.

Pfizer Press Release. Pfizer website. Pfizer announces the publication of final results from two pivotal phase 3 studies of crisaborole topical ointment in patients with mild to moderate atopic dermatitis. http://www.pfizer.com/news/press-release/press-release-detail/pfizer_announces_the_publication_of_final_results_from_two_pivotal_phase_3_studies_of_crisaborole_topical_ointment_in_patients_with_mild_to_moderate_atopic_dermatitis. July 13, 2016. Accessed on September 12, 2016.

Reitter B. Deflazacort vs. prednisone in Duchenne muscular dystrophy: trends of an ongoing study. Brain Dev. 1995;17 Suppl: 39-43.

R&D Insight database. Adis Insight website. http://bi.adisinsight.com/.

Radius Press Release. Radius website. JAMA publishes positive phase 3 data for abaloparatide in postmenopausal women with osteoporosis. http://investors.radiuspharm.com/releasedetail.cfm?ReleaseID=984545. August 16, 2016. Accessed on September 12, 2016.

Radius Press Release. Radius website. Radius announces FDA acceptance for filing of new drug application for abaloparatide-SC for the treatment of postmenopausal women with osteoporosis. http://ir.radiuspharm.com/releasedetail.cfm?ReleaseID=973511. May 31, 2016. Accessed September 12, 2016.

Taylor PC, Keystone EC, van der Heijde D, et al. Baricitinib versus placebo or adalimumab in patients with active rheumatoid arthritis (RA) and an inadequate response to background methotrexate therapy: results of a phase 3 study. [Abstract]. Arthritis Rheumatol. 2015; 67 (suppl 10). http://acrabstracts.org/abstract/baricitinib-versus-placebo-or-adalimumab-in-patients-with-active-rheumatoid-arthritis-ra-and-an-inadequate-response-to-background-methotrexate-therapy-results-of-a-phase-3-study/. Accessed on September 8, 2016.

Sanofi Genzyme Press Release. Sanofi Genzyme website. Sanofi and Regeneron announce that dupilumab used with topical corticosteroids (TCS) was superior to treatment with TCS alone in long-term phase 3 trial in inadequately controlled moderate-to-severe atopic dermatitis patients. http://news.genzyme.com/press-release/sanofi-and-regeneron-announce-dupilumab-used-topical-corticosteroids-tcs-was-superior-. June 6, 2016. Accessed on September 28, 2016.

Sanofi Genzyme Press Release. Sanofi Genzyme website. Sanofi and Regeneron announce positive dupilumab topline results from two phase 3 trials in inadequately controlled moderate-to-severe atopic dermatitis patients. http://news.genzyme.com/press-release/sanofi-and-regeneron-announce-positive-dupilumab-topline-results-two-phase-3-trials-in. April 1, 2016. Accessed on September 28, 2016.

Shionogi Newsroom. Shionogi website. Naldemedine meets primary endpoint in phase 3 study for the treatment of opioid-induced constipation. http://www.shionogi.co.jp/en/company/news/2015/pmrltj0000002dnc-att/e_150803.pdf. August 3, 2015. Accessed on September 16, 2016.

Shionogi Newsroom. Shionogi website. Shionogi announces that naldemedine met the primary endpoint in its first Japanese phase 3 study for the treatment of opioid-induced constipation in cancer patients. http://www.shionogi.co.jp/en/company/news/2015/pmrltj0000002cd5-att/e150624_1.pdf. June 24, 2015. Accessed on September 16, 2016.

Shionogi Newsroom. Shionogi website. Shionogi & Co., Ltd announces that naldemedine meets primary endpoint in a phase 3 study for the treatment of opioid-induced constipation. http://www.shionogi.co.jp/en/company/news/2015/pmrltj00000028ut-att/e150330.pdf. March 30, 2015. Accessed on September 16, 2016.

Sonesson C, Johanson PA, Johnson Eva, and Gause-Nilsson I. Cardiovascular effects of dapagliflozin in patients with type 2 diabetes and different risk categories: a meta-analysis. Cardiovasc Diabetol. 2016;15:37

Synergy Press Release. Synergy website. Synergy Pharmaceuticals presents additional phase 3 plecanatide data in chronic idiopathic constipation at Digestive Disease Week. http://ir.synergypharma.com/press-releases/detail/1816/synergy-pharmaceuticals-presents-additional-phase-3. May 21, 2016. Accessed on September 16, 2016.

Synergy Press Release. Synergy website. Synergy Pharmaceuticals presents new plecanatide phase 3 data in chronic idiopathic constipation at Digestive Disease Week. http://ir.synergypharma.com/press-releases/detail/1817/synergy-pharmaceuticals-presents-new-plecanatide-phase-3. May 22, 2016. Accessed on September 16, 2016.

Synergy Press Release. Synergy website. Synergy Pharmaceuticals Announces Positive Results in the First Phase 3 Trial of Plecanatide in Patients with Chronic Idiopathic Constipation (CIC). http://ir.synergypharma.com/press-releases/detail/1788/synergy-pharmaceuticals-announces-positive-results-in-the. July 17, 2015. Accessed on September 16, 2016.

Timi Study Group. DECLARE-TIMI 58. http://www.timi.org/index.php?page=declare-timi-58. Accessed on September 12, 2016.

UpToDate Database. UpToDate website. https://www.uptodate.com. Accessed October 21, 2016.

OPTUM®

optum.com/optumrx