
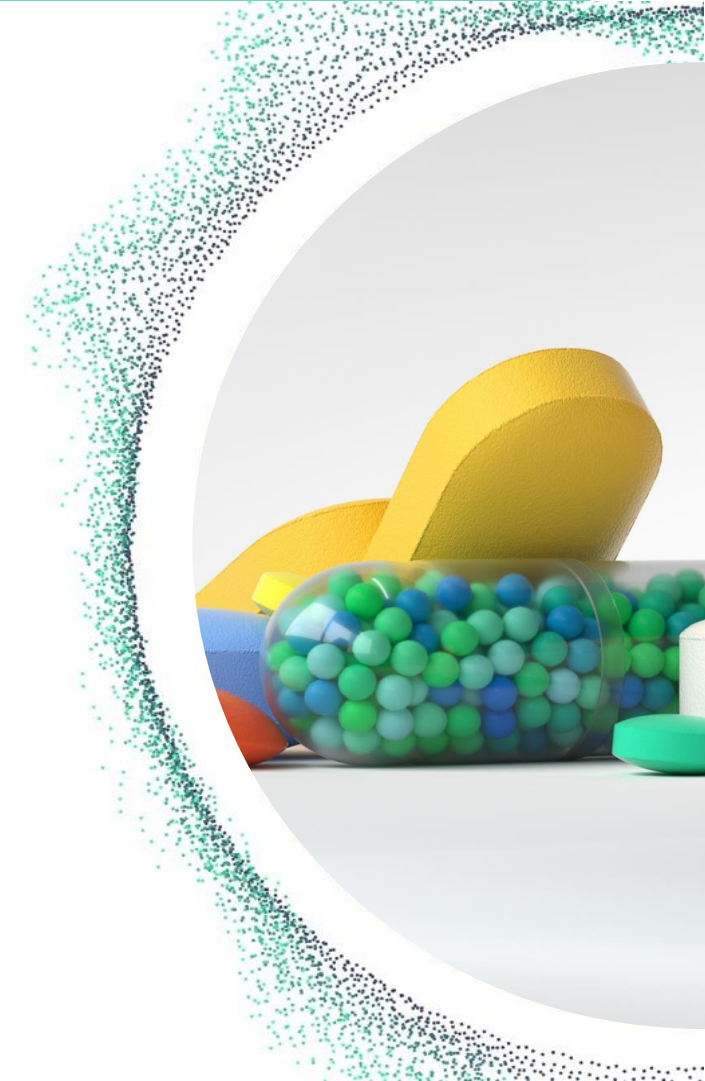


Key Potential Drug Launches in 2024

As a supplement to our well-known quarterly outlook report, Biomedtracker is pleased to present a longer-term look at some key late-stage drugs projected to hit the market in 2024. These drugs represent new drug classes, major changes to standards of care, and/or large market opportunities across the wide range of indications covered by Biomedtracker and Datamonitor Healthcare.

The information in this presentation, including likelihood of approval (LOA) ratings and upcoming catalysts, is up to date as of July 2023.

More details about each drug can be viewed instantly on Biomedtracker by clicking the  icon.



Contents

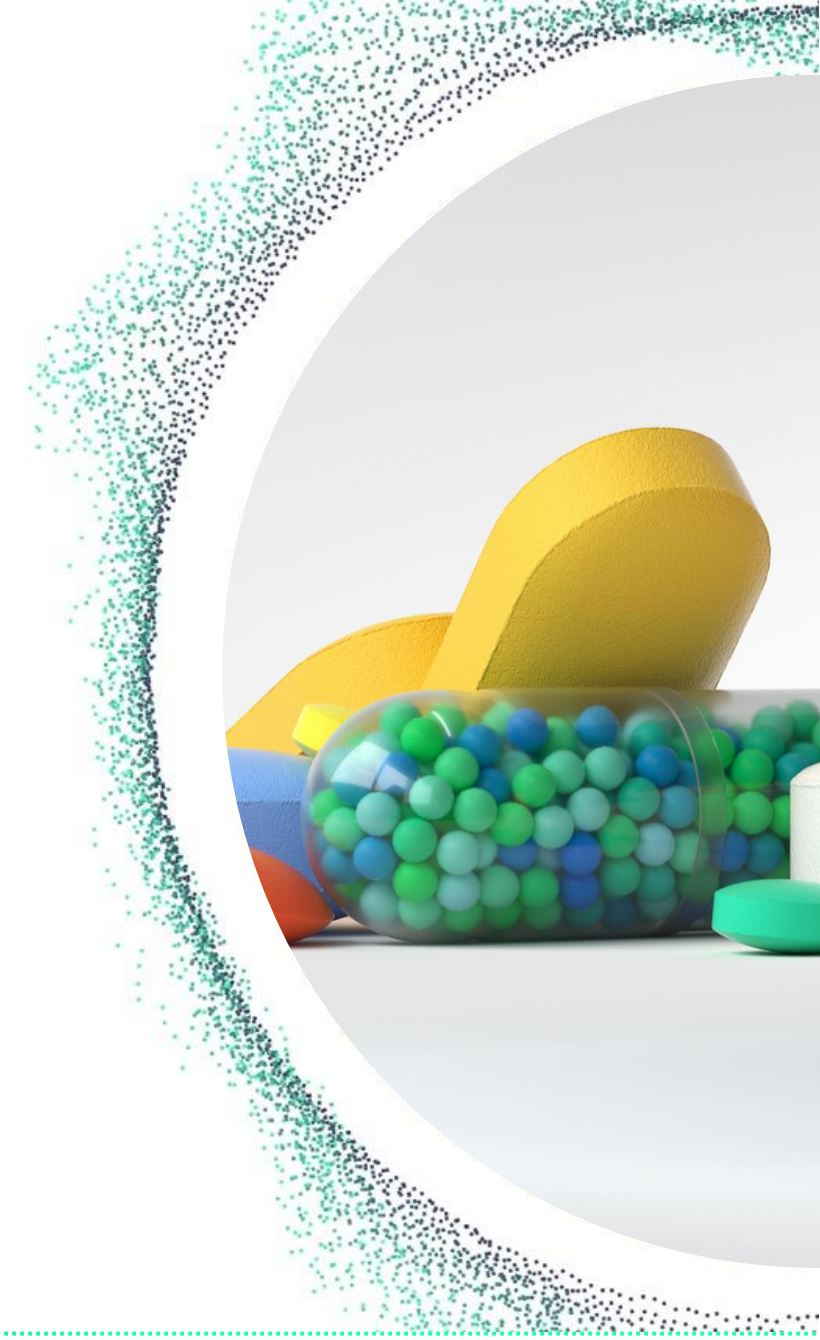
This report covers the following indications:

- **Allergy**
 - Atopic Dermatitis (Eczema)
- **Autoimmune/Immunology (A&I)**
 - Esophagitis
 - Graft vs. Host Disease (GVHD) - Treatment
 - Paroxysmal Nocturnal Hemoglobinuria (PNH)
 - Psoriatic Arthritis (PA)
 - Primary Biliary Cholangitis (PBC)
 - Ulcerative Colitis (UC)
- **Cardiovascular (CV)**
 - Hypertension (Systemic)
 - Paroxysmal Supraventricular Tachycardia
 - Pulmonary Hypertension (PH)
- **Dermatology**
 - Actinic Keratosis
 - Alopecia Areata
 - Hidradenitis Suppurativa
- **Endocrine**
 - Congenital Adrenal Hyperplasia (CAH)
 - Non-Alcoholic Steatohepatitis (NASH)
- **Hematology**
 - Hemophilia A and B
 - Thrombotic Thrombocytopenic Purpura (TTP)
- **Infectious Diseases**
 - BKV Infection
 - Meningococcal Vaccines
 - Molluscum Contagiosum
 - Respiratory Syncytial Virus (RSV) Prevention
 - Uncomplicated Urinary Tract Infections (uUTI)
- **Metabolic**
 - Galactosemia
 - Metachromatic Leukodystrophy (MLD)
 - Progressive Familial Intrahepatic Cholestasis (PFIC)
 - Niemann-Pick Disease Type C
- **Neurology**
 - Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- **Oncology**
 - Acute Myeloid Leukemia (AML)
 - Biliary Tract Cancer (BTC)
 - Breast Cancer
 - Bladder Cancer
 - Brain Cancer
 - Colorectal Cancer (CRC)
 - Hepatocellular (Liver) Cancer (HCC)
 - Gastric Cancer
 - Melanoma
 - Myelodysplastic Syndrome (MDS)
 - Non-Small Cell Lung Cancer (NSCLC)
 - Ovarian Cancer
 - Prostate Cancer
 - Sarcoma
 - Small Cell Lung Cancer (SCLC)
 - Uterine (Endometrial) Cancer
 - Waldenstrom Macroglobulinemia (WM)
- **Ophthalmology**
 - Dry Eye Disease
 - Glaucoma/Ocular Hypertension
 - Wet Age-Related Macular Degeneration (Wet AMD)
- **Psychiatry**
 - Schizophrenia
 - Major Depressive Disorder (MDD)
- **Respiratory**
 - Chronic Obstructive Pulmonary Disease (COPD)

[Click to jump directly to any of the disease groups](#)

[Allergy](#) • [A&I](#) • [CV](#) • [Dermatology](#) • [Endocrine](#) • [Hematology](#) • [Infectious Diseases](#) • [Metabolic](#) • [Neurology](#) • [Oncology](#) • [Ophthalmology](#) • [Psychiatry](#) • [Respiratory](#)

Allergy



NEMOLIZUMAB | GALDERMA | LOA: ABOVE AVERAGE | [↗](#)

Atopic Dermatitis (Eczema)

Targeting the pathway that triggers itch, nemolizumab is the first-in-class interleukin-31 receptor alpha inhibitor poised to treat atopic dermatitis and prurigo nodularis. It was licensed from Chugai in 2016 and was approved in Japan in 2022 for the treatment of itch associated with atopic dermatitis.

In its Phase III pivotal studies (ARCADIA 1 and ARCADIA 2), nemolizumab, in combination with background topical therapy, met all co-primary endpoints and key secondary endpoints after 16 weeks of treatment. Results showed that the drug not only improved itch, but also improved skin lesions, though detailed results will be presented at a scientific congress later in 2023. While results from a Phase IIb trial that allowed concomitant use of topical corticosteroids showed a reduction from baseline on EASI scores over time, efficacy may be modest.

The drug will join the increasingly crowded eczema market, which is dominated by anti-IL-4 and anti-IL-13 monoclonal antibody Dupixent, but has also seen the launch of the anti-IL-13 antibody Adbry and small molecule PDE4 and JAK inhibitors. Nemolizumab is anticipated to launch in the US in the second half of 2024.

Tags: New Drug Class

VTAMA | DERMAVANT SCIENCES | LOA: ABOVE AVERAGE | [↗](#)

Atopic Dermatitis (Eczema)

Vtama (tapinarof) is a first-in-class, aryl hydrocarbon receptor (AhR) agonist with once-daily topical cream. It was initially approved in 2022 in the US for treating psoriasis, and is on track for a supplemental New Drug Application (sNDA) submission for the treatment of atopic dermatitis (AD) in pediatric and adult patients in the first quarter of 2024.

Vtama met its primary and key secondary endpoints in its two identically designed pivotal trials (ADORING 1 and ADORING 2) in atopic dermatitis. Among topicals, the profile for Vtama looks favorable, with potential to compete as the most efficacious branded topical. Compared to Opzelura, which is a twice-daily topical formulation carrying a black box warning associated with oral JAK inhibitors, Vtama may be more attractive in dermatologists' eyes, especially when treating pediatric patients.

The drug is generally well tolerated in patients as young as two years old. However, ADORING 1 showed that nearly one in 10 patients taking Vtama (8.9%) developed folliculitis, though dermatologists would be well equipped to handle this side effect. Lower levels of folliculitis were seen in these studies than have been noted in psoriasis. Dermavant is also heralding consistent dosing regardless of age or indication as an advantage, though dermatologists are used to handling different dosages.

Tags: New Drug Class

ZORYVE | ARQT | LOA: ABOVE AVERAGE | [↗](#)

Atopic Dermatitis (Eczema)

Although not a first-in-class PDE4 inhibitor nor the first topical formula in the atopic dermatitis space, Zoryve (roflumilast) has shown promising efficacy with a favorable safety profile among the approved and pipeline topical non-steroid products.

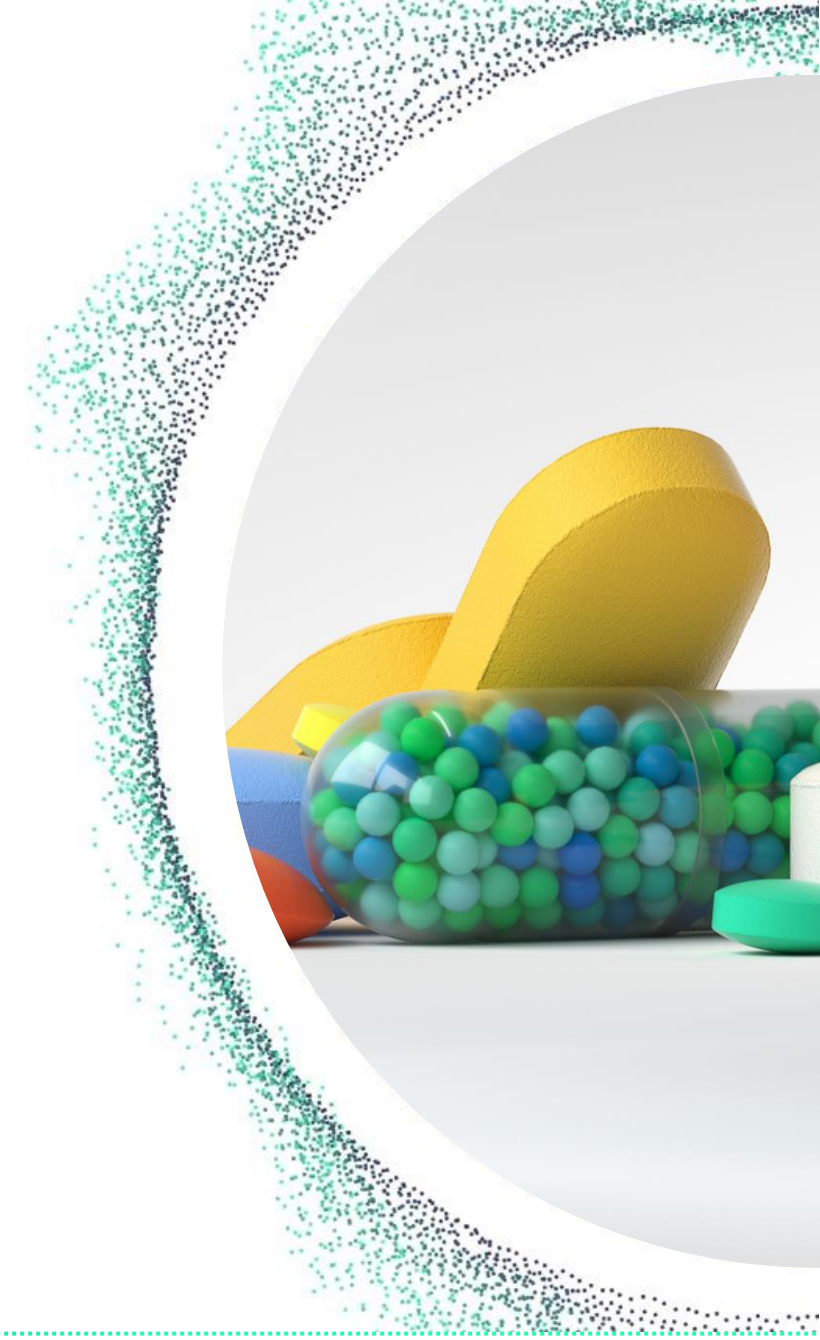
Zoryve performed well in its pivotal studies INTEGUMENT-1 and INTEGUMENT-2 by meeting primary endpoints of Investigator Global Assessment success after four weeks of treatment. The data were consistent across trials for Eczema Area and Severity Index and Worst Itch Numeric Rating Scale. While there is no head-to-head comparison of efficacy, Zoryve provides a once-daily dosing regimen, which is more convenient than twice-daily treatment with Eucrisa, and a relatively low risk of application site pain (burning and stinging), suggestive of its potential to replace Eucrisa in the coming years once approved.

This highly potent and selective topical PDE4 inhibitor may not only pull share from fellow PDE4 inhibitor Eucrisa, but also has demonstrated its efficacy as being on parity with Vtama, another novel entity that is approved in psoriasis and is also in late-phase development for atopic dermatitis. Zoryve is seen as having better tolerability than Vtama, which may cause folliculitis. Although Opzelura is seen as having high efficacy among topical non-steroidal options, its twice-daily usage is less convenient than once-daily candidates Zoryve and Vtama.

Arcutis is testing Zoryve in children 2–5 years of age (INTEGUMENT-PED) and anticipates the topline readout in the third quarter of 2023.

Tags: Label Expansion (New Indication)

Autoimmune/ Immunology



TAKECAB | PHAT | LOA: ABOVE AVERAGE | [↗](#)

Esophagitis

Vonoprazan, a novel first-in-class potassium-competitive acid blocker (PCAB) developed by Phathom Pharmaceuticals, suffered a delayed launch owing to a CRL issued by the FDA. The CRL was issued earlier in 2023 owing to specifications and controls for a nitrosamine drug substance-related impurity, N-nitroso-vonoprazan (NVP). The company has now addressed the CRL, which included a minor reformulation of the product, and the FDA has accepted the complete response to the CRL.

The drug had demonstrated a strong profile, with rapid and durable clinical superiority over lansoprazole in treating patients with moderate-to-severe eosinophilic esophagitis (EE) at two weeks and maintenance of healing in patients of all LA grades in the Phase III PHALCON-EE trial. Phathom expects Takecab to be used after multiple proton pump inhibitor (PPI) failures and in patients having an endoscopy, who at the point of prescribing Takecab have likely already failed a few PPIs. Approximately 50% of patients with EE and non-erosive reflux disease (NERD) progress through lines of therapy annually, which bodes well for a therapy that will likely be prescribed and reimbursed further down the treatment paradigm. Thus, a later line of therapy will not significantly affect prescription rates and potential sales.

Tags: New Drug Class

AXATILIMAB | SNDX | LOA: ABOVE AVERAGE | [↗](#)

Graft vs. Host Disease (GVHD) - Treatment

Despite the approvals of Jakafi, Imbruvica, and Rezurock as second- and third-line agents for the treatment of graft versus host disease (GVHD) in recent years, there remains a significant unmet medical need. Chronic GVHD (cGVHD), a long-term complication of allogeneic stem cell transplantation, occurs when the donor's immune cells attack the recipient's healthy cells. Axatilimab is a humanized monoclonal antibody targeting the CSF-1 receptor pathway involved in the expansion and infiltration of donor-derived macrophages that have been shown to mediate cGVHD. By directly inhibiting macrophages rather than targeting T or B cells, axatilimab hopes to provide a differentiated mechanism from currently available drugs for the treatment of cGVHD.

In September 2021, Incyte entered into an exclusive worldwide collaboration and license agreement to develop and commercialize axatilimab with Syndax Pharmaceuticals in which Incyte leads global activities for axatilimab across all indications. The Biological License Application for axatilimab is expected by the end of 2023, pending agreement with the US FDA, and will be supported by data from the Phase II AGAVE-201 trial which met its primary endpoint of overall response rate (ORR) at all doses. Further confirming axatilimab's efficacy, the AGAVE-201 trial enrolled a high percentage of patients previously treated with Jakafi and Rezurock and that had a longer time since diagnosis and a higher proportion of lung involvement. Axatilimab thus has the potential to be a major change to standard of care due to its effectiveness in non-responder patients and represents a novel drug class for cGVHD. Syndax could see axatilimab receive approval as soon as 2024 assuming discussions with the FDA are positive and determine that a Phase III clinical trial is not required for the application.

Tags: First Approval, New Drug Class, Practice Changing

IPTACOPAN | NVS | LOA: ABOVE AVERAGE | [↗](#)

Paroxysmal Nocturnal Hemoglobinuria (PNH)

Iptacopan is a first-in-class, oral, selective, small molecule inhibitor of complement factor B being developed by Novartis for PNH and a variety of related indications. PNH results from a genetic mutation affecting the complement system leading to hemolysis, which results in anemia, hemoglobinuria, thrombosis, and fatigue, as well as other symptoms, that can require blood transfusions. Current treatment options include bone marrow transplant (BMT) or medical therapy with Alexion (part of AstraZeneca)'s Soliris (eculizumab) and Ultomiris (ravulizumab), as well as Apellis Pharmaceuticals' Empaveli (pegcetacoplan) that target complement component 5 or 3 (C5 or C3); the drug treatments require injection. However, not all patients are willing to undergo BMT or respond to the medical treatments, meaning there is still a high unmet need for novel drugs, with iptacopan receiving breakthrough therapy designation and orphan drug designations from the FDA for PNH and similar recognition from the EMA.

In the Phase III APPOINT-PNH trial involving treatment-naïve PNH patients, the primary endpoint (a 2g/dL or more increase from baseline in hemoglobin [Hb] without the need for blood transfusions) was met by more than 90% of participants, although there was no active comparator. In the APPLY-PNH Phase III trial, iptacopan achieved significant improvements over anti-C5 therapy for both primary endpoints (a transfusion-free 2g/dL or more increase in Hb from baseline, and achieving at least 12g/dL Hb level) in patients already treated with anti-C5 therapy, with differences being clinically meaningful (82.3% versus 2.0%, and 68.8% versus 1.8%). Although it will be launching against established competitors, these benefits over anti-C5 therapy combined with oral administration could see iptacopan garner market share and meet the needs of many patients with PNH. With advanced development already under way for other underserved indications, including immunoglobulin A nephropathy and hemolytic uremic syndrome, iptacopan could be a lucrative new addition to Novartis's portfolio.

Tags: First Approval, New Drug Class, Potential Blockbuster

BIMZELX | UCB | LOA: ABOVE AVERAGE | [↗](#)

Psoriatic Arthritis (PA)

Bimzelx neutralizes both IL-17A and IL-17F and has a positive outlook in psoriasis, for which FDA approval is pending, though European approval was granted in 2021. In 2023, it has gained two additional marketing authorizations in the EU, for the treatment of adults with active psoriatic arthritis (PsA) and adults with active axial spondyloarthritis (axSpA) including non-radiographic axSpA (nr-axSpA) and ankylosing spondylitis (AS), also known as radiographic axSpA.

UCB has raised the bar in psoriatic arthritis, reporting positive topline results on ACR-50 in the Phase III BE OPTIMAL and BE COMPLETE studies in patients who are biologic-naïve and inadequate responders to current first-line anti-TNF biologics, respectively. Dramatic effects seen in the Phase IIb BE ACTIVE study, including between a third and half of patients achieving ACR-70 at week 48, have generated excitement among physicians. The submission of a BLA is anticipated in the third quarter of 2023.

Although the data seem promising, the approval of Bimzelx is overshadowed by several uncertainties after pre-license inspections by FDA. Following a complete response letter from the FDA, UCB resubmitted a BLA in November 2022 for the treatment of psoriasis. Nevertheless, an April 2023 FDA inspection delayed Bimzelx's approval for psoriasis. Three points were stated in the inspection report, highlighting UCB's inadequate supervision over document control in the Quality Unit, environmental and personnel monitoring in classified areas, and handling and rejection of in-process materials. UCB thus expects the FDA approval decision for psoriasis to be delayed to Q3 2023. It remains to be seen if this will impact timelines for a potential label expansion into psoriatic arthritis next year.

Tags: Potential Blockbuster

SELADELPAR | CBAY | LOA: ABOVE AVERAGE | [↗](#)

Primary Biliary Cholangitis (PBC)

PBC is a progressive liver condition that can lead to liver failure and the need for transplantation. Currently, ursodeoxycholic acid (UDCA) is the first-line medication recommended for PBC by leading US and European guidelines, with Intercept's Ocaliva recommended for non-responders or patients who cannot tolerate UDCA. Notably, Ocaliva is associated with a high rate of pruritus.

In the ASSURE study, Cymabay's seladelpar, a selective peroxisome-activated receptor- δ (PPAR- δ) agonist, showed improvement in GLOBE score, a surrogate measure of the potential for reducing the need for liver transplant. Encouragingly, seladelpar also achieved the primary outcome in the ENHANCE study, with up to 78.2% of patients achieving an alkaline phosphatase (ALP) level $<1.67 \times$ ULN. Above all, seladelpar consistently exhibited a well-tolerated safety profile, with a statistically significant decline in pruritus.

With the pivotal Phase III RESPONSE study due to read out in Q3 2023, if seladelpar shows a clear and sustained biochemical control and no worsening of itch, it is poised to be a strong contender to be the second-line PBC treatment of choice in 2024.

Tags: Practice Changing, New Drug Class

ETRASIMOD | PFE | LOA: ABOVE AVERAGE | [↗](#)

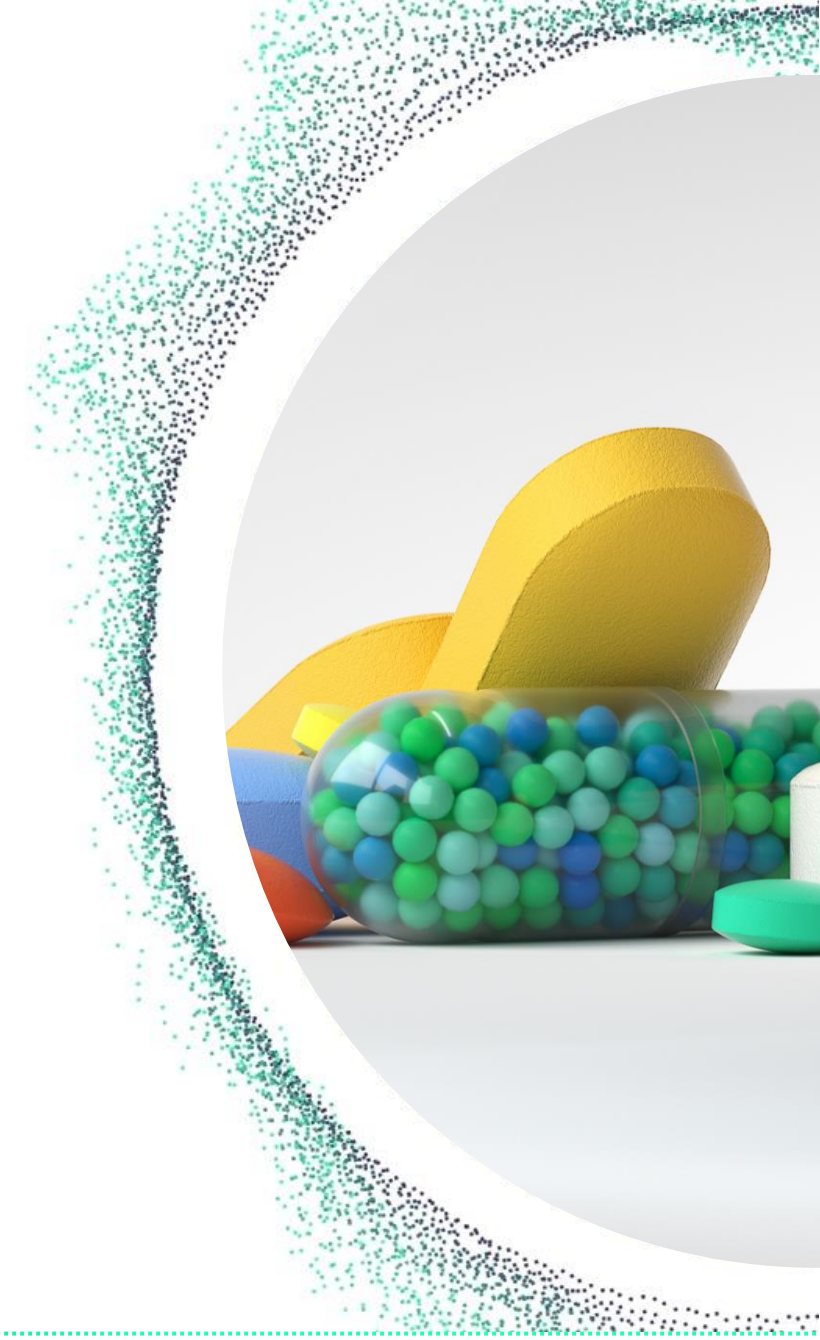
Ulcerative Colitis (UC)

Etrasimod will try to differentiate itself from other S1P receptor modulators owing to its better safety profile, as most of the drugs sharing the mechanism of action require dose titration as first-dose bradycardia is often observed. However, etrasimod did not require any dose titration, and exhibited minimal lowering of heart rate. The agent, with its quicker onset of action, fewer drug-drug interactions, and more rapid return to normal heart rate on discontinuation, will challenge Zeposia which is currently indicated for treating adults with moderate to severe active UC who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.

With Xeljanz (tofacitinib) facing loss of exclusivity by 2025, Pfizer aims to showcase the safety profile and the potential best-in-class efficacy of etrasimod as one of the major selling points to stay afloat in the UC market.

Tags: New Drug Class, First Approval

Cardiovascular



APROCITENTAN | JNJ | LOA: ABOVE AVERAGE | [↗](#)

Hypertension (Systemic)

Systemic hypertension remains a major modifiable risk factor for cardiovascular disease, with many patients not reaching blood pressure goals despite a wide variety of therapeutic options. Johnson & Johnson filed applications for aprocitentan for resistant systemic hypertension with US and EU regulators in December 2022 and January 2023, respectively. If successful, the product will become widely commercially available from early 2024. Endothelin receptor antagonists (ERAs) prevent endothelin-1 (ET-1) from binding to ETA and ETB receptors, which causes processes such as neurohormonal activation, vascular hypertrophy, and endothelial dysfunction.

The filing will be supported by data from its Phase III PRECISION trial where aprocitentan significantly reduced blood pressure in patients with resistant hypertension (uncontrolled blood pressure despite at least three background antihypertensive medications) and other co-morbidities. However, this was accompanied by edema in approximately 30% of patients, with >95% being mild to moderate in intensity. This appears to be a class effect, with Gilead's discontinued darusentan showing high rates of edema (21% of patients at different dosages) during its Phase III trial, which missed its primary endpoint. However, Johnson & Johnson believes that aprocitentan's risk-benefit profile will be acceptable to the FDA as 10–20% of the hypertensive population are resistant to standard treatments, representing a significant unmet need that is growing with an aging population.

Tags: First Approval, Potential Blockbuster, Practice Changing

ETRIPAMIL | MIST | LOA: ABOVE AVERAGE | [↗](#)

Paroxysmal Supraventricular Tachycardia (PSVT)

People with PSVT may have a heart rate of more than 200 beats per minute and experience various symptoms including palpitations, dyspnea, and light-headedness. Most episodes of PSVT do not require emergency interventions, but for those who experience prolonged events, worsening cardio-respiratory symptoms, or hemodynamic instability, intravenous adenosine, beta-blockers (BBs), calcium channel blockers (CCB), or synchronized cardioversion in an emergency department are required. Ongoing medical management can vary depending on the underlying mechanism, frequency of symptoms, and patient preference. Catheter ablation is often preferable as first-line treatment over long-term medical management in view of high curative rates and low risk of major complications. Medications for preventing PSVT episodes can include oral BBs, CCBs, class IC antiarrhythmics, class III antiarrhythmics, and digoxin, but if unsuccessful, patients may need to regularly attend an emergency department for treatment. PSVT episodes are unpredictable and there are no approved medications for self-treating acute SVT.

Milestone Pharmaceuticals' next-generation CCB offers convenient intranasal administration with the hope of reducing the need for emergency department visits for people who experience PSVT. Phase III results showed that etripamil is effective within 30 minutes for the majority of patients, with no safety concerns identified. Importantly, reductions in the need for medical interventions and emergency department visits were shown in the pooled analyses, which indicate that etripamil could lead to improved quality of life for people with PSVT and reductions in healthcare resource utilization. One caveat is that the placebo-controlled nature of the trials does not permit any conclusions to be drawn regarding etripamil's efficacy versus current practice for treating SVT episodes. Milestone is currently planning to submit a New Drug Application to the FDA for etripamil for PSVT in Q3 2023, which could see etripamil on the US market in 2024.

Tags: First Approval, Practice Changing

SOTATERCEPT | MRK | LOA: ABOVE AVERAGE | [↗](#)

Pulmonary Hypertension (PH)

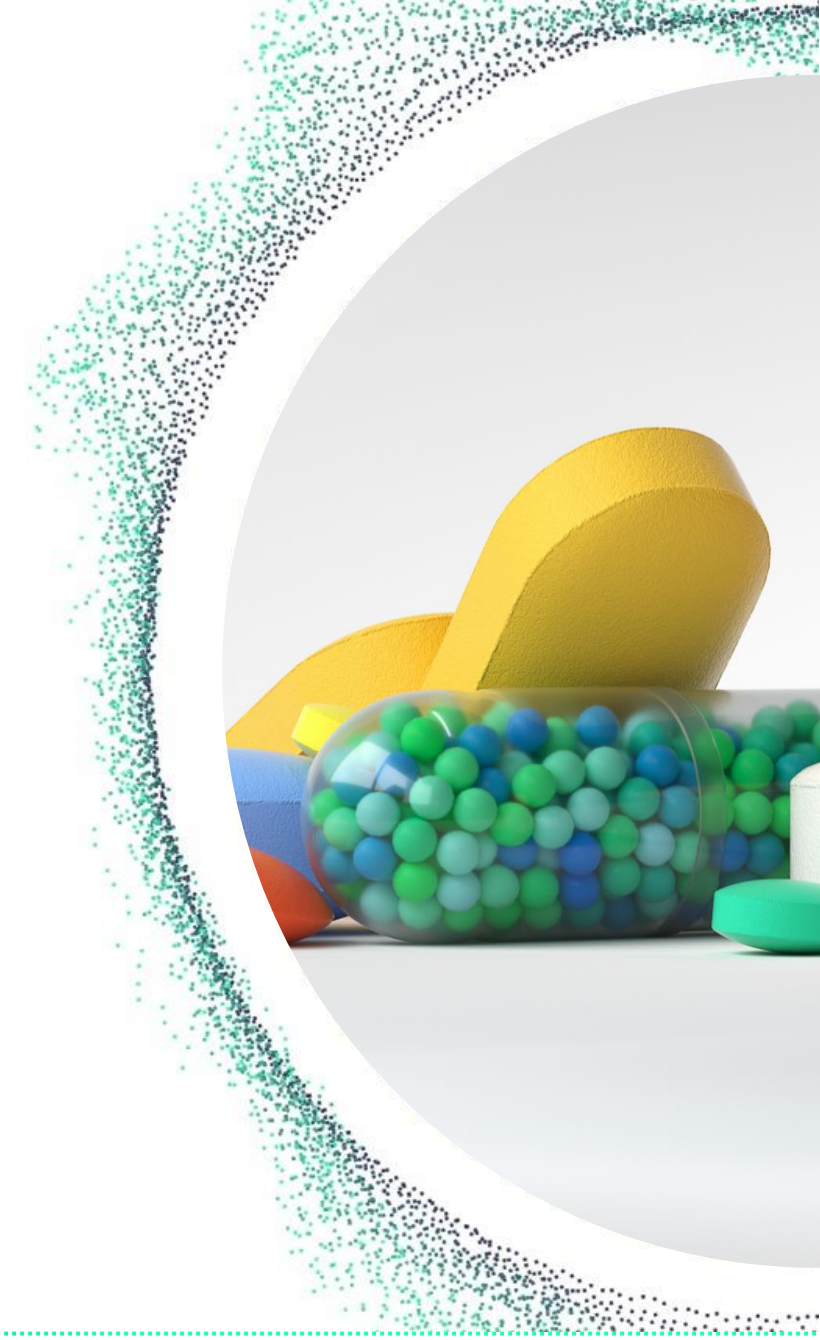
Merck & Co's sotatercept, acquired from Acceleron Pharma, is a promising first-in-class next-generation treatment for pulmonary hypertension (PH). Sotatercept acts via a distinct and novel mechanism to other drug classes by balancing bone morphogenetic protein receptor type II (BMPRII) signaling, which drives PH, thereby restoring vascular homeostasis. This would begin to address an important unmet need in the PH space, as most treatments are designed to treat the symptoms and improve quality of life rather than modifying the disease itself.

The company has applied for priority review with the FDA to accelerate the regulatory process; if successful, the company plans to launch sotatercept in early 2024. The filing will be based on the STELLAR Phase III trial results, where sotatercept attained compelling data on decreasing the risk of clinical worsening or death by 84% over placebo in group 1 PH (pulmonary arterial hypertension) patients. Comparatively, current treatments such as prostacyclins have historically achieved 20–40% reductions in morbidity/mortality events in trials (although some caution should be exercised when comparing trial data). Impressively, treatment with sotatercept led to a mean improvement of 40.8m in 6MWD from baseline, which was achieved on top of 61.3% of patients receiving triple therapy and 39.9% receiving prostacyclin infusion therapy, meeting STELLAR's primary endpoint requirements.

Sotatercept is also being evaluated in trials in historically neglected PH populations. The most anticipated results are from the Phase II CADENCE trial (primary completion date: January 2024), which would be an expansion into PH group 2 (PH due to left-sided heart disease), the most prevalent of the five groups (29% of the PH population versus 22% in group 1); there are currently no approved drug treatments for this group. If successful in this group, sotatercept's market share would be unchallenged, more than doubling its target population, thereby further enhancing its blockbuster sales potential.

Tags: First Approval, New Drug Class, Potential Blockbuster, Practice Changing

Dermatology



KLISYRI | ALM | LOA: AVERAGE | [↗](#)

Actinic Keratosis (AK)

Klisyri is a notable drug in the field of dermatology due to its innovative approach to treating actinic keratosis (AK), a common skin condition characterized by precancerous lesions caused by sun exposure. Unlike traditional treatments such as cryotherapy or surgical removal, Klisyri offers a novel approach through its mechanism of inhibiting tubulin polymerization within cells. This mechanism results in the selective destruction of AK lesions upon topical application, allowing for convenient at-home application. This marks a significant shift in the standard of care for AK, potentially providing a less invasive and more patient-friendly treatment option.

In previous Phase III trials, the primary objective of achieving complete clearance (100%) of AK lesions by Day 57 within the treated areas of the face or scalp was successfully met. Each individual study demonstrated a high level of statistical significance ($p < 0.0001$), further reinforcing the efficacy of the treatment. Additionally, the achievement of statistical significance ($p < 0.001$) was observed in both of the subgroups focusing on the face and scalp. These results underscore the robustness of the treatment's effectiveness in addressing AK lesions and its potential to significantly impact clinical practice. Klisyri has the potential to address a substantial market demand and improve outcomes for individuals dealing with actinic keratosis.

Tags: Practice Changing

CTP-543 | SUNP | LOA: ABOVE AVERAGE | [↗](#)

Alopecia Areata

CTP-543 is an oral, deuterium-modified analog of ruxolitinib (a selective inhibitor of Janus kinases JAK1 and JAK2) in development for the treatment of alopecia areata, an indication for which there are currently only two FDA-approved therapies. Although it is difficult to compare efficacy between trials, CTP-543 showed best-in-class potential over Pfizer's Litfulo and Eli Lilly's Olumiant, the two JAK inhibitors approved for alopecia, giving the drug strong commercial potential despite its late entrance to the market. Treatment was not associated with thromboembolic adverse events in trials, unlike the trials for Olumiant and Litfulo, but the label will likely contain a black box warning, if approved, consistent with the JAK class of drugs.

CTP-543 has received breakthrough therapy designation and fast track status for the treatment of adults with moderate-to-severe alopecia. Sun Pharmaceuticals plans to submit an NDA to the FDA during 2023, which will include data from two Phase III trials, for a potential launch in 2024. A long-term Phase III extension study is ongoing.

Tags: Practice Changing, Potential Blockbuster

COSENTYX | NVS | LOA: AVERAGE | [↗](#)

Hidradenitis Suppurativa

Cosentyx's prominence in dermatology is highlighted by its ability to meet a substantial unmet medical need in the treatment of hidradenitis suppurativa (HS). HS is a persistent and severe skin illness characterized by painful abscesses and inflammatory lesions which frequently result in decreased quality of life. Cosentyx's exceptional promise stems from its novel method of action which targets interleukin-17A, a key cytokine involved in inflammatory processes. In two Phase III trials for HS, Cosentyx displayed continued improvement even after the primary analysis at Week 16. More than 55% of patients achieved an HS clinical response (HiSCR) at Week 52, with over 60% being flare-free and over 50% experiencing reduced pain, a significant symptom of HS. Notably, response rates were higher in the Cosentyx groups compared to placebo, and these positive effects were maintained up to the trial's end at Week

52. In summary, Cosentyx showcased lasting effectiveness in treating HS, offering substantial relief to patients suffering from this condition.

Overall, Cosentyx has shown effectiveness in clinical studies in reducing the severity of HS lesions and accompanying symptoms. Given the lack of definite therapy options for HS, the arrival of Cosentyx provides new hope for patients and healthcare practitioners alike. If authorized for this indication, Cosentyx has the potential to change the landscape of HS care by addressing a critical need.

Tags: Practice Changing

Endocrine



CRINECERFONT | NBIX | LOA: ABOVE AVERAGE | [↗](#)

Congenital adrenal hyperplasia (CAH)

Congenital adrenal hyperplasia (CAH) typically results from a mutation affecting the 21-hydroxylase (21-OH) enzyme, leading to deficient production of adrenal hormones including cortisol and often aldosterone. Untreated CAH can lead to salt wasting, dehydration, and even death. Patients require steroid therapy to correct cortisol deficiency and reduce the high levels of adrenocorticotropic hormone (ACTH) that are stimulated as a result; high ACTH levels can cause excess levels of androgens that can affect female development as well as stature and fertility. However, high doses of glucocorticoid treatment can be required, but these agents have potentially serious side effects including increased cardiovascular risk, bone loss, fractures, growth impairment, muscle weakness, and increased infection risk. As such, steroid-free treatment options are highly desirable.

Crinecerfont is an oral, selective corticotropin-releasing factor type 1 receptor (CRF1) antagonist being developed by Neurocrine Biosciences for the treatment of classic CAH due to 21-OH deficiency. This steroid-independent agent blocks the CRF1 receptors in the pituitary gland, leading to a reduction in ACTH levels and lower adrenal androgen levels, with the hope of physiologic dosing of glucocorticoids reducing the risk of the complications of long-term steroid treatment. Phase II data demonstrated median reductions from baseline to Day 14 for 24-hour measurements of ACTH, 17-hydroxyprogesterone (17-OHP), and androstenedione (males and females). Androstenedione/testosterone ratio (males) ranged from -55.3% to -76.1%, and a more than 50% reduction from baseline for ACTH, 17-OHP, androstenedione (males and females), testosterone (females), and androstenedione/testosterone ratio (males) was achieved by 63%, 75%, 50%, 60%, and 67% of participants, respectively. The Phase III CAHtalyt trial is ongoing with topline data expected in Q4 2023, offering the potential for approval and launch in late 2024.

Tags: First Approval, Practice Changing, New Drug Class

RESMETIROM | MDGL | LOA: ABOVE AVERAGE | [↗](#)

Non-Alcoholic Steatohepatitis (NASH)

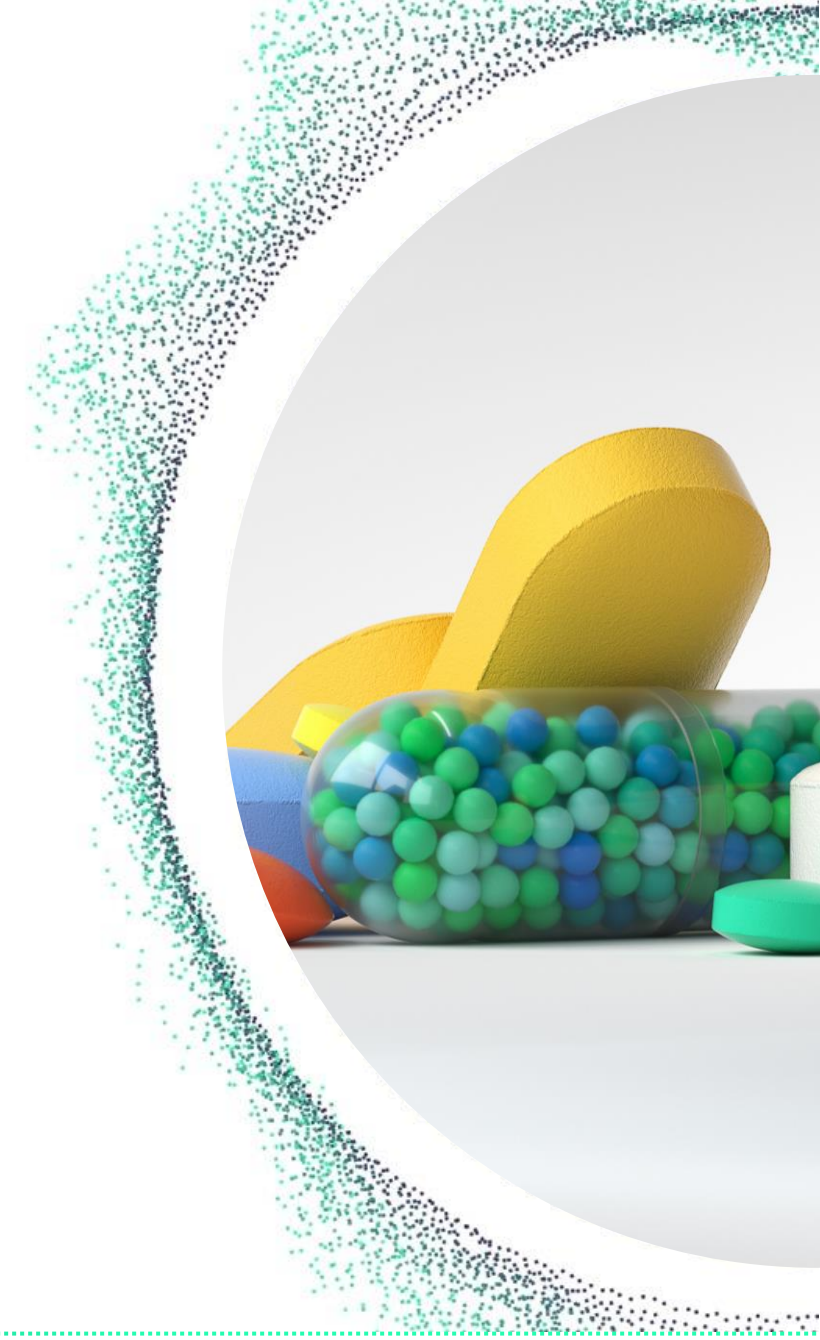
Madrigal has announced that the US submission for resmetirom has been completed, which, if approved, could make the drug the first therapy ever approved in the US for NASH, an important milestone for both the THR-beta class and this patient population's unmet need. Indeed, NASH represents a significant unmet need due to its heavy burden on healthcare systems and large prevalent population, both of which are expected to increase as disease awareness improves and more therapeutic options become available. Moreover, NASH is expected to become one of the leading etiologies of chronic liver disease and a main indication for liver transplantation, reinforcing the urgent need of finding an effective therapy.

The NDA submission was based on results from the pivotal Phase III MAESTRO-NASH study, where resmetirom 80mg and 100mg doses achieved both primary endpoints. Resmetirom treatment demonstrated statistically significant results, with up to 30% of recipients achieving NASH resolution and up to 26% of recipients improving liver fibrosis by ≥ 1 stage at 52 weeks. Above all, resmetirom was shown to be safe and well tolerated, with only a 7.7% discontinuation rate for the higher dose. Additionally, reductions in atherogenic lipids and lipoproteins were also observed in resmetirom treatment arms as compared with placebo, which enhances resmetirom's potential as cardiovascular disease is the leading cause of death for NASH patients.

The overall risk-benefit profile will position resmetirom as a desirable therapy. Resmetirom is projected to attain blockbuster sales, though its uptake could be limited by strong payer pressure if pricing is considered unreasonable. Barring no regulatory setbacks, resmetirom will enter the US market in early 2024.

Tags: Potential Blockbuster, First Approval, New Drug Class

Hematology



FITUSIRAN | SNY | LOA: BELOW AVERAGE | [↗](#)

Hemophilia A and B

Fitusiran is an RNA interference (RNAi) therapeutic that targets antithrombin in the liver with the aim of providing greater hemostatic control and more convenient administration than many of the currently available marketed products for hemophilia. This RNAi is being investigated for the treatment of all hemophilia A and B patients, irrespective of the patients' status regarding inhibitors to factor therapy. As well as this broad target population, fitusiran offers a much longer dosing interval compared with factor replacement.

The Phase III ATLAS clinical trials have shown that the drug is efficacious, with a median ABR of 1.08 which is in line with other drugs in the space. Unfortunately, fitusiran has been plagued with safety concerns which will likely limit its uptake upon its potential approval in late 2024. There have been two amendments to safety protocols as a result of adverse thrombotic events in trials, with the most notable being a fatality in its Phase II trial from an intercranial blood clot. As a result, the latest FDA-agreed amendment to the investigations is a lower dosing regimen of 50mg every two months as opposed to its original monthly dosing. However, the reduction in the dosing to once every two months could reduce the drug's efficacy, and therefore it is critical that fitusiran achieves a clean safety and efficacy profile comparable to standard of care in its upcoming Phase III data readout which is expected in late 2023.

Although fitusiran will not stand competition in the hemophilia A space, it has potential for hemophilia B patients with inhibitors where therapeutic options are limited to burdensome factor replacement or highly expensive gene therapy. However, this only represents a small fraction of the overall market, estimated at 1–5% of the population.

Tags: First Approval, New Drug Class

TAK-755 | TAK | LOA: ABOVE AVERAGE | [↗](#)

Thrombotic Thrombocytopenic Purpura (TTP)

Takeda's TAK-755 is the first recombinant ADAMTS13 replacement enzyme for congenital TTP (cTTP) that cleaves the von Willebrand factor. cTTP involves a defect in the protease ADAMTS13 and only accounts for a minority of overall TTP (less than one case per million in the general population), where most cases are acquired due to auto-antibodies.

Topline Phase III results suggest that TAK-755 is efficacious at preventing acute TTP events, which have a mortality rate of >90% if left untreated, and reduced the incidence of thrombocytopenia by 60% as compared to plasma-based therapy. TAK-755 has been granted priority review in the US due to the high unmet need in this patient population, placing a potential approval in January 2024.

Additionally, TAK-755 is also in development for immune TTP – a larger indication where the company will test whether it can disrupt the treatment paradigm by avoiding the need for plasma exchange (Cablivi is also being tested for this) – and sickle cell disease.

Tags: First Approval, New Drug Class, Practice Changing

Infectious Disease



SB-206 | NOVNI | LOA: ABOVE AVERAGE | [↗](#)

Antiviral – Other Treatments (Molluscum Contagiosum)

SB-206 (berdazimer gel, 10.3%) is engineered as a macromolecule that can be applied to the skin as a topical product, allowing for controlled release of nitric oxide. Novan has submitted a New Drug Application (NDA) for SB-206 for the topical treatment of molluscum contagiosum and received a PDUFA goal date of January 2024 for the application.

Results from the pivotal Phase III B-SIMPLE4 study provided the basis for the application, following disappointing results from the previous B-SIMPLE1 and B-SIMPLE2 studies. The efficacy data from the current B-SIMPLE4 study are very positive, with a larger vehicle- adjusted treatment difference observed on the primary endpoint of complete clearance of lesions at week 12 compared to the B-SIMPLE2 study (+12.7% vs +9.7%, respectively), and a statistically significant treatment effect manifesting as early as week 8 (+8.0%).

Tags: First Approval

ANTIBKV | MEMO THERAPEUTICS | LOA: AVERAGE | [↗](#)

Antiviral – Other Treatments (BKV Infection)

AntiBKV is a therapeutic antibody candidate identified through the screening of kidney transplant patients infected with BK virus which neutralizes all strains of BKV at low concentrations. There is currently no disease-modifying therapy available to treat BKV infection; it can only be treated by lowering immunosuppression. Positive data from a Phase I study demonstrated the safety and tolerability of multiple intravenous doses of AntiBKV. With its 100 times higher neutralization capacity than benchmark antibodies, AntiBKV could potentially be used for the treatment of BKV infection in kidney transplant recipients.

The efficacy of AntiBKV is currently being evaluated in a pivotal ongoing Phase II/III study in the US. Results from the study are expected in the third quarter of 2023, and, if positive, will support Memo's planned BLA submission in 2024.

Tags: First Approval, Practice Changing, New Drug Class

PF-06886992 | PFE | LOA: ABOVE AVERAGE | [↗](#)

Meningococcal Vaccines

Pfizer's PF-06886992 is currently leading a heated race with rival vaccine GSK3536819A from GSK to become the first approved pentavalent meningococcal vaccine, potentially addressing an unmet need for a simplified meningococcal vaccine schedule and broad serogroup coverage.

PF-06886992 is based on two of Pfizer's current meningococcal vaccines, Trumenba (meningococcal group B vaccine) and Nimenrix (meningococcal group A, C, W-135, and Y conjugate vaccine). The new vaccine candidate is administered via the intramuscular route in a suspension.

The pivotal Phase III study of PF-06886992 met all primary and secondary endpoints, with non-inferiority demonstrated for all five serogroups following two doses of PF-06886992 compared to two doses of Trumenba and one dose of Nimenrix. Notably, in individuals who had not previously received a meningococcal vaccine, the proportion of subjects with ≥ 4 -fold increases in immune responses was observed to be higher following PF-06886992 administration. PF-06886992 is poised to be the first pentavalent vaccine approved, with a set PDUFA goal date in October 2023, paving the way for a 2024 rollout.

Tags: Practice Changing, New Drug Class

GSK3536819A | GSK | LOA: ABOVE AVERAGE | [↗](#)

Meningococcal Vaccines

GSK3536819A is expected to be the second approved pentavalent meningococcal vaccine, and it will directly compete with rival PF-06886992 from Pfizer, which is currently under regulatory review by the FDA.

Similar to Pfizer's candidate, GSK3536819A is based on the antigenic components of GSK's licensed meningococcal vaccines, Bexsero (Meningococcal group B) and Menveo (Meningococcal group A, C, W-135, and Y). It is intended to be administered intramuscularly in two doses, six months apart.

Topline results from the pivotal Phase III in March 2023 demonstrated statistical non-inferiority compared to Bexsero and Menveo in individuals 10–25 years old, with GSK3536819A eliciting a clinically meaningful immune response. Currently, in the US, two separate vaccines needing four injections are required to protect against all five serogroups. With these robust data, GSK is aiming to convince regulators in time to launch its candidate in 2024 and compete with Pfizer's PF-06886992.

Tags: Practice Changing, New Drug Class

BEYFORTUS | AZN | LOA: AVERAGE | [↗](#)

Respiratory Syncytial Virus (RSV) Prevention

AstraZeneca and Sanofi's Beyfortus (nirsevimab) is an F protein monoclonal antibody administered in a single-dose intramuscular injection which received FDA approval in July 2023 for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease (LRTD) in newborns and infants.

It is on track to be launched onto the US market ahead of the 2023/24 RSV season following the CDC's ACIP unanimously voting for routine use in RSV LRTD prevention in newborns and infants under eight months of age born during or entering their first RSV season, as well as slightly older infants aged 8–19 months with an elevated risk of severe RSV who are entering their second RSV season.

The launch of Beyfortus will render Sobi's Synagis redundant in the pediatric population on account of it having a more convenient dosing schedule and approval in a broader infant population. Revenues for Beyfortus will also be bolstered by the additional approval of the monoclonal antibody in Europe, which occurred in 2022.

Tags: Potential Blockbuster, Practice Changing

MRNA-1345 | MRNA | LOA: ABOVE AVERAGE | [↗](#)

Respiratory Syncytial Virus (RSV) Prevention

Moderna's mRNA vaccine mRNA-1345 is set to become the third approved vaccine for use in RSV prevention in adults, with the company initiating a rolling BLA submission in the US and an MAA in the EU, in July 2023.

These filings are based on results from the pivotal Phase II/III ConquerRSV trial which showed that mRNA-1345 met both primary endpoints and reported 83.7% efficacy against RSV-LRTD as defined by two or more symptoms, as well as 82.4% efficacy in preventing at least three symptoms in adults aged 60 years or older.

mRNA-1345 will experience competition within the elderly RSV segment from Pfizer's Abrysvo and GSK's Arexvy which both received FDA approval in May 2023. Breakthrough Therapy Designation for the prevention of RSV-LRTD in adults aged 60 years or older was granted to mRNA-1345 in January 2023, and it previously received Fast Track designation in August 2021. These awards should help speed up the approval process for mRNA-1345, potentially allowing it to reach the market in time for the 2023/24 RSV season, which will give it the opportunity to compete with Abrysvo and Arexvy in their first year of launch.

Tags: First Approval

GEOTIDACIN | GSK | LOA: ABOVE AVERAGE | [↗](#)

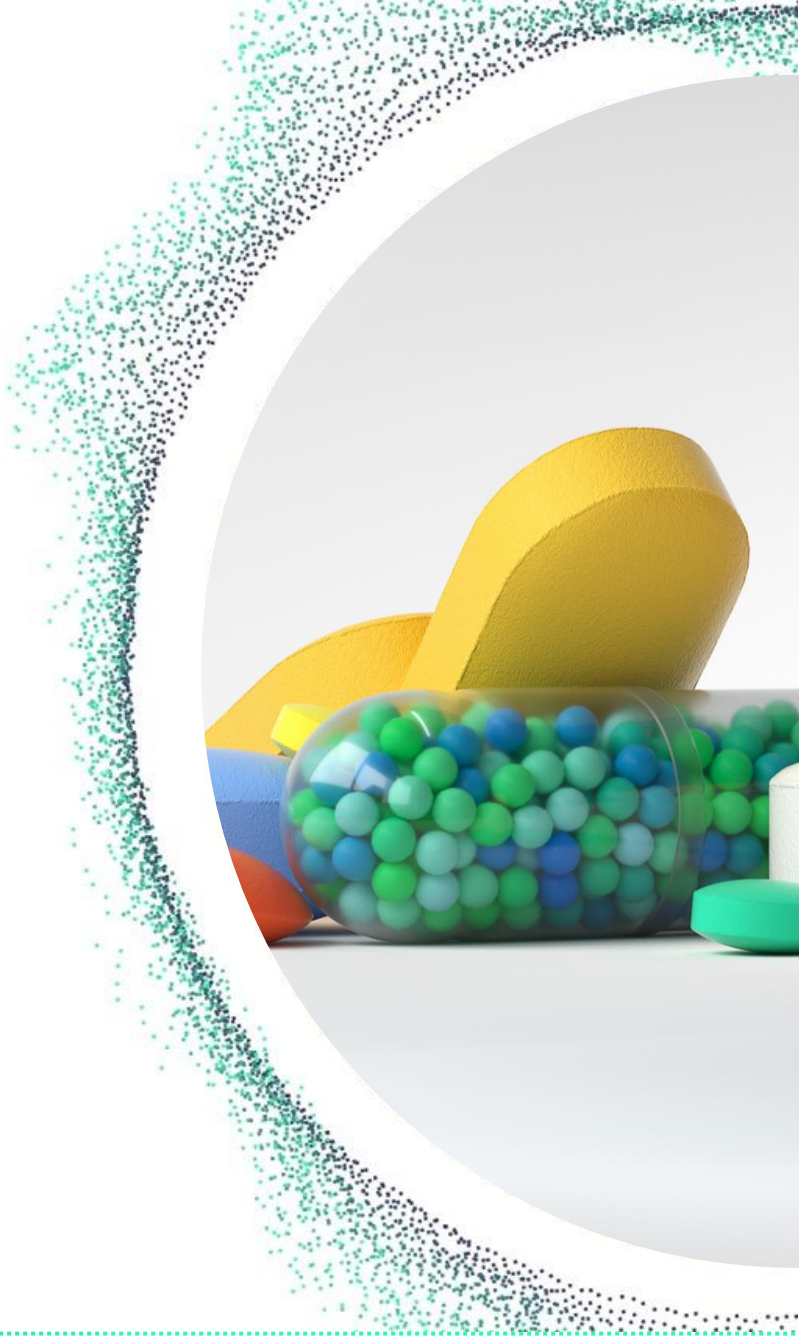
Uncomplicated Urinary Tract Infections (uUTI)

Gepotidacin (formerly GSK2140944) is GSK's answer to resistant strains of escherichia coli and staphylococcus saprophyticus in uncomplicated urinary tract infections (uUTI). This asset is a first-in-class triazaacenaphthylene antibiotic with a novel mechanism of action targeting bacterial DNA replication and two topoisomerase enzymes. In this way, the target pathways limit antibiotic resistance development, as mutations in both enzymes would be needed to affect gepotidacin's susceptibility. There is a serious medical unmet need in the uUTI population; of the approximately 15 million episodes of uUTI in the US alone each year, 25% have documented resistance to first-line treatment including fosfomycin, nitrofurantoin, or trimethoprim/sulfamethoxazole.

US and EU filings are expected during 2023 for uUTI treatment following the positive data release from two pivotal Phase III trials, EAGLE-2 and EAGLE-3. Both trials achieved primary endpoints with therapeutic success comparable to that of nitrofurantoin. Most notably, only 6% of patients across both trials required an additional antibiotic for uUTI treatment after 28 days. While the efficacy results alone would make it a strong contender as an alternative for antibiotic resistance cases, the minimal need for a combination therapy has the potential to make this treatment more attractive to regulators and insurers. Indeed, as multidrug-resistant populations expand, it is becoming more frequent to utilize combinations such as nitrofurantoin and amikacin, which not only increases treatment costs but also the patient's risk of adverse effects. Furthermore, therapeutic success with gepotidacin has been demonstrated in critical subgroups that are at higher risk of treatment failure, such as those with a history of recurrence. In addition to this, gepotidacin is being studied in urogenital gonorrhea (EAGLE-1 study), another market plagued by multidrug resistance; topline results are expected in the first half of 2024.

Tags: First Approval, New Drug Class

Metabolic



AT-007 | APLT | LOA: ABOVE AVERAGE | [↗](#)

Galactosemia

Applied Therapeutics' AT-007 (govorestat) is a novel, potent, investigational CNS-penetrant aldose reductase inhibitor in development for galactosemia and other rare metabolic diseases. Patients with galactosemia are unable to break down the sugar galactose (derived from lactose), which is converted into galactitol, a toxic metabolite, by aldose. Galactosemia has no known cure or approved drug treatment; management is based on an early diagnosis and elimination of lactose from the diet. If untreated, galactosemia can cause rapid, unexpected death due to infection and possibly brain damage, liver disease, and cataracts. The FDA has awarded both orphan drug and pediatric rare disease designations to AT-007 for the treatment of galactosemia, with orphan medicinal product designation also granted by the EMA.

Data from the ACTION-Galactosemia Kids Phase III trial involving 47 children aged 2–17 years with galactosemia showed that AT-007 narrowly missed the primary endpoint, the Global Statistical Test, but was associated with clinical benefit on activities of daily living, behavioral symptoms, cognition, adaptive behavior, and tremor. AT-007 was reported to be safe and well tolerated, with no treatment-related serious adverse events observed. Applied Therapeutics has announced that a pre-NDA meeting with the FDA is planned during 2023, with an application to the EMA for marketing authorization also scheduled to occur before the end of 2023.

Tags: First Approval, Practice Changing

OTL-200 | ORTX | LOA: AVERAGE | [↗](#)

Metachromatic Leukodystrophy (MLD)

Orchard Therapeutics' OTL-200 (Libmeldy in Europe) is a lentiviral vector-based gene therapy consisting of autologous CD34+ cells encoding the arylsulfatase A (ARSA) gene which has been developed for the treatment of MLD. MLD is a fatal neurodegenerative disease that is rapidly progressive and is estimated to affect 40,000 to 160,000 patients globally, with 2,500 of those located in the US.

In December 2020, OTL-200 was approved as Libmeldy in Europe, making it the first approved treatment for MLD patients, and Orchard is now focusing on gaining FDA approval in the first half of 2024. Pricing of gene therapies remains a significant barrier to uptake, and in Europe the current wholesale price of Libmeldy is listed at \$3.2m per dose. For the US, a placeholder price of \$2.8m has been estimated by the Institute for Clinical and Economic Review (ICER), which would be in line with other FDA-approved gene therapies that have reached the market.

Tags: Potential Blockbuster, Practice Changing

IB1001 | INTRABIO | LOA: ABOVE AVERAGE | [↗](#)

Niemann-Pick Disease Type C

IntraBio's IB1001 is in Phase III development for Niemann-Pick disease Type C (NPC), a rare indication for which there are currently no FDA-approved therapies, making this a significant market opportunity. The drug is an orally administered modified amino acid thought to stabilize the nerve cells responsible for balance and coordinating movement. Its mechanism of action is multi-modal and involves altering glucose and antioxidant metabolism, reducing lysosomal storage, and reducing neuroinflammation in the cerebellum. In the Phase III trial, IB1001 met the primary endpoint by demonstrating a statistically significant and clinically meaningful 1.37-point reduction on the Scale for the Assessment and Rating of Ataxia (SARA) compared to placebo. The secondary endpoints were also met with statistical significance and the drug demonstrated a positive safety and tolerability profile, with no drug-related serious adverse events.

IB1001 is competing with several pipeline therapies to become the first FDA-approved treatment for NPC; a race that it seems to be winning. Global regulatory submissions for IB1001 in NPC are expected shortly, which should allow for a potential launch in 2024. The drug has received fast track designation, US and European orphan drug designations, and rare pediatric disease designation in the US for the treatment of NPC. IB1001 is also being developed for other orphan indications which have no FDA-approved therapies, including GM1 and GM2 gangliosides, and inherited cerebellar ataxias.

Tags: First Approval

MOUNJARO | LLY | LOA: ABOVE AVERAGE | [↗](#)

Obesity

Eli Lilly's tirzepatide is a once-weekly glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist that was approved by the FDA in May 2022 under the brand name Mounjaro for type 2 diabetes. On top of its impressive efficacy for glycemic control, it also has the additional benefit of marked weight reduction, offering the potential for a game-changing new therapeutic option to battle the obesity pandemic which is associated with serious outcomes including cardiovascular events. With only Novo Nordisk's Wegovy (semaglutide) offering mean weight reductions above 10%, tirzepatide's ability to drive average weight loss in excess of 25% after more than one year's treatment offers a practice-changing alternative once available for obesity. Until recently, prescription weight loss agents offered only up to 10% mean weight loss and came with safety concerns, meaning that patients with obesity and associated co-morbidities only had metabolic surgery as a highly efficacious approach. However, like all major surgery, this comes with risks and can also mean a lifetime of micronutrient deficiency and gastrointestinal issues after the intervention. Tirzepatide's efficacy can bridge the gap between lifestyle modifications and metabolic surgery and offers an effective option for those with less severe obesity or those who do not want to or cannot undergo surgery.

The SURMOUNT Phase III trial program for tirzepatide was initiated in 2019 and included six major studies enrolling more than 5,000 patients with and without diabetes assessing weight reduction and weight maintenance. In 2022, the FDA granted fast track designation for the investigation of tirzepatide for obesity or overweight with weight-related co-morbidities, and a rolling NDA submission was initiated incorporating delivery of data from the SURMOUNT program as it completed. Considering the reports of off-label prescribing of Mounjaro for obesity and with high prevalence of the disease, blockbuster sales of tirzepatide for obesity are expected to be achieved rapidly.

Tags: Practice Changing, Potential Blockbuster

LIVMARLI | MIRM | LOA: ABOVE AVERAGE | [↗](#)

Progressive Familial Intrahepatic Cholestasis (PFIC)

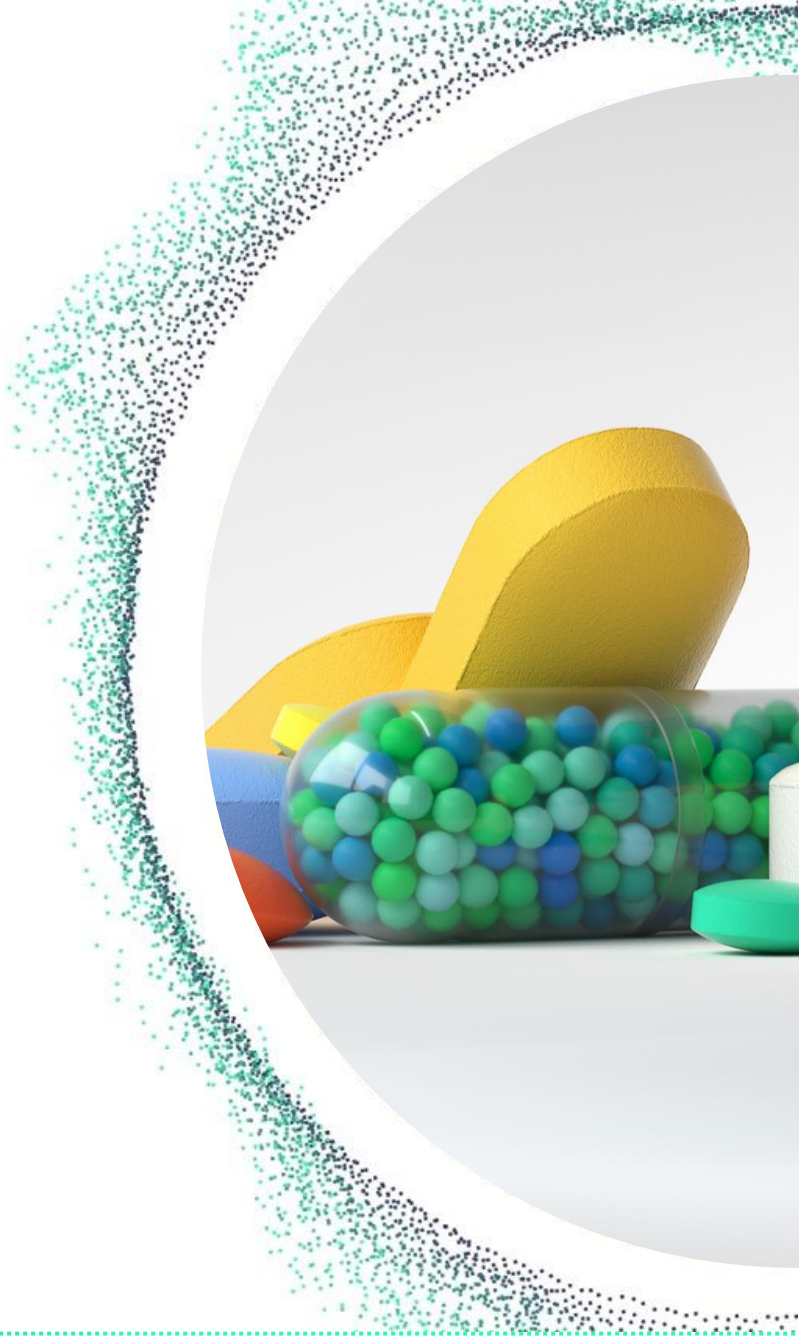
Mirum is developing Livmarli for the treatment of progressive familial intrahepatic cholestasis (PFIC), specifically pruritus, an indication for which there is currently only one FDA-approved therapy, Albireo's Bylvay. PFIC is a genetic disease caused by defects in biliary epithelial transporters (PFIC subtypes impact different transporters), resulting in cholestasis. Livmarli is an orally administered ileal bile acid transporter (IBAT) inhibitor which reduces bile accumulation in the liver to improve liver function. It has already been approved by the FDA and EMA for the treatment of Alagille syndrome (ALGS), and has received US and European orphan drug designation and breakthrough therapy designation in the US for the treatment of PFIC.

In the Phase III trial for PFIC, Livmarli treatment led to a statistically significant reduction in ItchRO(Obs) severity scores compared to placebo, the primary endpoint, indicating an improvement in pruritus. Additionally, there was a statistically significant decrease in serum bile acids compared to placebo. These effects have been sustained so far in the open-label extension study. Although it is difficult to compare between studies, an increased dosage appears to have given Livmarli a slight competitive edge over Bylvay in terms of efficacy. Additionally, Livmarli may be differentiated by its stronger efficacy in treating PFIC type 2 patients who have variations in the gene that predicts non-functional or complete absence of the bile salt export pump protein.

A supplemental NDA for Livmarli in the treatment of cholestatic pruritus in PFIC was submitted to the FDA in February 2023, with a PDUFA date set for December 2023. An early 2024 launch is expected in the US, if approved. A supplemental filing was also submitted in Europe in April 2023.

Tags: Practice Changing, Label Expansion (New Indication)

Neurology



HYQVIA | TAK | LOA: ABOVE AVERAGE | [↗](#)

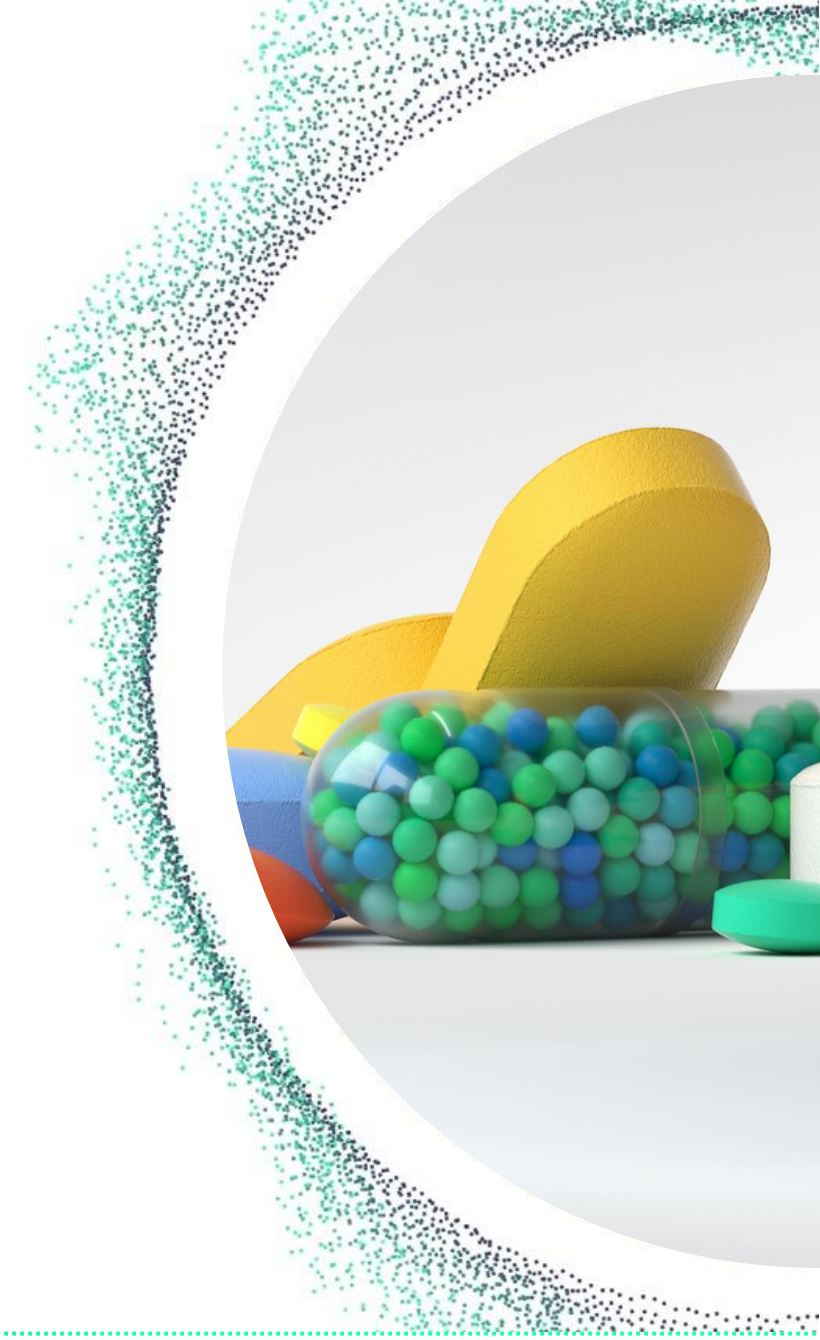
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Takeda's HyQvia, an immunoglobulin (Ig) infusion with recombinant human hyaluronidase for use as a maintenance therapy in adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP), hopes to be the first monthly subcutaneous Ig injection on the market and could see US approval as soon as 2024. The current standard of care for CIDP is intravenous Ig, which is administered over several hours every three weeks and is burdened by side effects such as injection site reactions, nausea, and headaches. Takeda hopes to carry on HyQvia's successes in primary immunodeficiency, for which it received approval from the FDA back in 2014. However, to succeed in the well-established immunoglobulin market currently dominated by CSL and Grifols, Takeda hopes the utilization of Halozyme's ENHANZE technology based on recombinant hyaluronidase to facilitate more Ig into the bloodstream will give it an edge over its competitors by reducing the number of infusions and enhancing efficacy over the standard of care.

The pivotal Phase III ADVANCE-CIDP 1 trial, in which the majority of patients received dosing at four-weekly intervals, met its primary endpoint of showing a significant reduction in relapse rate compared to placebo. Patients from ADVANCE-CIDP 1 who remained relapse-free were offered to continue in the open-label extension ADVANCE-CIDP 3, which will assess HyQvia's long-term safety and efficacy. Regulatory filings for HyQvia for use as maintenance therapy in CDP were submitted to the FDA and EMA in fiscal year 2022 and are presumably supported by the robust data from ADVANCE-CIDP 1 as well as the drug's well-established safety profile demonstrated across trials in patients with primary immunodeficiency.

Tags: Label Expansion (New Indication)

Oncology



IOMAB-B | ATNM | LOA: ABOVE AVERAGE | [↗](#)

Acute Myeloid Leukemia (AML)

Radiolabeled CD45-targeting antibody lomab-B is Actinium Pharmaceuticals' lead asset, and it is being evaluated in relapsed/refractory (R/R) AML patients as a low-intensity conditioning regimen prior to hematopoietic stem cell transplant (HSCT) in the Phase III SIERRA trial. Topline results from the trial were published in February 2023 and showed that conditioning therapy with lomab-B led to higher rates of allo-HSCT in R/R AML patients, with all 66 patients administered the drug able to undergo an allo-HSCT. The trial met its primary endpoint of durable CR of six months following initial complete remission after HSCT. Notably, the patients were not required to first attain a CR before the transplant, thus halving the time between conditioning therapy and transplant. In addition, 74.6% of the patients treated with lomab-B achieved an initial remission after their transplant, a significant increase over the control arm where only 6.3% of patients entered remission after transplant. The depth and durability of the remission are also important factors, and 22% of the lomab-B-treated patients who achieved post-transplant remission had a durable CR at six months, with a one-year OS rate of 92% and a two-year OS rate of 60%. The median OS achieved by patients treated with lomab-B was 6.4 months, compared with 3.2 months in the control arm patients who did not cross over, and the one-year survival rate was 26.1%. These are significant improvements in a population with limited treatment options who have few available opportunities for survival benefits, and lomab-B could fulfill a significant unmet need if approved.

For a positive outlook, lomab-B would benefit from having the full force of a big company's commercial presence, which is something that Actinium Pharmaceuticals and commercialization partner Immedica may struggle with, as radiolabeled antibodies have not been extremely commercially successful in the past, in part because of difficulties in the logistics associated with their delivery.

Tags: First Approval

UPROLESELAN | GLYC | LOA: ABOVE AVERAGE | [↗](#)

Acute Myeloid Leukemia (AML)

GlycoMimetics' first-in-class E-selectin inhibitor uproleselan has demonstrated promising efficacy in early-phase trials in relapsed/refractory (R/R) AML, and a pivotal Phase III trial is currently assessing its efficacy in the same patient population in combination with salvage chemotherapy regimens MEC and FAI versus chemotherapy alone. Uproleselan was granted breakthrough therapy designation for the treatment of adult R/R AML by the FDA in May 2017 following the release of data from a Phase I/II trial. The drug also has fast track designation. The Phase I/II trial evaluating uproleselan in combination with MEC demonstrated a median OS of 8.8 months, which compares well to the median OS of 5.2–5.4 months reported in the literature for MEC alone.

An event-based final analysis of OS from uproleselan's pivotal trial was expected at the beginning of 2023, but with the number of events slowing, the projected timeline for the trial was extended in June 2023 to the second quarter of 2024, when – if positive – the data are expected to support a filing for regulatory approval. Another Phase III trial for uproleselan is evaluating the drug in combination with MEC in Chinese patients with R/R AML at first or second relapse who are eligible to receive induction chemotherapy. Sponsored by Apollomics, GlycoMimetics' development partner, and with a primary completion date of October 2023, the trial is designed to support a potential filing in China.

Tags: First Approval, New Drug Class

ZELTHERVA | SLS | LOA: ABOVE AVERAGE | [↗](#)

Acute Myeloid Leukemia (AML)

Typically, AML patients who relapse or become refractory to treatment following two lines of therapy have a poor outcome, with allogeneic stem cell transplant (allo-SCT) the only potentially curative option in this setting. Not all patients can access transplantation, however, due to their age, co-morbidities, or lack of a donor. Sellas Life Sciences' therapeutic vaccine Zeltherva is being developed as a maintenance treatment in the rather specialized group of patients who have achieved hematologic complete remission after second-line therapy (CR2) and are ineligible for allo-SCT. Zeltherva's target, antigen WT1, is widely overexpressed on leukemic blasts, and lower levels of WT1 are associated with long-term remission. The Phase III REGAL trial, the basis for Zeltherva's expected BLA filing, passed a significant milestone in April 2023 when the Independent Data Monitoring Committee performed a prespecified risk-benefit assessment of unblinded data from the study and recommended its continuation as planned. With no data from REGAL available, we rely on data from a pilot Phase I/II study, published in April 2020, which showed that at a median follow-up of 19.3 months, the median OS reached by Zeltherva-treated patients on their second remission was 16.3 months (vs 5.4 months for the best standard therapy control). It remains to be seen whether these heavily pretreated patients can mount an effective and sustained immune response following vaccination with Zeltherva, but should the drug receive regulatory approval, it would offer a much-needed therapeutic option to a patient population characterized by a high unmet need. And with prior-line treatments expected to increase patients' derived clinical benefit, the size of Zeltherva's target CR2 population is likely to increase in the future.

Sellas has also announced plans for a Phase IIa trial of Zeltherva in combination with Venclexta and azacitidine, a doublet that has become the standard of care in first-line AML patients ineligible for intensive induction; no such trial has been registered yet at the time of publication.

Tags: First Approval

ZANIDATAMAB | JAZZ | LOA: ABOVE AVERAGE | [↗](#)

Biliary Tract Cancer (BTC)

Jazz Pharmaceuticals' zanidatamab is a next-generation HER2 antibody that is differentiated by its ability to simultaneously bind two non-overlapping epitopes of HER2. This unique design results in multiple mechanisms of action including dual HER2 signal blockade, increased binding and removal of HER2 protein from the cell surface, as well as antibody-dependent cellular cytotoxicity. Zanidatamab is being investigated in multiple clinical trials for HER2-expressing solid tumors and has breakthrough therapy and fast track designations for patients with previously treated HER2-expressing BTC, a setting with no approved HER2-targeted agent and which is zanidatamab's first potential commercial indication. Zanidatamab in combination with chemotherapy has fast track designation for the treatment of first-line gastroesophageal adenocarcinoma (GEA).

At ASCO 2023, updated results were presented from HERIZON-BTC-01, a single-arm Phase IIb study that reported a 41% ORR, a 12.9-month median duration of response, and a 5.5-month median PFS. A BLA submission seeking accelerated approval for second-line BTC and supported by HERIZON-BTC-01A is expected by the end of 2023. The FDA has agreed that a confirmatory Phase III trial will evaluate zanidatamab for first-line metastatic BTC.

Phase III data for first-line GEA are expected in 2024. Apart from BTC and GEA, Jazz Pharmaceuticals is planning to explore zanidatamab for breast cancer including the neoadjuvant setting and the post-Enhertu or Enhertu-intolerant setting. Finally, zanidatamab is also being evaluated for other HER2-positive tumors, including those with few approved HER2-targeted agents. Jazz Pharmaceuticals has estimated that peak sales of zanidatamab could eventually reach \$2bn per year.

Tags: First Approval, Potential Blockbuster, Practice Changing

DAY101 | DAWN | LOA: ABOVE AVERAGE | [↗](#)

Brain Cancer

DAY101 is an investigational, oral, brain-penetrant, highly selective type II pan-RAF kinase inhibitor which is currently being evaluated in an ongoing pivotal Phase II trial (FIREFLY-1) for the treatment of pediatric, adolescent, and young adult patients with relapsed pediatric low-grade glioma (pLGG). pLGG is the most common brain tumor diagnosed in children, accounting for 30–50% of all CNS tumors, and with a high 10-year OS rate of 85–96%. Children who do not achieve remission following surgical resection often face years of adverse effects from long-term chemotherapy and/or radiation therapy.

Day One has reported positive data from the Phase II FIREFLY-1 study and has also initiated a pivotal Phase III study (FIREFLY-2/LOGGIC) with DAY101 in newly diagnosed patients with pLGG. Although coming from a relatively small patient sample, the 67% overall response rate is positive in a population that had received a median of three prior lines of therapy, and is superior to the 20–25% response rate typically seen with standard-of-care single-agent chemotherapy in this patient population. The majority of adverse events (AEs) were grade 1–2, with grade ≥ 3 AEs seen in 36% of patients. Importantly, there were no discontinuations of treatment due to AEs, which bodes well for a treatment which patients will be receiving on a long-term basis. The company anticipates the rolling NDA submission of DAY101 to complete in October 2023 following a submission of an amended clinical study report that will include safety and efficacy data from a June 2023 data cutoff.

Tags: Practice Changing, First Approval

IMFINZI | AZN | LOA: AVERAGE | [↗](#)

Bladder Cancer

Imfinzi was dealt a severe setback after the FDA rescinded its second-line metastatic approval in the bladder cancer indication, but AstraZeneca is hoping to re-enter to market with an approval in the muscle-invasive bladder cancer (MIBC) space based on the Phase III NIAGARA trial. However, the perioperative NIAGARA regimen may struggle to compete with rival PD-1 inhibitor Opdivo, which has already been shown to nearly double disease-free survival in the CheckMate 274 trial, unless comparable data from this trial are released.

Tags: Label Expansion (New Indication)

CAPIVASERTIB | AZN | LOA: BELOW AVERAGE | [↗](#)

Breast Cancer (HR+/HER2-)

Capivasertib is set to be the second PI3K/AKT inhibitor approved in the HR+/HER2- breast cancer space, after competing PI3K inhibitor Piqray was approved in May 2019. Capivasertib is being studied in the Phase III CAPItello-291 trial in combination with fulvestrant for HR+/HER2- patients who have recurred or progressed after aromatase inhibitor treatment, where data have shown that capivasertib significantly increased PFS in the overall and biomarker-altered population over placebo. The second-line metastatic setting is an area of high unmet need, with many patients developing estrogen receptor 1 (ESR1) mutations after prior treatment with an aromatase inhibitor, making them more difficult to treat. Furthermore, CDK4/6 inhibitors are the standard of care in the first-line metastatic setting, but there are limited data on the efficacy of sequencing these agents, making physicians reluctant to prescribe a second CDK4/6 inhibitor after initial treatment. This has left a gap in the treatment algorithm, with effective second-line therapies needed to address this.

While capivasertib did meet the primary endpoint of the Phase III trial, its safety profile was less than favorable, with 9.3% of patients experiencing grade 3 or above diarrhea, and 12.1% experiencing grade 3 or above rash. AKT inhibitors are associated with severe diarrhea, which has damaged their reputation as a class and may hurt capivasertib's chances of uptake once approved. Nonetheless, a lower percentage of patients experienced a grade 3 or 4 adverse event on capivasertib than on Piqray (as per the Phase III SOLAR-1 trial), which may reassure physicians who are wary of class-wide toxicities seen with the AKT inhibitors. Capivasertib has subsequently been given fast track status by the FDA, reflecting these positive results, and will likely gain approval in the US towards the end of 2023 or in early 2024.

Tags: First Approval

KISQALI | NVS | LOA: AVERAGE | [↗](#)

Breast Cancer (HR+/HER2-)

Kisqali is expected to be submitted for US approval in the lucrative adjuvant setting for HR+/HER2- breast cancer and become the second CDK4/6 inhibitor approved in this setting for this indication. Kisqali has demonstrated a 25.2% decrease in risk of recurrence in adjuvant HR+/HER2- breast cancer patients compared to endocrine therapy alone, with the lowest invasive disease-free survival (iDFS) HR observed in node-negative disease (HR=0.630). Importantly, it has demonstrated this efficacy across a wide range of subgroups, including in node-positive disease. Competitor Verzenio has already secured an approval in high-risk node-positive adjuvant HR+/HER2- breast cancer and will likely dominate in this subset of patients, but Kisqali may be able to boost sales with a wider approval across subgroups.

The two CDK4/6 inhibitors are expected to compete fiercely, with physician familiarity expected to play a large role in which agent is preferred in the adjuvant setting. Verzenio showed stronger efficacy in the Phase III monarchE trial, but data were limited to the high-risk setting, and Kisqali showed a benefit across multiple risk groups. Furthermore, Kisqali's OS is currently tracking stronger than Verzenio's, which could sway physician opinion as OS is the gold standard of oncology endpoints. Safety signals between Kisqali and Verzenio are generally comparable; Verzenio is associated with gastrointestinal adverse events, whereas EKG monitoring is required with Kisqali. Both of these classes of adverse events have the potential to be burdensome depending on the patient's lifestyle and the physician's preference.

Tags: Label Expansion (Existing Indication), Potential Blockbuster

ENHERTU | DAIICHI SANKYO | LOA: AVERAGE | [↗](#)

Breast Cancer (HER2+)

HER2-directed antibody-drug conjugate (ADC) Enhertu has had significant success across all three subtypes of breast cancer and is currently being investigated in a suite of trials in the early-stage setting. The Phase III DESTINY-Breast11 trial looking at Enhertu in the neoadjuvant setting in HER2+ breast cancer is expected to be one of the first of these trials to yield results and lead to an approval in the lucrative early-stage setting. It is expected that Daiichi Sankyo will file for approval based on the Phase III DESTINY-Breast11 results in 2024, greatly expanding Enhertu's reach within the breast cancer space and generating substantial revenues in this large patient population.

Tags: Label Expansion (Existing Indication)

BRAFTOVI | PFE | LOA: ABOVE AVERAGE | [↗](#)

Colorectal Cancer (CRC)

Pfizer's RAF kinase inhibitor Braftovi established a strong OS and ORR benefit in the Phase III BEACON-CRC trial as part of a doublet regimen with Erbitux in second-line metastatic CRC expressing BRAF V600E, leading to its approval in April 2020. Aiming to boost Braftovi's commercial outlook, Pfizer registered the BREAKWATER Phase III trial, which targets the larger, more lucrative first-line setting. Interim data from the Phase II ANCHOR-CRC study exploring a triplet of Braftovi/Erbitux/Mektovi (a MEK inhibitor) showed a promising median OS of 17.2 months and a median PFS of 5.8 months in first-line BRAF V600E mutants, giving a glimpse into Braftovi's potential success in the first-line setting. The toxicity of the triplet is, however, problematic, and so BREAKWATER focuses only on Braftovi/Erbitux.

BRAF V600E mutants represent 5–12% of the patient population, with a significant overlap with MSI-H tumors where the Braftovi/Erbitux regimen is expected to compete with PD-1 inhibitors. The BREAKWATER trial excludes patients with MSI-H tumors unless these patients are specifically ineligible for checkpoint inhibitors, a way of acknowledging that PD-1 inhibitors may be used preferentially over BRAF blockade where possible. If successful, however, Braftovi would be a welcome addition to the CRC treatment algorithm.

Tags: Label Expansion (New Indication)

LUMAKRAS | AMGN | LOA: ABOVE AVERAGE | [↗](#)

Colorectal Cancer (CRC)

Amgen's irreversible KRAS G12C inhibitor Lumakras has shown clinical activity as a monotherapy in KRAS G12C-mutated solid tumors, including CRC. The Phase III CodeBreak 300 study is investigating the combination of Lumakras and Vectibix in previously treated CRC patients with KRAS G12C mutation.

Data from the Phase Ib CodeBreak 101 trial showed that Lumakras in combination with Vectibix and chemotherapy regimen FOLFIRI yielded an ORR of 58.1% (all partial responses) and a disease control rate of 93.5% in metastatic CRC patients treated with a median of two prior lines. The addition of Vectibix to Lumakras could bypass a resistance mechanism to the latter drug, and in addition could provide an efficacy boost. CodeBreak 300 does not include a chemotherapy add-on, so it remains to be seen whether the promising clinical activity seen in CodeBreak 101 will be sustained by the Lumakras/Vectibix doublet.

Tags: Label Expansion (New Indication)

FRUQUINTINIB | TAK | LOA: ABOVE AVERAGE | [↗](#)

Colorectal Cancer (CRC)

Approved in China in 2022 under the brand name Elunate, VEGFR inhibitor fruquintinib has demonstrated promising PFS and OS in the heavily pretreated population. The Phase III FRESCO-2 trial seeks to expand its development in the US as a supplement to best supportive care (BSC) in CRC patients who are refractory to at least two prior rounds of treatment. Data from FRESCO-2 showed that fruquintinib added to BSC led to a median OS of 7.4 months (vs 4.8 months for BSC alone) and a median PFS of 3.7 months (vs 1.8 months for BSC alone) in a patient population previously treated with a median of three lines. The disease control rate was 55.5% in the fruquintinib arm compared with 16.1% for patients in the BSC arm. Third- and later-line mCRC are an area of high unmet need, with current therapies reaching an mPFS of only 1.5–2 months, and the improvements seen in the fruquintinib arm are therefore significant and exciting. Subgroup analysis data from FRESCO-2, however, have shown that there were significantly more treatment-emergent adverse events in the fruquintinib arm (80.7% vs 53% for BSC), with grade ≥ 3 hypertension and grade ≥ 3 palmar-plantar erythrodysesthesia of particular concern, as they are both debilitating toxicities which can lead to treatment discontinuation. With a PDUFA date set for November 2023, it remains to be seen whether the FDA will tip the balance of efficacy versus toxicity in favor of fruquintinib.

Tags: First Approval

KRAZATI | MRTX | LOA: ABOVE AVERAGE | [↗](#)

Colorectal Cancer (CRC)

Small molecule KRAS inhibitor Krazati is the first such agent in CRC. It is being evaluated in the KRYSTAL-10 trial in combination with Erbitux, targeting second-line KRAS G12C-mutated CRC patients. This expression profile limits the drug's outreach to only 3–4% of the CRC population, but it offers a rare chemotherapy-free option for advanced disease. Granted a breakthrough therapy designation for G12C-mutated advanced CRC by the FDA in December 2022, Krazati (in combination with Erbitux) demonstrated an ORR of 46%, a median PFS of 6.9 months, and a median OS of 13.4 months at a median follow-up of 17.5 months in the Phase I/II KRYSTAL-1 trial. If these results are replicated in KRYSTAL-10, the doublet has a high chance of becoming the standard of care for G12C-mutated CRC patients with advanced disease who have been treated with one previous line, and will at least partially fulfill an unmet need for a population that currently has a poor prognosis.

Tags: Label Expansion (New Indication)

ZOLBETUXIMAB | ASTELLAS | LOA: ABOVE AVERAGE | [↗](#)

Gastric Cancer

Zolbetuximab is a first-in-class monoclonal antibody which targets the cell adhesion protein Claudin 18.2, which is overexpressed in approximately 40% of gastric cancers. The current gastric cancer treatment paradigm splits patients via the presence of one actionable biomarker; namely, human epidermal growth factor 2 (HER2). HER2-negative disease represents 80% of the market and hence is the most lucrative space for agents to enter. The Phase III SPOTLIGHT and GLOW trials investigated zolbetuximab in combination with chemotherapy as a front-line treatment for metastatic or locally advanced HER2-negative gastric cancer. Both of these trials met the primary endpoint of improving PFS compared to placebo plus chemotherapy. If the drug is to be approved it would require patients to be screened for Claudin 18.2 expression, diversifying the biomarker portfolio within gastric cancer. Zolbetuximab has been estimated to reach blockbuster status by 2028.

Current treatment options are limited for patients with HER2-negative gastric cancer, with Bristol Myers Squibb's PD-1-targeted inhibitor Opdivo (nivolumab) standing as the only approved targeted therapy in this setting. While Opdivo reigns as the market leader of the gastric cancer space, zolbetuximab is anticipated to steal considerable share. The survival data for both agents look to be comparable; however, zolbetuximab looks set to offer a potentially improved safety profile compared to Opdivo, with SPOTLIGHT reporting a similar incidence of treatment-related adverse events in both the placebo and zolbetuximab arms. In the Phase III CheckMate 649 trial, on the other hand, the incidence of serious treatment-related adverse events was higher in the Opdivo arm compared to placebo. This positions zolbetuximab as an attractive alternative, especially for patients who are immunodeficient. Zolbetuximab also has the potential to carve a niche for itself in patients who are poorly immunogenic. While Opdivo is approved regardless of PD-1 expression and is often prescribed in HER2-negative patients with combined positive score (CPS) <1 , this is predominantly due to the lack of effective available therapies for these patients, as the survival benefit from CheckMate 649 was observed in patients with CPS ≥ 1 . If zolbetuximab is afforded the approval, it can be expected that the drug will steal market share from Opdivo in these patients who are PD-1-negative/PD-1-low.

Tags: First Approval, Practice Changing, Potential Blockbuster

IMFINZI | AZN | LOA: AVERAGE | [↗](#)

Hepatocellular (Liver) Cancer (HCC)

Patients with locoregional HCC are currently treated with transarterial chemoembolization (TACE), radiofrequency ablation, and resection, and lack immunotherapy or targeted therapy treatment options. Imfinzi is in development as a part of multiple combinations for the treatment of locoregional HCC, including in combination with TACE, with or without bevacizumab, in the Phase III EMERALD-1 trial. Although data are lacking for this combination in this setting, topline data are expected during 2023, which should pave the way for an approval in 2024. The Phase III EMERALD-3 trial is also investigating Imfinzi plus TACE in combination with Imjudo in locoregional HCC; however, an approval for this combination is not expected until 2026.

Imfinzi is currently approved for the first-line treatment of advanced or metastatic HCC; however, in this setting it competes with standard-of-care Tecentriq and bevacizumab. If Imfinzi receives an approval for the treatment of these patients, it will be the first immunotherapy approved for these patients and will have full monopoly of the market, carving a niche for itself in the treatment of HCC.

Tags: Practice Changing, Label Expansion (Existing Indication)

LN-144 | IOVA | LOA: ABOVE AVERAGE | [↗](#)

Melanoma

Iovance Biotherapeutics' Contego (LN-144), a ready-to-infuse autologous cell therapy product containing tumor-infiltrating lymphocytes (TILs), is poised to become the first TIL therapy approved after demonstrating remarkable results in the pivotal Phase II innovaTIL-01 study. In the pivotal cohort, Contego demonstrated an overall response rate (ORR) of 32.4% and a disease control rate of 72.1% in heavily pretreated advanced melanoma patients, most of whom had already progressed on both a PD-1 inhibitor and a CTLA-4 inhibitor. Currently, patients who have progressed on a PD-1 inhibitor and a CTLA-4 inhibitor have limited treatment options, and retreatment with either immune checkpoint inhibitors or chemotherapy yields a poor response rate, with a 29% ORR seen with Keytruda and low-dose Yervoy retreatment and a 4–10% ORR seen with chemotherapy.

Contego has previously been granted regenerative medicine advanced therapy (RMAT) designation, fast track status, and orphan drug designation as a treatment for advanced melanoma. However, in 2020, the FDA indicated that Iovance's potency assays, which are required for a BLA submission, were inadequate. After this unexpected setback, a BLA submission was accepted in August 2022 following a meeting with the FDA. The submission was completed in March 2023, and a PDUFA date has been set for November 2023.

Tags: Practice Changing, New Drug Class, First Approval

IMETELSTAT | GERN | LOA: ABOVE AVERAGE | [↗](#)

Myelodysplastic Syndrome (MDS)

Geron has filed a New Drug Application to the FDA for the use of its first-in-class telomerase inhibitor imetelstat in the treatment of low-intermediate risk MDS patients with anemia who have failed on or are ineligible for erythropoiesis-stimulating agent (ESA) therapy. The submission is based on impressive Phase III IMerge data, and an approval decision is anticipated in February 2024. Importantly, the IMerge trial targets a patient setting of high unmet need with limited effective treatment options approved. In April 2023, the company announced that IMerge had met its primary endpoint of improving the percentage of participants without any red blood cell (RBC) transfusion during any consecutive eight-week periods. In these impressive topline results, it was demonstrated that imetelstat improved hemoglobin levels, alleviated symptoms of anemia, and induced durable transfusion independence across various subgroups of non-del(5q) lower risk MDS patients.

The practice-changing subgroup analysis from IMerge revealed imetelstat to be the first efficacious agent in non-del(5q) patients regardless of ring sideroblast (RS) status, paving the way for imetelstat to carve itself a crucial niche and emerge as a pioneer in the refractory lower risk MDS setting. An approval irrespective of RS status would armor imetelstat with a key differentiating advantage over the only other approved targeted therapy in the non-del(5q) space, namely Bristol Myers Squibb's Reblozyl (luspatercept), and would seize a previously untapped large market opportunity. Exploratory variant allele frequencies (VAF) analysis from the IMerge trial investigating genes commonly mutated in MDS also demonstrated imetelstat to have the revolutionary potential to be the first disease-modifying agent to enter the market, further solidifying the drug's competitive edge. Equipped with these impressive clinical data, imetelstat looks set to become the new standard-of-care treatment for ESA-refractory non-del(5q) lower risk MDS patients.

Tags: First Approval, Practice Changing

SAR408701 | SNY | LOA: ABOVE AVERAGE | [↗](#)

Non-Small Cell Lung Cancer (NSCLC)

Sanofi's tusamitamab ravtansine (SAR408701) is an antibody-drug conjugate (ADC) directed towards CEACAM5, a cell surface protein with limited expression in normal tissue and overexpression in approximately 20% of non-squamous NSCLC cases. The overall response rate of 20.3% and disease control rate of 64.1% seen in patients with high CEACAM5 expression in a Phase I/II study are promising, although there were some safety concerns due to the 27.2% of evaluable patients who experienced a corneal treatment-related adverse event that led to a dose modification.

Notably, 70.3% of patients in this study had previously received treatment with a PD-1 inhibitor, and currently patients who have progressed on immunotherapy treatment have few, if any, treatment options available to them. Enhertu was the first targeted therapy to receive an approval in the post-immunotherapy setting in 2022, although its label is limited to the approximately 2–4% of patients who have a HER2 mutation. Furthermore, the results seen with tusamitamab ravtansine compare favorably to the approved therapies currently used for these patients – docetaxel, which has a historical ORR of 9–14%, and docetaxel in combination with Cyramza, which has a historical ORR of 23%.

Results from the pivotal Phase III CARMEN-LC03 study of tusamitamab ravtansine for the second-line or later treatment of NSCLC patients with CEACAM5-positive tumors are expected during 2023, and assuming the data are positive, Sanofi plans to submit a BLA by the end of 2023.

Tags: Practice Changing, First Approval

IMFINZI | AZN | LOA: ABOVE AVERAGE | [↗](#)

Ovarian Cancer

Imfinzi is currently being evaluated in combination with platinum-based chemotherapy and bevacizumab followed by maintenance Imfinzi, bevacizumab, and Lynparza in the Phase III DUO-O trial for the treatment of advanced ovarian cancer patients in the first-line and maintenance settings. PARP inhibitors, platinum-based chemotherapy, and bevacizumab currently dominate the first-line treatment setting of ovarian cancer; however, Lynparza's label is restricted to the one in three women who present with a BRCA mutation or are HRD-positive. AstraZeneca is hoping that a label expansion into the lucrative first-line BRCA wild-type market will boost its treatable patient population.

Although there are multiple checkpoint inhibitor and PARP inhibitor combinations being developed for the front-line and front-line maintenance settings, DUO-O is the first Phase III trial to release data. In DUO-O, the combination demonstrated at 37.3-month median PFS in newly diagnosed HRD-positive, BRCA wild-type advanced ovarian cancer patients, which is a statistically significant and clinically meaningful improvement over the 23.0-month median PFS seen with platinum-based chemotherapy and bevacizumab alone. However, DUO-O utilized a bevacizumab and chemotherapy comparator arm, when a Lynparza, bevacizumab, and chemotherapy comparator arm would have been more reflective of the current treatment algorithm for HRD-positive patients. Nevertheless, the median PFS seen in DUO-O is superior to the data seen in the Phase III PAOLA-1 study, where Lynparza, bevacizumab, and chemotherapy demonstrated a median PFS of 28.1 months in newly diagnosed BRCA wild-type, HRD-positive advanced ovarian cancer patients. Most importantly, the DUO-O study is the first study to show benefit in BRCA wild-type, HRD-negative patients against an active comparator arm, as PARP inhibitors have typically shown weak data in this setting. A 20.9-month median PFS was seen when patients with previously untreated BRCA wild-type, HRD-negative advanced ovarian cancer were treated with the DUO-O regimen, which is a 3.5-month benefit over the median PFS seen with chemotherapy and bevacizumab alone in the same patient population. The DUO-O regimen is expected to be the first to be approved in this setting, after which the market will become more competitive.

Tags: Practice Changing, Label Expansion (New Indication)

PLUVICTO | NVS | LOA: AVERAGE | [↗](#)

Prostate Cancer

Pluvicto made history in 2022 when it was approved for pretreated metastatic castration-resistant prostate cancer (mCRPC) patients, becoming the first PSMA-targeted radiotherapy approved in the prostate cancer space. It has since become an important part of the prostate cancer treatment algorithm despite encountering manufacturing issues towards the start of its launch. Novartis is looking to capitalize on the success of Pluvicto, and is investigating it in several other settings, including the metastatic hormone-sensitive prostate cancer (mHSPC) setting as outlined in the Phase III PSMAddition trial.

An approval for Pluvicto in the mHSPC setting would give it the potential to generate significant profit, as it is much larger than the pretreated mCRPC population, the only setting in which it is currently approved. However, next-generation androgen receptor antagonists Xtandi and Zytiga are well cemented as the standards of care in the mHSPC treatment paradigm, and comparable efficacy and safety in this setting will need to be demonstrated by Pluvicto in order to usurp Xtandi and Zytiga from their current dominance. Furthermore, Novartis will need to ensure that its supply chain is robust, as manufacturing issues initially held it back in the mCRPC setting.

Tags: Label Expansion (Existing Indication), Potential Blockbuster

AFAMITRESGENE AUTOLEUCEL | ADAP | LOA: ABOVE AVERAGE | [↗](#)

Sarcoma

Adaptimmune's afamitresgene autoleucel (afami-cel) is an autologous T-cell therapy in which the patient's T cells are modified to express a T-cell receptor (TCR) engineered to recognize melanoma-associated antigen A4 (MAGE-A4) peptides bound to the MHC receptor. Patients undergo leukapheresis for collection of T cells for processing and manufacture of the afami-cel product, which is then administered as a single infusion following lymphodepleting chemotherapy. If approved, afami-cel will be the first commercially available engineered T-cell therapy for a solid tumor indication.

SPEARHEAD-1 enrolled patients with advanced synovial sarcoma (SS). Patients had to have tumors expressing MAGE-A4 and had to be positive for the HLA-A*02 allele (the allele is expressed in approximately 41% of the population). The trial met its primary endpoint with an ORR of 39% (17/44) by independent review. The median duration of response was approximately 12 months. These data are similar to results from a Phase I trial which reported an ORR of 41% (23/59) and a median duration of response of 52 weeks.

In terms of safety, SPEARHEAD-1 reported cytokine release syndrome in 66% of patients, most of which were grade 1 and 2 with just a single grade 3 event. Grade 3 or higher cytopenia was reported in 16% of patients at week 4.

Based on these positive Phase II results, Adaptimmune initiated a rolling BLA in December 2022 for patients with advanced SS. The submission is expected to be completed in Q4 2023, with accelerated approval expected in late 2024. A second cohort of SPEARHEAD-1 is fully enrolled and will serve as confirmatory evidence for a full approval. With around 1,800 SS patients dying every year across the US, UK, France, Germany, Italy, and Spain, Adaptimmune estimates that, factored for expression of MAGE-A4 and HLA-A*02, 496 SS patients may be eligible for afami-cel every year. To date, afami-cel has not shown strong activity in other tumor types that express MAGE-A4, so Adaptimmune is developing a next-generation T-cell product (ADP-A2M4CD8) where the TCR is expressed along with the CD8 receptor in CD4-positive T cells. ADP-A2M4CD8 is currently being evaluated in the SURPASS Phase I clinical trial enrolling patients with a variety of solid tumors. At ESMO 2022, ADP-A2M4CD8 reported an ORR of 44% in patients with ovarian cancer, urothelial cancer, or head and neck cancer. A pivotal Phase II trial, SURPASS-3, is enrolling patients with platinum-resistant ovarian cancer.

Tags: First Approval, New Drug Class

SERPLULIMAB | SHANGHAI HENLIUS BIOTECH | LOA: AVERAGE | [↗](#)

Small Cell Lung Cancer (SCLC)

Novel anti-PD-1 antibody serplulimab is in Phase III development in front-line extensive-stage (ES) SCLC. Data from the Phase III ASTRUM-005 trial showed that when added to etoposide and carboplatin, the drug significantly improved the OS of treatment-naïve patients compared with chemotherapy only (15.4 months vs 10.9 months), meeting the trial's primary endpoint. The median PFS was also improved in the serplulimab arm compared with the chemotherapy arm (5.7 months vs 4.3 months), while the treatment-related adverse events were similar between the two trial arms.

SCLC is characterized by rapid progression and metastasis, with most patients presenting with ES disease at diagnosis. The advent of PD-1/PD-L1 inhibitors in the front-line treatment of ES SCLC marked a milestone for a hard-to-treat population that used etoposide combined with platinum agents as a standard of care for decades. PD-L1 inhibitors Tecentriq and Imfinzi, both in combination with etoposide and a platinum agent, are currently the preferred regimens for first-line ES SCLC as listed in the 2023 NCCN guidelines, having led to median OS values of 12.3 months and 12.9 months, respectively, in the IMpower133 and CASPIAN Phase III trials. Keytruda plus chemotherapy also improved the median PFS in the same patient population but did not significantly improve OS in the KEYNOTE-064 trial.

The numerically superior median OS yielded by serplulimab in ASTRUM-005 would therefore satisfy an unmet need in the first-line population – that of a more effective treatment – and would also provide a boost for what would be a third-to-market drug. Henlius has announced plans to submit a BLA to the FDA for serplulimab in 2024, supported by the data from ASTRUM-005. The study, however, had certain limitations, including having a short follow-up in the non-Asian population, recruiting no US patients, and including only a small number of patients with brain metastases. It remains to be seen, therefore, how heavily these limitations will weigh against a positive FDA outcome, especially as the agency has become increasingly stringent in its demands for clinical trials to include US sites should developers seek a US approval.

Tags: First Approval

TORIPALIMAB | CHRS | LOA: AVERAGE | [↗](#)

Small Cell Lung Cancer (SCLC)

Already approved in China under the brand name Tuoyi for a number of oncology indications, PD-1 inhibitor toripalimab is also in Phase III development for extensive-stage (ES) SCLC in the EXTENTORCH trial, in combination with etoposide and a platinum agent. In July 2023, supported by data from the Phase III EXTENTORCH trial, China's NMPA accepted a supplemental NDA seeking approval for toripalimab in combination with etoposide and a platinum agent for first-line ES SCLC. No numerical data have been made available at the time of this report's publication, but the drug's developers have indicated that toripalimab met both PFS and OS primary endpoints of the trial, becoming the first PD-1 inhibitor in the world to do so. Its chances of success with the FDA, however, are likely to be hampered by the lack of sites recruiting US patients in the EXTENTORCH trial, which is a significant and difficult barrier to surpass. Furthermore, with two PD-L1 inhibitors already approved for first-line ES SCLC (Tecentriq and Imfinzi), and with no clear picture of the magnitude of toripalimab's survival benefits in this patient population, it is difficult to ascertain whether the drug can hold off the competition in this space. Another agent, serplulimab, vying for a slice of the same market is also aiming for an FDA approval, but just like toripalimab it may be constrained by its lack of testing in a US/Western population.

Tags: First Approval

IMFINZI | AZN | LOA: ABOVE AVERAGE | [↗](#)

Small Cell Lung Cancer (SCLC)

PD-L1 inhibitor Imfinzi is in Phase III development for limited-stage

SCLC (disease that has not spread beyond one side of the chest). Approximately 30% of SCLC cases are diagnosed with limited-stage disease, with these patients typically treated with concurrent chemoradiation (cCRT) and prophylactic cranial irradiation. Despite good response to cCRT, outcomes remain poor and the median PFS for these patients is around 15 months, with median OS reaching around 25 months. A high unmet need, therefore, remains for these patients, with the standard of care unchanged for several decades.

The ADRIATIC trial is evaluating Imfinzi, alone or in combination with CTLA-4 inhibitor Imjudo, in patients who responded to four cycles of cCRT. With no data yet available from the ADRIATIC trial, there is significant excitement for a therapy or a combination regimen that could improve the outcomes of cCRT. AstraZeneca expects the first data from the ADRIATIC trial to become available in the second half of 2023, and, if positive, they could pave the way for an entry for Imfinzi in the SCLC space.

Tags: Label Expansion (New Indication)

TISLELIZUMAB | BGNE | LOA: AVERAGE | [↗](#)

Small Cell Lung Cancer (SCLC)

BeiGene's PD-1 inhibitor tislelizumab is in Phase III development for first-line extensive-stage (ES) SCLC, in combination with a platinum agent and etoposide, in a trial recruiting Chinese patients only. There are limited data for tislelizumab in this indication, with only Phase II results from a small number of Chinese first-line ES SCLC patients (n=17) available. This Phase II trial showed that when added to etoposide and a platinum agent doublet, tislelizumab had encouraging antitumor activity, leading to a median OS of 15.6 months, a median PFS of 6.9 months, and an ORR of 77%. These data compare well with the efficacy achieved by the current standard of care, etoposide and platinum, but with cross-trial comparisons fraught with danger, it will be essential to see the values for such endpoints from a controlled, larger trial.

In its Q2 2023 results, Novartis – BeiGene's partner in the drug's development – indicated its intention to submit an application for regulatory approval with the FDA in 2024. As tislelizumab is only being tested in Chinese patients, the FDA is likely to request further clinical data to ascertain the drug's efficacy in a Western population.

Tags: First Approval

XPOVIO | KPTI | LOA: ABOVE AVERAGE | [↗](#)

Uterine (Endometrial) Cancer

Approved in the US for multiple myeloma and DLBCL, first-in-class XPO1 inhibitor Xpovio is also in development for endometrial cancer in the Phase III SIENDO and XPORT-EC-042 trials. Both trials are assessing Xpovio as maintenance after therapy with platinum and a taxane (SIENDO) or a platinum agent (XPORT-EC-042), both targeting advanced/recurrent endometrial cancer patients who respond to systemic therapy. Primary results from SIENDO showed improvements in median PFS for the intent-to-treat population, but these were not clinically meaningful. An exploratory analysis of a prespecified subgroup of patients with TP53 wild-type disease, however, showed promising results; at a follow-up of 25.3 months, Xpovio-treated patients with TP53 wild-type disease had a median PFS of 27.4 months versus 5.2 months for patients treated with chemotherapy only. In addition, median PFS was not reached for Xpovio-treated TP53 wild-type MMR-proficient (pMMR) endometrial cancer versus 4.9 months for TP53 wild-type pMMR patients in the control arm. These data provide further support for the XPORT-EC-042 trial, which is focusing on TP53 wild-type patients only.

Advanced/recurrent endometrial cancer is associated with a poor prognosis, with the current standard of care in the first-line setting (carboplatin plus paclitaxel) yielding a median PFS of 13 months and a median OS of 37 months. The data from SIENDO, therefore, are sending a positive signal that Xpovio maintenance can improve these outcomes. Half of advanced/recurrent cases are associated with a TP53 wild-type phenotype, which in turn is found in both pMMR and dMMR/MSI-H tumors, with the latter subgroup mostly targeted by immune checkpoint inhibitors. With a clear unmet need remaining for pMMR tumors (comprising approximately 70% of TP53 wild-type endometrial cancer cases), Xpovio maintenance treatment has the potential to prolong systemic therapy response, provide a much-needed therapeutic option for these patients, and boost the drug's commercial outlook.

Tags: Label Expansion (New Indication)

IMFINZI | AZN | LOA: ABOVE AVERAGE | [↗](#)

LYNPARZA | AZN | LOA: AVERAGE | [↗](#)

Uterine (Endometrial) Cancer

The Phase III DUO-E trial is assessing Imfinzi in combination with platinum-based chemotherapy followed by Imfinzi and Lynparza or Imfinzi alone as maintenance therapy in newly diagnosed or recurrent Stage III or IV endometrial cancer patients. In May 2023, AstraZeneca announced positive topline results from the DUO-E trial, indicating that a statistically significant and clinically meaningful improvement in PFS was observed, with a greater clinical benefit seen in the combination of Lynparza and Imfinzi as maintenance therapy.

With the current standard of care for advanced endometrial cancer being chemotherapy, long-term outcomes in the first-line setting are poor, with a significant unmet need remaining for novel, more efficacious treatments. There are no numerical data yet available from the DUO-E trial, so it remains to be seen how clinically significant the benefit of adding a PARP inhibitor (Lynparza) to immune checkpoint blockade was when compared with placebo.

Tags: Label Expansion (New Indication)

CLR 131 | CLRB | LOA: AVERAGE | [↗](#)

Waldenstrom Macroglobulinemia (WM)

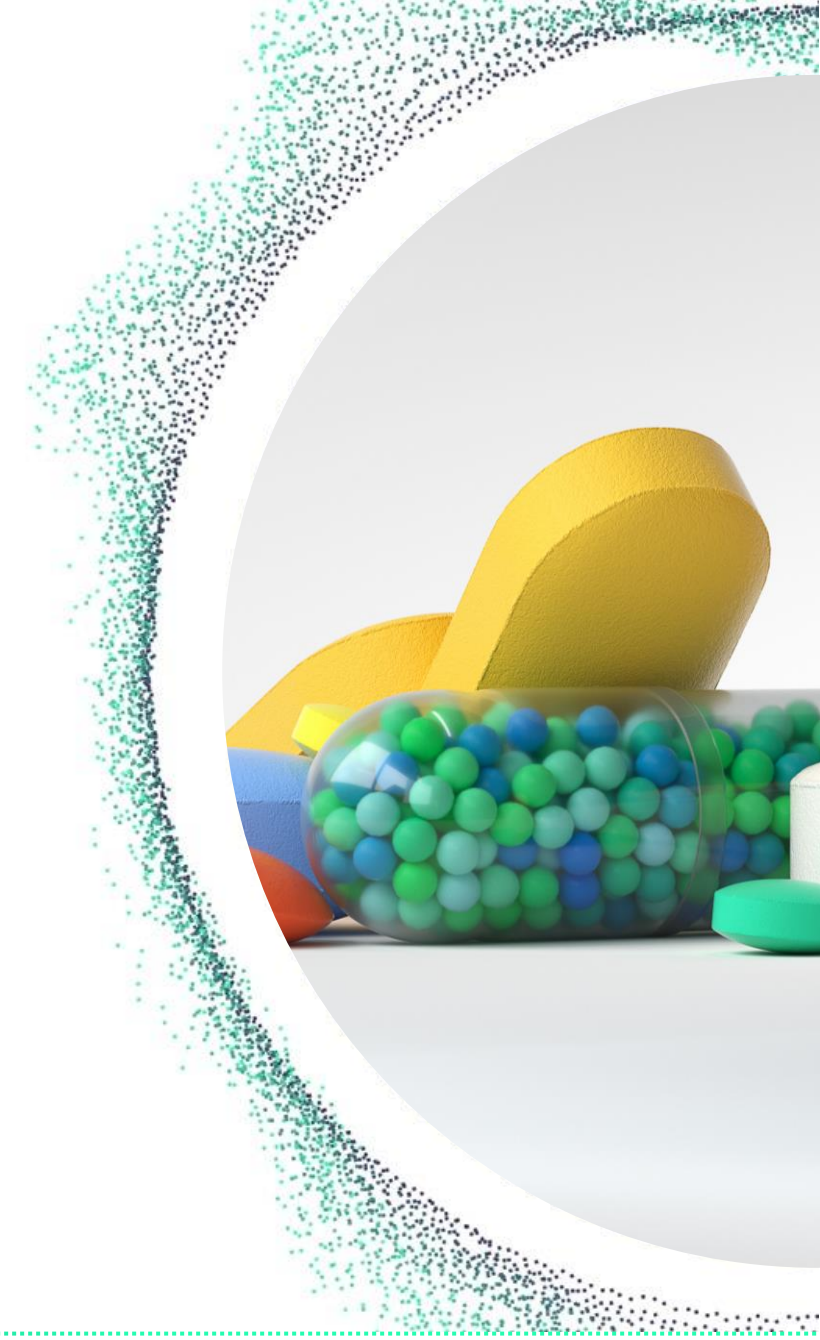
Cellectar Biosciences' CLR 131 (iopofosine I-131) is an iodine-131-containing phospholipid ether (PLE) that enters the cell by incorporating into lipid rafts. Targeting lipid rafts is a novel approach for targeting cancer cells, with the rationale being that compared to normal cells, cancer cells have more lipid rafts and the rafts are larger and more stable (days versus nanoseconds). Furthermore, while normal cells predominately use endogenously produced lipids, cancer cells require exogenous lipids, with lipid rafts representing the primary uptake mechanism.

A Phase IIa study, CLOVER-1, reported a 100% ORR in six third-line WM patients who had failed a BTK inhibitor. There was one complete response (CR) and five partial responses, and the median duration of response was >18 months. CLR 131 also showed activity in late-line multiple myeloma and relapsed/refractory B-cell NHL. In multiple myeloma, CLR 131 reported a 32% ORR in 28 sixth-line or later patients, while in B-cell NHL it reported a 50% ORR and a 25% CR rate in patients with a median of two prior lines of therapy.

A pivotal cohort of CLOVER-1 is enrolling 50 third-line WM patients who failed a BTK inhibitor or had a suboptimal response. The single-arm trial is evaluating a fixed-dose regimen, with patients given CLR 131 on days 1, 15, 57, and 71. Topline data are expected during H2 2023, and if the data are positive, an NDA submission is expected in Q4 2023 or Q1 2024. CLR 131 has fast track designation for WM, so approval could occur in H2 2024.

Tags: First Approval, New Drug Class

Ophthalmology



REPROXALAP | ALDX | LOA: ABOVE AVERAGE | [↗](#)

Dry Eye Disease

Aldeyra's lead product candidate, reproxalap, represents a first-in-class topical reactive aldehyde species (RASP) scavenger, currently in development for dry eye disease (DED) and allergic conjunctivitis. In the Phase III trial for DED, reproxalap was found to be statistically superior to vehicle (the control arm) for the primary endpoints of Schirmer test (a measure of ocular tear production) and ≥ 10 mm Schirmer test responder proportions. The 17% increase in response over vehicle in the ≥ 10 mm responder analysis is a greater response than published for currently available topical therapies for DED, which are typically in the range of 7–10%. The Phase II head-to-head trial demonstrated a significant reduction in patient-reported DED symptoms following reproxalap treatment compared to Novartis's Xiidra, a marketed therapy, as well as significantly lower levels of ocular discomfort, blurry vision, and dysgeusia (taste disturbance).

The clinical package for reproxalap in DED is comprehensive, with Aldeyra submitting an NDA covering symptoms (ocular dryness) and three sign endpoints (ocular redness, Schirmer test, and Schirmer test responder proportions) based on data from five clinical trials. The NDA was accepted by the FDA in February 2023, and a US approval decision is expected in November 2023. If approved, reproxalap has the potential to be the first DED drug with at least two labeled objective signs.

Tags: New Drug Class, Practice Changing

IDOSE-TRAVOPROST | GKOS | LOA: ABOVE AVERAGE | [↗](#)

Glaucoma/Ocular Hypertension

iDose-Travoprost (iDose TR) is a microinvasive intraocular implant designed to continuously deliver therapeutic levels of a proprietary formulation of the active ingredient (travoprost) into the anterior chamber of the eye. If approved, the implant can offer long-lasting eye drop-free therapeutic effects and could significantly improve patient quality of life.

In the two Phase III pivotal trials (GC-010 and GC-012) which enrolled patients with open-angle glaucoma or ocular hypertension, implantation with iDose TR with both fast- and slow-release formulations achieved the prespecified primary endpoint and demonstrated non-inferiority to the active control, a twice-daily 5% topical timolol ophthalmic solution, through three months. Around 93% of patients who received slow-release travoprost with the iDose TR implant had disease that was well controlled on the same or fewer intraocular pressure (IOP)-reducing topicals at one year after a single administration of the implant, compared to only 67% of those who received twice-daily topical timolol. In addition, 81% of patients in the slow-release iDose TR arm were completely free of IOP-reducing topicals at one year.

Since adherence to topical eye drops tends to be low, these data support Glaukos's premise that an implantable drug-device will be a more convenient alternative for glaucoma patients without having to sacrifice efficacy or safety.

Tags: Practice Changing, Potential Blockbuster

LYTENA VA | OTLK | LOA: ABOVE AVERAGE | [↗](#)

Wet Age-Related Macular Degeneration (Wet AMD)

Lytenava is a version of bevacizumab formulated specifically for ophthalmic use in wet AMD. Although Outlook Therapeutics submitted a BLA for Lytenava in March 2022, the FDA requested additional information in order to complete the filing. The company voluntarily withdrew its BLA, and then resubmitted a revised version in late August 2022. If approved, the drug aims to eliminate the safety problems associated with off-label Avastin, while also expanding access to patients in markets where Avastin is not available.

In the NORSE TWO Phase III study, Lytenava demonstrated clinical superiority over Lucentis. In the intent-to-treat (ITT) primary dataset, the percentage of patients who gained at least 15 letters who were treated with Lucentis was 23%, compared to 41.7% in those treated with Lytenava ($p=0.0052$). Improvements in the key secondary endpoint, best corrected visual acuity (BCVA) score change from baseline to month 11 in the primary ITT dataset, were also statistically significant and clinically relevant ($p=0.0043$). A mean change in BCVA of 5.8 letters was observed with Lucentis, while the mean change with Lytenava was 11.2 letters. The safety profile of Lytenava appeared benign, distinguishing it from off-label Avastin. Outlook Therapeutics has stated that the drug will be “responsibly priced” and will reduce the cost of care for patients on anti-VEGF therapy, although it will no doubt be priced higher than off-label Avastin.

Tags: First Approval

SOZINIBERCEPT | OPT | LOA: ABOVE AVERAGE | [↗](#)

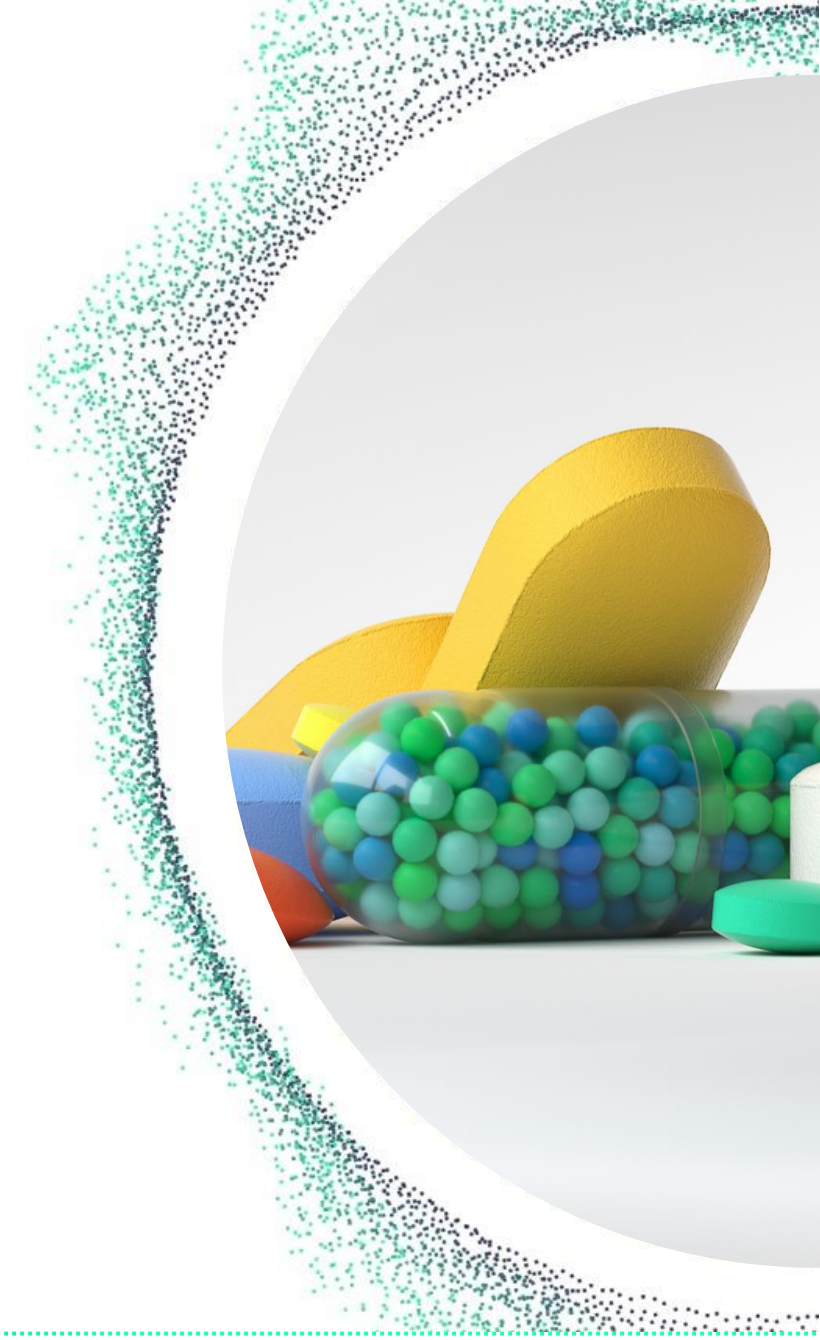
Wet Age-Related Macular Degeneration (Wet AMD)

Opthea's OPT-302 is a soluble form of vascular endothelial growth factor receptor 3 (VEGFR-3) which blocks the activity of both VEGF-C and VEGF-D. The drug is designed to be utilized in combination with Lucentis or Eylea, which inhibit VEGF-A, in order to completely block the VEGF family of proteins. Pivotal Phase III trials testing OPT-302 in combination with Eylea (COAST trial) and Lucentis (ShORe trial) have been initiated, and topline results are expected during the second half of 2023.

Thus far, Phase II data in combination with Lucentis have demonstrated only modest efficacy improvements over Lucentis alone, with a 3.4-letter average improvement and only around 4.5% more patients achieving a >15-letter gain. As a combination, the drug is expected to be priced at a premium, and without providing improvements in dosing schedules, the commercial potential of OPT-302 hinges mainly on its clinical efficacy.

Tags: New Drug Class, First Approval

Psychiatry



KARXT | KRTX | LOA: ABOVE AVERAGE | [↗](#)

Schizophrenia

Karuna Therapeutics' KarXT combines the first-in-class M1/M4-preferring muscarinic receptor agonist xanomeline, which was previously discontinued due to side effects, with a pan-muscarinic receptor antagonist, trospium (approved outside of schizophrenia), which does not cross the blood-brain barrier and enables safe usage. The drug is being primarily developed for the treatment of acute psychosis in adults with schizophrenia. Effect sizes in Phase III trials so far compare well to widely prescribed antipsychotics such as Risperdal, but KarXT's differentiating factors include its rapid onset of action, its strong tolerability profile, and its potential to treat cognitive symptoms. There are currently no approved treatments for cognitive symptoms in schizophrenia, so this is a significant market opportunity.

KarXT's unique mode of action means it does not directly compete with any approved or pipeline therapies and has the potential to become first in class. A

main drawback is its twice-daily administration, which is more inconvenient than available antipsychotics with once-daily or longer dosing schedules. Sumitomo Pharma's investigational drug SEP-363856, dosed once daily, will potentially be its biggest indirect competitor as a first-in-class trace amine-associated receptor 1 (TAAR1) agonist, although the drug recently failed two Phase III trials.

Karuna plans to submit an NDA for KarXT in schizophrenia in the third quarter of 2023, so an FDA approval decision is to be expected in 2024. Data from two Phase III long-term safety and tolerability trials are also expected in 2024. Another Phase III trial, ARISE, will evaluate the safety and efficacy of KarXT as an adjunctive treatment in adults who have an inadequate response to their current antipsychotic therapy, which is likely to be more reflective of how the drug would be used in the real world, if approved.

Tags: New Drug Class, First Approval

SELTOREXANT | JNJ | LOA: ABOVE AVERAGE | [↗](#)

Major Depressive Disorder (MDD)

Seltorexant is a first-in-class antagonist at the hypocretin/orexin 2 receptor, currently under development by Johnson & Johnson for both MDD and insomnia. In one Phase IIb trial for MDD patients with sleep disturbances, a statistically significant reduction in MADRS score was seen at week three but not at week six, suggesting that effects could taper over time. Although seltorexant showed only modest efficacy as an adjunctive treatment in this study – specifically at the lowest dose – the drug’s target population is SSRI/SNRI-inadequate responders, a notoriously challenging group to treat who benefit from access to as much therapeutic diversity as possible.

An additional, smaller Phase IIb study pitted seltorexant against an active comparator, quetiapine. Although overall discontinuation rates were similar, the seltorexant group experienced a greater improvement in MADRS score and a lower treatment-related discontinuation rate than the quetiapine arm after 24 weeks of treatment, quelling worries that effects may not be long-lasting and supporting previous safety and tolerance data. Informed by these two Phase IIb studies, two Phase III studies were launched. One was terminated due to interim analysis data, but the other is still under way with results expected in Q3 or Q4 2023.

Assuming results from the in-progress Phase III study are generally consistent with prior trials, Johnson & Johnson is likely to submit an NDA before the end of 2023, with the intention of a 2024 launch.

Tags: New Drug Class, First Approval

CAPLYTA | ITCI | LOA: ABOVE AVERAGE | [↗](#)

Major Depressive Disorder (MDD)

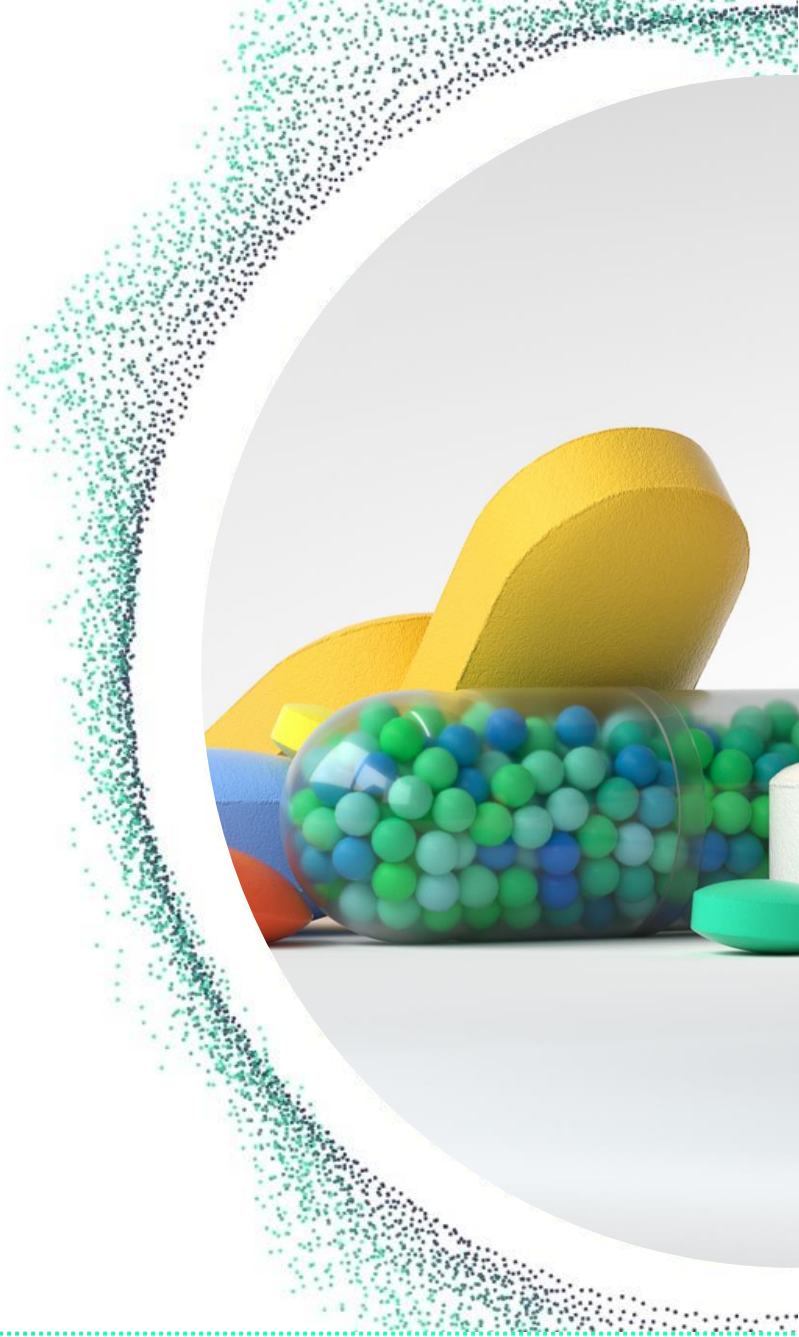
Caplyta was first approved for schizophrenia in December 2019, and the label was expanded to include bipolar disorder, specifically bipolar depression, two years later in December 2021. There is a long history of using antipsychotics to treat MDD, and, like other atypical antipsychotics, Caplyta modulates both serotonin and other monoamines, particularly dopamine, although the exact mechanism of action is unknown. Intra-Cellular Therapies' decision to pursue a further label expansion into MDD will give this drug a wide patient population, although it will likely be relegated to refractory patients.

In the Phase III Study 403 trial, Caplyta was explored as a monotherapy in MDD with mixed features, as well as bipolar I and II. For the combined patient population, Caplyta demonstrated a statistically significant reduction of 5.7 points on the MADRS total score compared to placebo at week six ($p < 0.0001$), and an even higher 5.9-point reduction over placebo in the MDD subpopulation. These results are unsurprising given the drug's prior success and ultimate approval in bipolar depression, but are notable nonetheless.

Four other Phase III trials for Caplyta in MDD are ongoing, two of which are set to finish before the end of 2023. Interestingly, however, despite the drug's success as a monotherapy in MDD, all four trials are assessing Caplyta as an adjunctive treatment. Intra-Cellular has indicated that it plans to file an sNDA in 2024, and, assuming it is submitted early in the year, the drug may gain approval and be able to launch in MDD before the end of 2024.

Tags: Label Expansion (New Indication)

Respiratory



ENSIFENTRINE | VRNA | LOA: ABOVE AVERAGE | [↗](#)

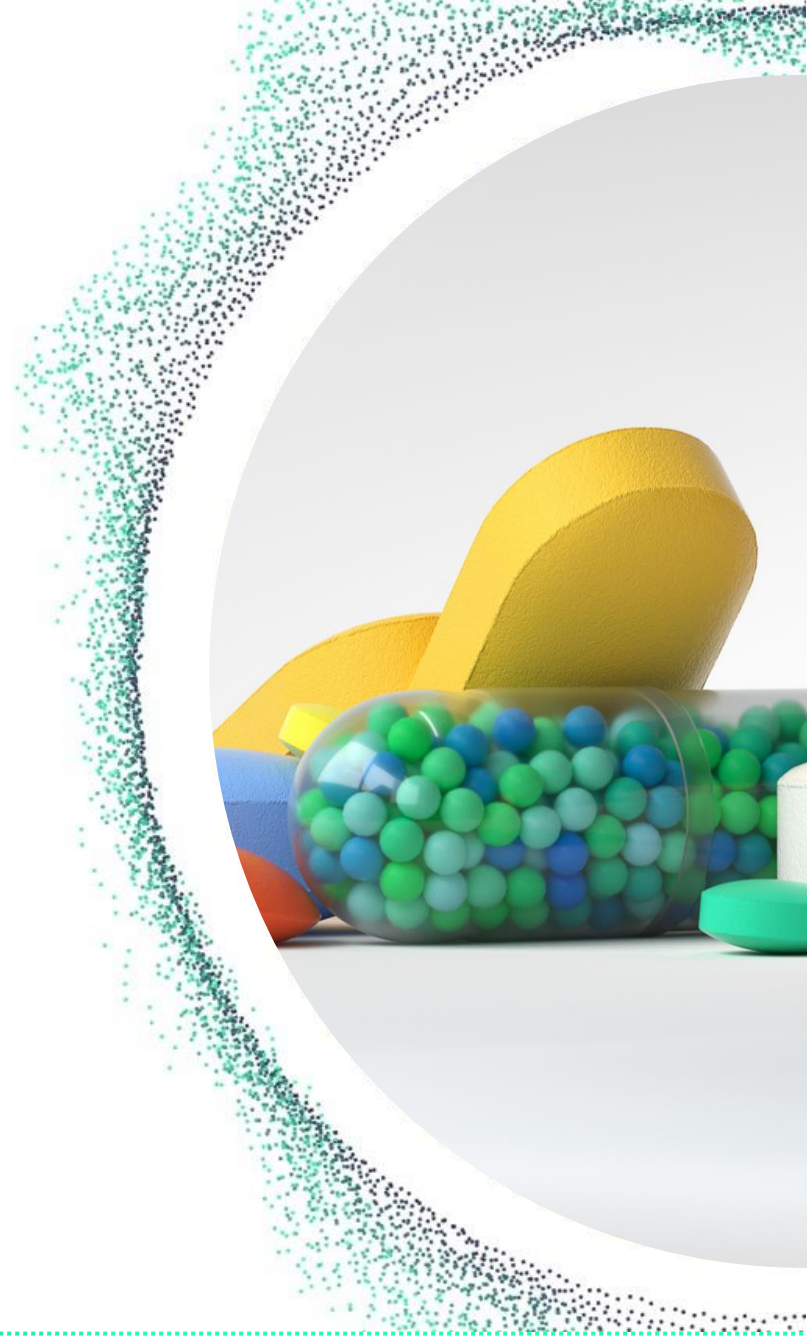
Chronic Obstructive Pulmonary Disease (COPD)

Ensifentrine (RPL 554) is a dual inhibitor of PDE3 and PDE4, and is the only inhaled formulation in this class in the COPD treatment landscape as compared to competitors that are available as oral tablets. Ensifentrine's nebulized formulation will help circumvent GI side effects seen with Daliresp, while the bifunctional PDE3 and PDE4 inhibition may provide both bronchodilatory and anti-inflammatory effects. Although nebulization is less convenient than tablets or inhalers, this method of administration ensures that COPD patients receive the correct medication dosage without much inhalation skill. The prospect of a novel therapy to combat COPD would understandably excite pulmonologists, particularly in the treatment of more severe patients who are refractory to dual or triple therapies.

Verona Pharma's ensifentrine met the primary endpoint in both of its Phase III trials, ENHANCE-1 and ENHANCE-2, with the week 12 placebo-corrected change from baseline in FEV1 area under the curve 0–12 hours post dose (FEV1 AUC 0–12) at 87mL and 94mL in moderate-to-severe disease where 69% and 55% patients were taking a concomitant LAMA or LABA, respectively. The increased peak FEV1 at a consistent magnitude on Day 1, Week 6, Week 12, and Week 24 suggested ensifentrine's durability. Ensifentrine treatment further reduced the rate of moderate/severe exacerbation and postponed the time to first exacerbation significantly compared to placebo treatment. Together with a clean safety profile, this drug may be useful as both a monotherapy and an add-on treatment.

Tags: New Drug Class, Potential Blockbuster

Appendix



Appendix

Drugs covered (listed alphabetically):

AFAMI-CEL | ADAP | [↗](#)
ANTIBKV | MEMO THERAPEUTICS | [↗](#)
APROCITENTAN | JNJ | [↗](#)
AT-007 | APLT | [↗](#)
AXATILIMAB | SNDX | [↗](#)
BEYFORTUS | AZN | [↗](#)
BIMZELX | UCB | [↗](#)
BRAFTOVI | PFE | [↗](#)
CAPIVASERTIB | AZN | [↗](#)
CAPLYTA | ITCI | [↗](#)
CLR-131 | CLRB | [↗](#)
COSENTYX | NVS | [↗](#)
CRINECERFONT | NBIX | [↗](#)
CTP-543 | SUNP | [↗](#)
DAY101 | DAWN | [↗](#)
ENHERTU | DAIICHI SANKYO | [↗](#)
ENSIFENTRINE | VRNA | [↗](#)
ETRASIMOD | PFE | [↗](#)
ETRIPAMIL | MIST | [↗](#)
FITUSIRAN | SNY | [↗](#)
FRUQUINTINIB | TAK | [↗](#)
GEPOTIDACIN | GSK | [↗](#)
GSK3536819A | GSK | [↗](#)

HYQVIA | TAK | [↗](#)
IB1001 | INTRABIO | [↗](#)
IDOSE-TRAVOPROST | GKOS | [↗](#)
IMETELSTAT | GERN | [↗](#)
IMFINZI | AZN | [↗](#)
IOMAB-B | ATNM | [↗](#)
IPTACOPAN | NVS | [↗](#)
KARXT | KRTX | [↗](#)
KISQALI | NVS | [↗](#)
KLISYRI | ALM | [↗](#)
KRAZATI | MRTX | [↗](#)
LIVMARLI | MIRM | [↗](#)
LN-144 | IOVA | [↗](#)
LUMAKRAS | AMGN | [↗](#)
LYNPARZA | AZN | [↗](#)
LYTENAVA | OTLK | [↗](#)
MOUNJARO | LLY | [↗](#)
MRNA-1345 | MRNA | [↗](#)
NEMOLIZUMAB | GALDERMA | [↗](#)
OTL-200 | ORTX | [↗](#)
PF-06886992 | PFE | [↗](#)

PLUVICTO | NVS | [↗](#)
REPROXALAP | ALDX | [↗](#)
RESMETIROM | MDGL | [↗](#)
SAR408701 | SNY | [↗](#)
SB-206 | NOVN | [↗](#)
SELADELPAR | CBAY | [↗](#)
SELTOREXANT | JNJ | [↗](#)
SERPLULIMAB | HENLIUS | [↗](#)
SOTATERCEPT | MRK | [↗](#)
SOZINIBERCEPT | OPT | [↗](#)
TAK-755 | TAK | [↗](#)
TAKECAB | PHAT | [↗](#)
TISLELIZUMAB | BGNE | [↗](#)
TORIPALIMAB | CHRS | [↗](#)
UPROLOSELAN | GLYC | [↗](#)
VTAMA | DERMAVANT | [↗](#)
XPOVIO | KPTI | [↗](#)
ZANIDATAMAB | JAZZ | [↗](#)
ZELTHERVA | SLS | [↗](#)
ZOLBETUXIMAB | ASTELLAS | [↗](#)
ZORYVE | ARQT | [↗](#)

Biomedtracker is an independent research service that offers proprietary clinical assessments of developmental drugs within a comprehensive and intuitive drug information database. Clients from the pharmaceutical, biotech, and investment industries rely on Biomedtracker for its insight on the likelihood of approval, commercial potential, and future data and regulatory catalysts for drugs within the competitive landscape of every important disease and indication. Over recent years, Biomedtracker has become the leader in providing objective information alongside evidence-based clinical assessments and investment research on pipeline drugs worldwide.

DATAMONITOR HEALTHCARE

CITELINE COMMERCIAL

Datamonitor Healthcare provides a total business information solution to the pharmaceutical and healthcare industries. Datamonitor Healthcare provides expertise in therapeutic, strategic, and company market analysis, and competitive intelligence to the global pharmaceutical and healthcare markets, enabling them to ultimately make valuable and profitable decisions.

Copyright © 2023 Pharma Intelligence UK Limited (Citeline), a Norstella company

This report is published by Citeline (the Publisher). This report contains information from reputable sources and although reasonable efforts have been made to publish accurate information, you assume sole responsibility for the selection, suitability and use of this report and acknowledge that the Publisher makes no warranties (either express or implied) as to, nor accepts liability for, the accuracy or fitness for a particular purpose of the information or advice contained herein. The Publisher wishes to make it clear that any views or opinions expressed in this report by individual authors or contributors are their personal views and opinions and do not necessarily reflect the views/opinions of the Publisher