Drugs to Watch 2024 revisited

Where are they now?

Clarivate

Drugs to Watch: Where are they now?

Aflibercept

EYLEA® HD

What is the current status of this drug?

EYLEA HD has now established itself as a pivotal therapy for treating wet age-related macular degeneration (AMD), diabetic macular edema (DME), and diabetic retinopathy (DR). Available across all G7 countries, EYLEA HD achieved a significant milestone, with net product sales in the United States reaching $1.2 billion for the full year 2024, cementing its blockbuster status. This high-dose formulation of aflibercept (8 mg) has shown efficacy in extending dosing intervals, thereby reducing patients' treatment burden. Its ability to maintain visual and anatomic improvements with fewer injections has made it a preferred choice in the major markets. Additionally, recent phase 3 data have shown promising results for macular edema secondary to retinal vein occlusion (RVO), strengthening its position as a leading therapy for retinal diseases.

What happened to the drug in 2024 / early 2025?

The period spanning 2024 and early 2025 was marked by several notable events for EYLEA HD. In early 2024, the drug received regulatory approval in the E.U., the U.K. and Japan for the treatment of wet AMD and DME, significantly expanding its market reach. In September 2024, the European Commission approved the pre-filled syringe version, offering a more convenient, safer, and faster treatment option compared with the vial formulation. In December 2024, the phase 3 QUASAR trial yielded positive results, demonstrating that EYLEA HD (dosed Q8W, or every eight weeks) was noninferior in visual gains to Eylea (dosed Q4W) for treating macular edema secondary to RVO, highlighting its clinical efficacy in retinal disorders. Additionally, three-year data from the PULSAR and PHOTON trials in wet AMD and DME, respectively, showed sustained visual gains and anatomic improvements with extended dosing intervals.

Has this met your expectations?

EYLEA HD has met Clarivate's sales expectations in the United States, becoming a blockbuster as soon as 2024, and reinforcing its position as a leading treatment option for wet AMD, DME, and DR. Despite facing fierce competition from Roche's VABYSMO and from the original formulation of Eylea throughout 2024, EYLEA HD gained traction in the ophthalmology space. This success is largely attributed to physicians' positive experience with aflibercept and its capacity to prolong dosing intervals and offer stronger retinal drying compared with other available drugs. These advantages have been key factors in helping the drug achieve strong sales performance and widespread adoption among patients and healthcare providers.

Why did it succeed or fail to meet expectations?

EYLEA HD experienced rapid uptake upon its launch in the United States, with substantial quarter-over-quarter increases in net sales. However, Regeneron reported lower-than-expected sales for EYLEA HD during Q4 2024. Clarivate's primary market research in the United States suggests that these headwinds are due to reimbursement issues related to EYLEA HD's narrower label compared with VABYSMO, which allows Q4W (every four weeks) dosing intervals, and to the absence of a pre-filled syringe formulation in this market. Nonetheless, the anticipated label expansion to include Q4W dosing, along with the potential approval of the pre-filled syringe during 2025 will likely revert this sales trend in the coming year.

What other milestones or challenges does the drug face in meeting the forecast?

Looking ahead, EYLEA HD has several important milestones and challenges to navigate. Regulatory approval for a pre-filled syringe version in the United States and supplemental biologics license applications (sBLAs) for the Q4W dosing interval in wet AMD, DME, and DR are pending and, if approved, will give prescribers even more flexibility in the use of EYLEA HD, which may encourage more switching from the original version of EYLEA to EYLEA HD. In addition, Regeneron has submitted an sBLA for the treatment of macular edema secondary to RVO, whose review of which is expected in 2025. However, the drug continues to face competition from other IVT treatments, particularly from Eylea and Vabysmo, which may negatively impact its uptake. In addition, EYLEA HD must continue to demonstrate its value proposition to payers and healthcare providers to sustain its market position before promising emerging agents, such as one-time gene therapies including AbbVie / Regenxbio's ABBV-RGX-314, enter the space.

Drugs to Watch: Where are they now?

Budesonide delayed release

TARPEYO® | Kinpeygo®

What is the current status of this drug?

Budesonide delayed release is launched in the United States, E.U., China and Singapore. Developed by Calliditas Therapeutics, budesonide delayed release received full approval in the United States in 2023 as TARPEYO. In 2024, Asahi Kasei acquired Calliditas Therapeutics, making it a wholly owned subsidiary and expanding Asahi Kasei's presence in the global renal market.

Stada Arzneimittel AG is responsible for marketing budesonide delayed release in the European Union and United Kingdom and has since received full marketing authorization in July 2024 as Kinpeygo.

Budesonide delayed release has also received approval in Taiwan, Hong Kong, and South Korea and is commercialized in those markets by Everest Medicines.

Viatris is developing budesonide delayed release in Japan, where it is currently in Phase 3 clinical trials.

What happened to the drug in 2024 / early 2025?

TARPEYO sales reported by Calliditas Therapeutics were SEK 771.6 million (US $76.5 million) in the United States for the period January to June 2024. Asahi Kasei reported TARPEYO sales of $54 million in the U.S. for Q3 2024 (for the period October to December 2024). The U.S. FDA granted TARPEYO Orphan Drug exclusivity, expiring in December 2030 following the drug's full approval in December 2023.

Stada reported that Kinpeygo contributed 0.7% to its total revenues of EUR 4.059 billion in 2024.

TARPEYO's growth was driven by patient transitions from older corticosteroid therapies and its inclusion in the draft 2024 KDIGO guidelines for patients at risk of progressive kidney function loss. Additionally, sales were boosted by the full marketing authorization of Kinpeygo in Europe for treating adults with primary IgAN.

Has this met your expectations?

Our earlier projections estimated sales of $0.74 billion by 2029. However, our revised forecast is now lower at $0.48 billion by 2029. This adjustment aligns our estimates with the indicated population for TARPEYO / Kinpeygo use, specifically adults with primary IgAN who are at risk for disease progression. Based on our revised estimates, TARPEYO / Kinpeygo performance has been in line with our expectations.

Why did it succeed or fail to meet expectations?

TARPEYO / Kinpeygo specifically targets the mucosal B cells in the Peyer's patches, which are cells that are responsible for producing Gd-IgA1 complexes. By targeting these cells, TARPEYO / Kinpeygo slows the decline in kidney function, thereby acting as a disease modifying therapy. Unlike other systemic steroids, TARPEYO / Kinpeygo is minimally absorbed, leading to fewer side effects even with prolonged use. This advantage is prompting high-risk patients to switch from traditional corticosteroid treatments.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

TARPEYO / Kinpeygo faces several challenges as it aims to meet its forecast:

- The high price of TARPEYO / Kinpeygo compared to traditional corticosteroid therapies.
- Competition from a growing market of nonsteroidal disease-modifying agents, such as Novartis's FABHALTA (iptacopan, approved in the United States in August 2024), Travere Therapeutics' FILSPARI (sparsentan, approved in the United States in February 2023), Novartis's atrasentan (VANRAFIA) and zigakibart, Vera Therapeutics' atacicept, and Otsuka's sibeprenlimab. Long-term patient stability on these novel nonsteroidal therapies may reduce the need for acute treatment with corticosteroid therapies like TARPEYO / Kinpeygo.

Drugs to Watch: Where are they now?

Datopotamab deruxtecan

Dato-DXd | DATROWAY®

What is the current status of DATROWAY?

DATROWAY was granted FDA approval in January for the later-line treatment of metastatic HR-positive / HER2- negative breast cancer patients, based on the Phase 3 TROPION-Breast01. The antibody drug conjugate (ADC) is now:

- Launched in the United States
- Approved in Japan (launch is pending price listing and is expected in 2025)
- Approved in the European Union

What happened to the drug in 2024 / early 2025?

- September 2024: DATROWAY failed to improve OS versus chemotherapy in the Phase 3 TROPION-Breast01 trial: OS: 18.6 vs. 18.3 months (HR: 1.01, P not significant).
- December 2024: DATROWAY is approved in Japan for the treatment of adult patients with HR-positive / HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) unresectable or recurrent breast cancer after prior chemotherapy. DATROWAY is the first TROP-2 directed therapy to be approved in Japan for HR-positive / HER2-negative breast cancer.
- January 2025: DATROWAY is approved in the United States for the treatment of adults with unresectable or metastatic HR-positive / HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease (data from TROPION-Breast01).
- January 2025: DATROWAY was recommended for approval by the EMA's CHMP for the treatment of adult patients with unresectable or metastatic HR-positive / HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received endocrine therapy and at least one line of chemotherapy in the advanced setting.
- April 2025: DATROWAY was granted approval by the EC following a position opinion from the EMA's CHMP.

Has this met your expectations?

The recent E.U. approval was in line with our forecasts. However, physician uptake could be negatively impacted by the lack of demonstrated OS benefit and bears watching.

The antibody drug conjugate (ADC) is now launched in the United States, approved in Japan and approved in the European Union.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

Challenges:

- The failure of the TROPION-Breast01 trial to improve OS—a dual primary endpoint—might compromise the adoption of this agent. Notably, TRODELVY showed an OS advantage in the Phase 3 TROPICS-02 (14.5 months vs. 11.2 months [HR: 0.79]) versus physician's choice of treatment in second-line+ HR-positive / HER2-negative disease, and ENHURTU demonstrated an OS improvement in the HR-positive HER-low subgroup in DESTINY-Breast04 (OS: 23.9 months vs. 17.5 months [HR: 0.64]).

- The first-to-market TROP2-targeted agent TRODELVY is available across the G7 for second-line or later HR-positive / HER2-negative metastatic breast cancer, and a third TROP2-targeted agent (sacituzumab tirumotecan) is expected to enter this market in 2028, intensifying competition within the TROP2 class of ADCs in this segment.

- Questions remain regarding the optimal therapy sequence. ENHURTU is becoming the standard of care in second-line metastatic HR-positive breast cancer (we expect the preferential use of ENHURTU across the G7 in the second-line HR-positive / HER2-negative setting) and is anticipated to gain a first-line label expansion in 2026. There is a need for robust data to establish ADC efficacy following prior treatment with an ADC and to determine whether all patients would benefit from an ADC-based sequencing strategy. Despite ENHURTU's use in HR-positive / HER2-low patients, a TROP2 ADC could still potentially be used in sequence because it is not yet clear if there would be any cross-resistance based on the payload (deruxtecan).

- Over the forecast period, label expansions for DATROWAY, either as monotherapy or in combination with IMFINZI, are expected in various triple-negative breast cancer populations, including in the early-stage and first-line metastatic settings:

  - We expect the approval of DATROWAY for the treatment of first-line metastatic triple-negative breast cancer patients ineligible for a PD-1/PD-L1 inhibitor, based on the Phase 3 TROPION-Breast02 trial.

  - We expect approval of DATROWAY plus IMFINZI in all the major-markets in previously untreated metastatic triple-negative breast cancer patients whose tumors express PD-L1 (CPS ≥ 10), based on the TROPION-Breast05 trial.

  - We anticipate approval of DATROWAY plus IMFINZI in the major markets for early-stage triple-negative breast cancer patients who do not achieve a pCR, based on the TROPION-Breast03 trial.

- Based in preliminary data, we do not expect that neoadjuvant DATROWAY plus IMFINZI will show superior pCR rates compared with chemotherapy plus KEYTRUDA in the Phase 3 TROPION-Breast04 trial; thus, we do not anticipate the approval of this regimen in patients with early-stage (II-III) triple-negative breast cancer or HR-low / HER2-negative disease.

- Given that all three TROP2-targeting agents—DATROWAY, TRODELVY and sacituzumab tirumotecan—will compete across various triple-negative and HR-positive / HER2-negative breast cancer populations, the intense competition between these agents in key treatable populations limits the potential of individual therapies.

Sales forecasts:

- Almost $2.5 billion of sales in 2033 in the major markets for breast cancer.

What is the current status of NSCLC?

- It is under regulatory review in the U.S., but for a different sub-indication than previously.
- The regulatory filing was withdrawn in the E.U., so the drug is back to being in phase 3 as its highest development status in Europe.

What happened to the drug in 2024 / early 2025?

- February 2024: the FDA accepted for review a filing for previously treated advanced nonsquamous NSCLC, based on TROPION-Lung01.
- March 2024: the EMA validated a European filing for the same indication.
- September 2024: Data showed that the dual primary endpoint of OS had not been met in the overall population of TROPION-Lung01 but had shown a trend toward improvement in nonsquamous patients.
- November 2024: based on FDA feedback, AstraZeneca and Daiichi withdrew the TROPION-Lung01 BLA filing, and submitted instead a BLA filing seeking accelerated approval for *EGFR*-mutated metastatic NSCLC after prior systemic therapies including an *EGFR*-directed agent, based on the Phase 2 TROPION-Lung05 trial.
- December 2024: based on CHMP feedback, AstraZeneca and Daiichi withdrew the European TROPION-Lung01 filing; no alternative filing submission was reported.
- January 2025: the FDA accepted the TROPION-Lung05 BLA for priority review with a PDUFA date of July 12, 2025.

Why did it succeed or fail to meet expectations?

Given the evolving data from TROPION-Lung01, the withdrawal of those filings comes as no surprise.

Based on encouraging pooled efficacy data from previously treated *EGFR*-mutated patients treated in TROPION-Lung05 and TROPION-Lung01, we cautiously forecast that the BLA filing based on these data will secure accelerated approval of datopotamab deruxtecan in the United States for metastatic *EGFR*-mutated NSCLC previously treated with an *EGFR*-targeted agent and platinum chemotherapy.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

Gaining approval based on the AVANZAR trial in the first-line setting, which is a much larger patient population compared with the later-line settings and therefore a larger market opportunity, will be crucial for this drug.

In the later-line *EGFR*-mutated setting, we cautiously forecast that the Phase 3 TROPION-Lung15 trial in *EGFR*-mutated advanced nonsquamous NSCLC progressing on TAGRISSO, will act as the confirmatory trial in the United States, and will secure approval of DATROWAY in this setting in the E.U. and Japan. Success in this trial therefore is crucial for DATROWAY's use in the late-line settings.

Drugs to Watch: Where are they now?

Efanesoctocog alfa

ALTUVIIIO™ | ALTUVOCT

What is the current status of this drug?

Efanesoctacog alfa was approved in the United States in February 2023 and is marketed there as ALTUVIIIO. It was approved in the E.U. in June, 2024 and is marketed there as ALTUVOCT. ALTUVIIIO / ALTUVOCT has been launched in the United States, Germany, and Switzerland. It has also received approval in Japan, Macau, Taiwan, and Hong Kong, and is now commercially available in Japan and Taiwan.

Sanofi and Sobi collaborate on developing and commercializing ALTUVIIIO / ALTUVOCT for hemophilia A. Sanofi holds the rights in North America and all other regions, excluding Sobi's territory, which includes Europe, Russia, the Middle East, and some North African markets.

What happened to the drug in 2024 / early 2025?

Sanofi reported that ALTUVIIIO'S 2024 sales reached $743 million (€682 million), with 90% of the revenue coming from the United States. Meanwhile, Sobi reported $43.4 million (SEK 436 million) in revenue from ALTUVOCT in its commercialized regions, including Germany and Switzerland, bringing the total 2024 revenue for ALTUVIIIO / ALTUVOCT to $786 million. ALTUVIIIO / ALTUVOCT experienced significant growth in 2024, driven by patients transitioning from older FVIII therapies and, from non-factor treatments like HEMLIBRA. This growth highlights the therapy's strong market.

Has this met your expectations?

The drug outperformed our expectations.

Earlier projections estimated **$1.77 billion** in sales by 2029, but given its strong start in **FY 2024,** we now anticipate sales reaching **$1.85 billion** by 2029.

Why did it succeed or fail to meet expectations?

ALTUVIIIO / ALTUVOCT offers the advantage of once-weekly dosing, significantly reducing the treatment burden compared to therapies that require multiple doses per week. This convenience is a key factor driving patients to switch from other FVIII treatments to ALTUVIIIO. Additionally, some patients prefer to stay on FVIII therapy rather than transition to Hemlibra, making ALTUVIIIO an appealing option. For patients who experience breakthrough bleeds while on Hemlibra, switching back to FVIII therapy, such as ALTUVIIIO, provides a viable alternative. This flexibility in treatment options helps cater to individual patient needs and preferences, enhancing overall treatment satisfaction and adherence.

What other milestones or challenges does the drug face in meeting the forecast?

ALTUVIIIO / ALTUVOCT faces the following challenges as it aims to build toward its forecast:

- Challenges with intravenous administration, especially in pediatric population: Intravenous administration in children is challenging due to the complexity of the process, risks of complications, difficulty in finding veins, and the need for central venous access devices. Additionally, young children often struggle with compliance, making the procedure stressful and potentially traumatic for both the child and their caregivers. Skilled healthcare professionals and supportive care are essential to address these challenges.

- Competition from upcoming non-factor therapies: Non-factor therapies like Pfizer's HYMPAVZI (marstacimab; approved by the U.S. FDA in Oct 2024) and Sanofi's fitusiran (PDUFA March 28, 2025) present significant advantages over factor replacement therapies like ALTUVIIIO / ALTUVOCT. They offer less frequent dosing schedules, subcutaneous administration, and potentially lower immunogenicity, making them attractive alternatives for patients and healthcare providers. As these therapies continue to advance and gain regulatory approvals, they are likely to reshape the treatment landscape for hemophilia A, posing a substantial challenge to ALTUVIIIO / ALTUVOCT.

ALTUVIIIO / ALTUVOCT offers the advantage of once-weekly dosing, significantly reducing the treatment burden compared to therapies that require multiple doses per week.

Drugs to Watch: Where are they now?

Ensifentrine

RPL554 | OHTUVAYRE™

What is the current status of this drug?

Ensifentrine was approved for the treatment of COPD by the FDA in June 2024 under the brand name OHTUVAYRE. The manufacturer, Verona, is in the process of filing for regulatory approval in Europe. There do not seem to be any imminent plans to file for regulatory approval in Japan.[1]

What happened to the drug in 2024 / early 2025?

OHTUVAYRE has experienced better-than-expected uptake since its launch in late 2024, despite its high cost. The company reported that the drug is being prescribed to a broad range of COPD patients, including those on background single, dual or triple therapy.

Has this met your expectations?

The initial uptake has exceeded expectations.

Why did it succeed or fail to meet expectations?

Given the high cost of the drug and its dosing (twice daily, nebulized formulation), we were concerned that physicians and patients would show some reluctance in using the agent; however, initial data indicate that the drug is addressing an unmet need for a more efficacious agent in the COPD space.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

OHTUVAYRE coverage by insurance companies on a preferred tier would greatly boost its uptake.

OHTUVAYRE has experienced better-than-expected uptake since its launch in late 2024, despite its high cost.

[1] https://www.veronapharma.com/news/verona-pharma-reports-fourth-quarter-and-full-year-2024-financial-results-and-provides-corporate-update/

Drugs to Watch: Where are they now?

Exagamglogene autotemcel and lovotibeglogene autotemcel

Exa-cel | CASGEVY™ and Lovo-cel | LYFGENIA™

What is the current status of this drug?

Exagamglogene autotemcel, branded as CASGEVY, is approved for treating patients aged 12 and older with sickle cell disease (SCD) experiencing recurrent vaso-occlusive crises (VOCs) and for transfusion-dependent beta-thalassemia (TDT).

CASGEVY received its first approval in November 2023 from the U.K.'s Medicines and Healthcare Products Regulatory Agency for the treatment of SCD and TDT. The United States FDA approved CASGEVY for SCD in December 2023, followed by approval for TDT in January 2024. In February 2024, the EC granted approval for both SCD and TDT. CASGEVY has also received approval in Saudi Arabia, Bahrain, the UAE, Canada, and Switzerland.

CRISPR Therapeutics and Vertex Pharmaceuticals collaborated on developing and commercializing CASGEVY for SCD and TDT.

What happened to the drug in 2024 / early 2025?

The period spanning 2024 and early 2025 was marked by several notable events for CASGEVY.

Vertex reported that CASGEVY's sales in 2024 amounted to $10 million. The first commercial patient was infused with CASGEVY in Q3 2024. To date, over 50 patients have initiated cell collection across approved geographies (the U.S., E.U., and the Middle East). Additionally, Vertex has activated more than 50 authorized treatment centers across approved geographies.

CASGEVY has made significant global progress in terms of reimbursement:

- In the United States, Vertex has confirmed reimbursement pathways in all 25 high prevalence SCD states. Additionally, Vertex has reached an agreement with the U.S. Centers for Medicare & Medicaid Services (CMS) to participate in its cell and gene therapy access model (CGT), which aims to provide enhanced Medicaid access for eligible patients and facilitate outcomes-based payment arrangements with cell and gene therapy manufacturers.

- In the United Kingdom, Vertex has secured access for both TDT and SCD.

- In the E.U., Vertex has obtained reimbursement for individuals with SCD or TDT in Luxembourg, established hospital-based reimbursement in Austria, and received approval from the Italian Medicines Agency for early access on a case-by-case basis for treating TDT or SCD.

- In the Middle East, Vertex has achieved hospital-based reimbursement for SCD or TDT in Saudi Arabia and national reimbursement for eligible patients in Bahrain.

Positive long-term data presented at ASH and EHA 2024 further demonstrated the durability of CASGEVY's transformative benefits. Its safety profile remains consistent with that of busulfan conditioning and autologous HSCT.

Has this met your expectations?

The drug has underperformed relative to our expectations.

Why did it succeed or fail to meet expectations?

The adoption of CASGEVY during its first year on the market has been slower than anticipated due to a lengthy and time-intensive treatment process, slow center activation, and reimbursement issues.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

Looking ahead, CASGEVY is expected to witness several milestones and challenges as it builds its forecast:

- Two global phase 3 clinical trials are evaluating CASGEVY in children aged 5 to 11 with severe SCD and TDT. Patient enrollment for these trials is complete, with dosing expected to finish in 2025. If the trials are successful and the therapy receives expanded approval for this younger age cohort, this outcome would expand the eligible patient population. Vertex is also working on advancing preclinical assets for myeloablative conditioning agents with milder side effects, which could further broaden the eligible patient population.

- CASGEVY will face competition from bluebird bio's gene therapy, LYFGENIA (lovotibeglogene autotemcel [lovo-cel]), which approved for adults and adolescents with SCD and a history of vaso-occlusive events. However, bluebird bio's financial challenges and its focus on the U.S. market only are likely to limit LYFGENIA's impact on CASGEVY's market adoption.

What is the current status of this drug?

Lovotibeglogene autotemcel, branded as LYFGENIA, was approved by the FDA for the treatment of sickle cell disease (SCD) in patients aged 12 years and older with a history of vaso-occlusive events (VOEs). It is only approved and commercialized in the United States.

What happened to the drug in 2024 / early 2025?

Bluebird bio reported LYFGENIA sales of $11.6 million for 2024 and the first cell collection was completed for a total of 21 patients. As of March 2025, 11 patients have received their infusion of LYFGENIA. Additionally, the company has scaled to more than 70 qualified treatment centers (QTCs) for the administration of LYFGENIA and the company's beta thalassemia gene therapy ZYNTEGLO (betibeglogene autotemcel).

Positive long-term data presented at ASH 2024 demonstrate that patients with SCD and a history of silent stroke showed no stroke recurrence through nine years of follow up.

Bluebird bio has signed outcomes-based agreements for LYFGENIA with multiple national payer organizations. The company has also reached an agreement with the CMS to offer an outcomes-based agreement for LYFGENIA under the Cell and Gene Therapy (CGT) access model.

In February 2025, bluebird bio entered into a definitive agreement to be acquired by private equity firms Carlyle and SK Capital Partners, with the transaction expected to provide bluebird bio with the necessary capital to scale its gene therapy operations. Subsequently, in March 2025, bluebird bio received an unsolicited non-binding written acquisition proposal from Ayrmid. As of this writing, the Board of Directors is reviewing this offer.

Has this met your expectations?

The drug has underperformed relative to our expectations.

Why did it succeed or fail to meet expectations?

LYFGENIA has experienced slow uptake primarily due to its complex and lengthy treatment process and reimbursement issues, including challenges in securing prior authorization. However, 2024 sales and the number of SCD patients undergoing cell collection since approval indicate that LYFGENIA is keeping pace with CASGEVY in terms of adoption, despite the latter's higher pricing.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

LYFGENIA must continue to demonstrate its safety to maintain its market position, especially given its boxed warning for the risk of hematologic malignancy. Ongoing long-term follow-up studies to monitor safety and efficacy are expected to further establish its effectiveness, durability, and safety. Additionally, LYFGENIA is being evaluated in a phase 3 study for SCD patients aged 2 to12. If trial results are positive and the therapy is approved for this age group, this would expand its eligible patient pool to include the younger pediatric population.

LYFGENIA will face competition from other gene therapies for SCD, particularly CASGEVY, which may negatively impact its uptake.

Drugs to Watch: Where are they now?

Mirikizumab

LY-3074828 | Omvoh™

What is the current status of this drug?

Mirikizumab (Omvoh) was approved for ulcerative colitis (UC) in October 2023 and launched in key markets, including the U.S. and Europe. The drug was also recently approved for Crohn's disease (CD) in January 2025. Omvoh has performed well, with company reported sales of $132 million in 2024, reflecting strong commercial performance.

What happened to the drug in 2024 / early 2025?

Mirikizumab has faced (and will continue to face) tough competition in the UC market from both established therapies and newly approved IL-23 inhibitors. The FDA approved SKYRIZI (risankizumab) for UC in June 2024, followed by TREMFYA (guselkumab) in September 2024. The introduction of these well-established IL-23 inhibitors is expected to create fierce competition, as both drugs are already recognized in other inflammatory conditions and have strong physician prescribing familiarity.[2]

Has this met your expectations?

Yes, mirikizumab has met our expectations for 2024, demonstrating strong clinical efficacy and establishing itself in the inflammatory bowel disease (IBD) market. As the first IL-23 inhibitor approved for UC, it holds a unique position in the treatment landscape and the recent approval for CD in January 2025 further strengthens its market potential. However, with increasing competition and the potential entry of new therapies in the coming years, maintaining its market share will require strategic differentiation and continued real-world evidence to support its long-term value.

Why did it succeed or fail to meet expectations?

Mirikizumab has met expectations, benefiting from its position as the first IL-23 inhibitor approved for UC. While it will face competition from existing targeted therapies and the later approved drugs from the same drug class (i.e., SKYRIZI and TREMFYA), its early entry provides an initial market advantage. Additionally, its recent approval for CD (January 2025) has further expanded its potential in the IBD space. Increasing physician familiarity and emerging long-term safety and efficacy data are expected to support wider adoption, strengthening its role in the IBD treatment landscape.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

Mirikizumab's path to achieving its forecasted blockbuster status will depend on several key milestones and challenges. Expanding market penetration in both UC and CD will be critical, particularly as real-world data on long-term efficacy and safety become available. However, challenges remain, including competition from established targeted therapies, including TNF inhibitors, JAK inhibitors, and CAM inhibitors.

Additionally, the subsequent FDA approvals of SKYRIZI and Tremfya provide physicians with alternative IL-23 options that had already demonstrated long-term safety and efficacy in psoriasis and psoriatic arthritis. Differentiating itself within the IL-23 class will be essential for mirikizumab to maintaining physician preference. Moreover, the recent approval of Stelara biosimilars is expected to impact the market landscape in the coming years, further intensifying competition.

For mirikizumab to withstand competition in the crowded UC market, expanding label indications, exploring combination therapies, and gaining regulatory approvals in new markets could further enhance its commercial success. Overall, continued physician adoption, favorable pricing strategies, and compelling real-world evidence will be key factors in ensuring mirikizumab's position in the UC treatment landscape.

$132M

in sales in 2024, reflecting strong commercial performance.

[2] https://www.reuters.com/business/healthcare-pharmaceuticals/us-fda-expands-jjs-psoriasis-drug-inflammatory-bowel-disease-2024-09-11/

Drugs to Watch: Where are they now?

Niraparib + abiraterone acetate

AKEEGA™

What is the current status of this drug?

AKEEGA remains approved only for its original indication in BRCA-mutated metastatic castration-resistant prostate cancer (mCRPC), with no additional approvals in the major markets since our January 2024 report.

What happened to the drug in 2024 / early 2025?

Throughout 2024 and into early 2025, AKEEGA has solidified market presence in the United States, Germany, and France. However, it has encountered reimbursement challenges in key European markets — specifically, Spain, Italy, and the United Kingdom — which have slowed adoption.

Has this met your expectations?

Overall, AKEEGA has not fully met expectations. While it remains a viable treatment option in markets where it is approved, its overall performance has been constrained by reimbursement hurdles and intense competition from other PARP inhibitors.

Why did it succeed or fail to meet expectations?

AKEEGA's fixed-dose combination (FDC) format offers the convenience of a single pill, which is appealing to patients managing multiple medications. However, many oncologists view the lack of dosing flexibility as a drawback, as it prevents independent adjustments of the PARP inhibitor or ARPI components, complicating side effect management.

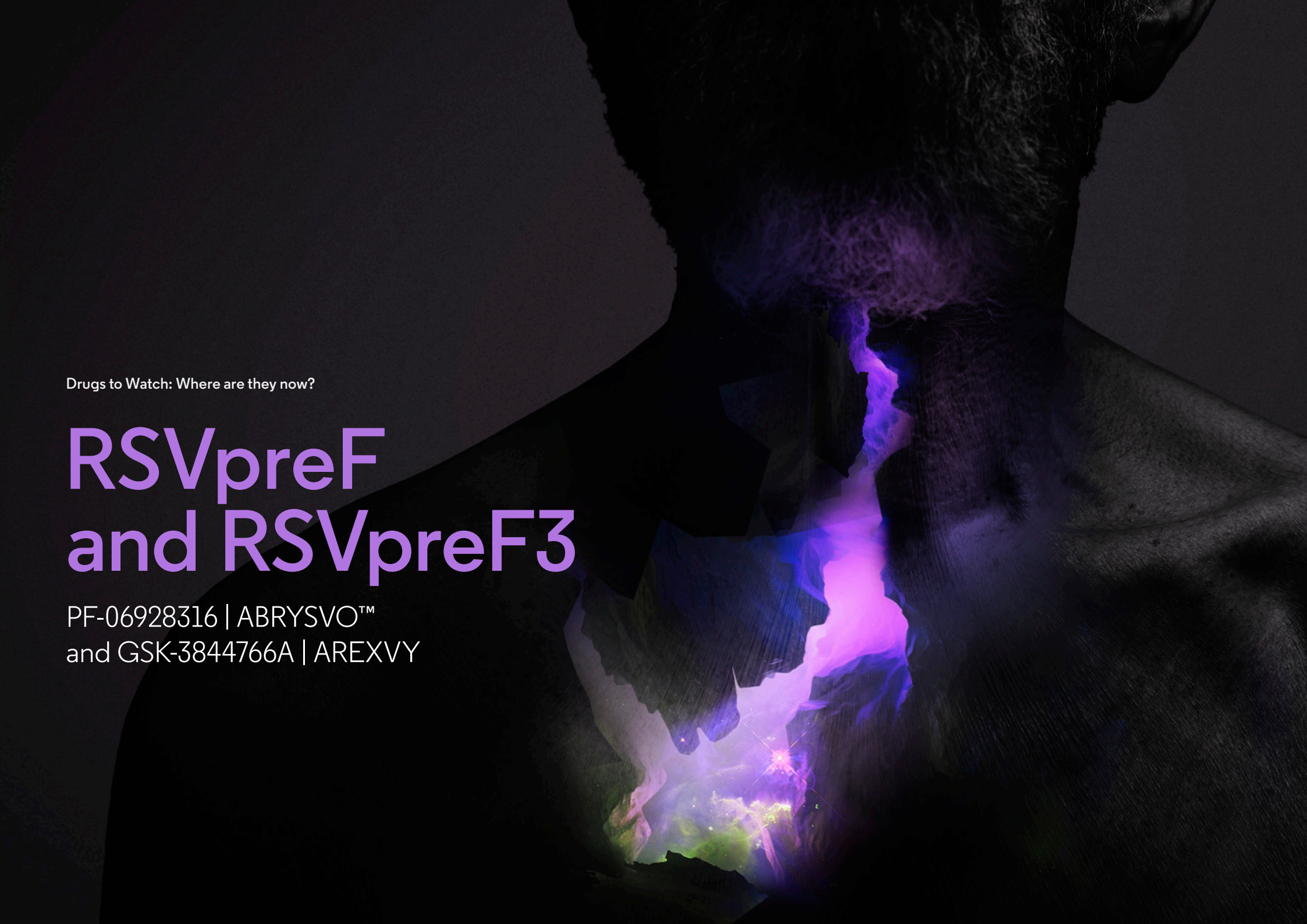
Moreover, competing PARP inhibitors such as Pfizer's TALZENNATALZENNA and AstraZeneca's LYNPARZA are well established in the mCRPC space. These alternatives not only offer greater dosing flexibility, but cross-trial comparisons suggest they might be more efficacious in both BRCA- and non-BRCA-mutated patients, further limiting AKEEGA's competitive edge.

Beyond clinical concerns, insufficient promotional efforts in Europe and the high cost of a full treatment course have also hindered adoption, making it difficult for AKEEGA to gain traction in an increasingly competitive market.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

A key milestone for AKEEGA is the upcoming readout from the Phase 3 AMPLITUDE trial in HRR-mutated metastatic hormone-sensitive prostate cancer (mHSPC) later this year. A positive outcome could enable a label expansion into this lucrative setting, which is currently untapped by PARP inhibitors. However, the trial's control arm — abiraterone — has already proven highly effective in this setting, setting a high bar for AKEEGA to surpass.

At the same time, Pfizer is actively pursuing its own label expansion for TALZENNA in mHSPC with the ongoing Phase 3 TALARPO-3 trial. While TALZENNA's data in this setting are not yet available, AKEEGA must demonstrate efficacy and safety that are at least equal to, if not superior to, TALZENNA to secure a competitive advantage. Beyond clinical performance, successfully navigating physician concerns over flexibility and payer negotiations in key markets will be critical to AKEEGA to fully capitalize on this potential expansion and strengthen its commercial outlook.



Drugs to Watch: Where are they now?

RSVpreF and RSVpreF3

PF-06928316 | ABRYSVO™
and GSK-3844766A | AREXVY

What is the current status of ABRYSVO?

ABRYSVO was initially granted U.S. and E.U. approval for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in people 60 years of age and older and pregnant individuals at 32 through 36 weeks gestational age for the prevention of LRTD and severe LRTD in infants from birth through 6 months of age. It has also been approved in the Japan in 2024 for both populations.

Additionally, it has also been approved in the United States and Europe for the adults aged 18-59 at increased risk.

What happened to the drug in 2024 / early 2025?

In 2024 and early 2025, ABRYSVO saw significant progress and expanded approvals. In January 2024, Japan's MHLW approved ABRYSVO for maternal immunization to protect infants against RSV, with the approval expanding in March 2024 to include adults aged 60 or older. February 2024 brought positive top-line data from the Phase 3 RENOIR trial, demonstrating durable efficacy in older adults aged 60 or older over two seasons. The data demonstrated that vaccine efficacy against RSV-LRTD, defined by three or more symptoms, after disease surveillance in season two was 77.8% (95.0% CI: 51.4, 91.1); vaccine efficacy following season one was 88.9% (95.0% CI: 53.6%, 98.7%), which demonstrates durable efficacy after two seasons.

By April 2024, the Phase 3 MONeT trial results were announced, showing strong immune responses in adults aged 18-59 with chronic conditions and immunocompromised adults aged 18 and older. Following these promising results, the FDA approved ABRYSVO in October 2024 for adults aged 18-59 at increased risk. Finally, in April 2025, the E.U. expanded its approval of ABRYSVO for adults aged 18-59, based on the Phase 3 MONeT trial results.

Has this met your expectations?

Although ABRYSVO offers broad protection against RSV for various age groups and effectively prevents RSV-associated LRTD in both older adults, high-risk younger adults, and infants through maternal immunization, it has fallen short of sales expectations, experiencing a global decline of 62% in Q4 2024 versus Q4 2023, as per company.

Why did it succeed or fail to meet expectations?

ABRYSVO failed to meet the sales expectations primarily due to a significant reduction in vaccination rates among older adults in the United States, driven by a narrowing market opportunity following the latest recommendations from the ACIP (recommendation for adults aged 75 and older and aged 60-74 with comorbidities). However, as per company, this decline has been partially offset by improved market share for the adult indication and strong demand for the maternal indication (following its launch in December 2023).

Another challenge has been the need for ongoing monitoring of vaccine efficacy and safety, especially concerning potential adverse events.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

Expanded approvals / launch of ABRYSVO for different populations like adults aged 18-49 in the United States and E.U., strong clinical trial results and ongoing real-world effectiveness studies would boost its uptake. However, it must ensure long-term efficacy for more seasons, address safety concerns (e.g., risk of developing Guillain-Barré syndrome), and expand awareness and uptake among target populations. Key opinion leaders (KOLs) interviewed by Clarivate highlight additional challenges, such as low acceptance of maternal vaccination and competition from monoclonal antibodies, which offer comparable protection directly to infants. Additionally, pregnant women's hesitancy to receive vaccinations impacts the vaccine's uptake and effectiveness in protecting newborns during critical early months.

What is the current status of AREXVY?

Since AREXVY's approval in the U.S., E.U., and Japan for the prevention of respiratory syncytial virus (RSV) -associated lower respiratory tract disease (LRTD) in adults aged 60 and older in 2023, it has also received expanded approval for adults aged 50-59 at increased risk for severe RSV outcomes in these countries. It has shown durable efficacy over multiple RSV seasons.

What happened to the drug in 2024 / early 2025?

There have been different developments and expanded approval of AREXVY in 2024 and early 2025. In June 2024, the FDA approved AREXVY for adults aged 50-59 at increased risk. This was followed by the E.C. authorizing AREXVY for the same age group in August 2024, after a positive recommendation from the CHMP in July 2024.

In October 2024, two significant trials were completed: the phase 3b trial (RSV OA=ADJ-025) met its co-primary endpoints, demonstrating robust immune responses in non-immunocompromised adults aged 18-49, and the phase 2b trial (RSV OA=ADJ-023) showed promising immune responses in immunocompromised adults aged 18 or older. Finally, in November 2024, the Japan's Ministry of Health, Labour and Welfare (MHLW) approved AREXVY for adults aged 50-59 at increased risk.

Has this met your expectations?

Despite AREXVY providing durable protection against RSV over multiple seasons and demonstrating efficacy in older adults, including those with underlying medical conditions, it has not met sales expectations. AREXVY experienced a decline in both annual and quarterly sales in 2024.

Why did it succeed or fail to meet expectations?

Challenges:

- AREXVY faced several hurdles in 2024 sales performance. In the United States, the decline in sales was primarily driven by reduced demand, which was influenced by the ACIP issuing a more limited recommendation for individuals aged 60 to 74. Despite these challenges, AREXVY successfully maintained its market-leading position in the retail (pharmacy) sector, per the company, where the majority of doses are administered.

Success:

- A robust network of retail pharmacies, being widely accessible to the population, has facilitated AREXVY's uptake, substantially contributing to its sales growth and market-leading position in this sector.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

Outside of the United States, sales growth was driven by positive recommendations for use across markets and initial stockpiling of product for dispensing. AREXVY is approved in 59 markets, with 17 countries having national RSV vaccination recommendations and six, including the United States, having reimbursement programs. Continued label expansion of AREXVY for different population like adults aged 50-59, positive data, and ongoing studies (for adults aged 18-49) will drive market dominance and sales growth.

Critical to AREXVY's success are ensuring long-term protection (meaning that the vaccine provides sustained immunity over an extended period, reducing the need for frequent booster doses and ensuring continuous defense against RSV), addressing safety concerns (e.g., risk of developing Guillain-Barré syndrome), and expanding vaccination coverage among older adults.

Overcoming a decline in vaccination rates owing to the ACIP's more limited recommendation in 2024, which negatively impacted sales and which presents an ongoing challenge for the coming years.

Competition from other RSV vaccines has also influenced AREXVY's market performance. GSK anticipates limited growth in the near term but remains optimistic about long-term prospects as public health recommendations evolve and international penetration increases.

Drugs to Watch: Where are they now?

Talquetamab

TALVEY™

What is the current status of this drug?

TALVEY is launched in Europe and the United States (conditional and accelerated approval, respectively).

What happened to the drug in 2024 / early 2025?

There have been no regulatory updates. However, updated data from the pivotal phase 1/2 MonumenTAL-1 trial and preliminary data from the phase 1b TRIMM-2, MonumenTAL-2, and RedirecTT-1 trials were presented at congresses in and published in journals, demonstrating impressive efficacy in relapse / refractory (R/R) patients.

Has this met your expectations?

TALVEY has met our expectations by continuing to perform well in R/R patients. We expect this trend to continue throughout the 2023-2033 forecast period.

Why did it succeed or fail to meet expectations?

Data from the MonumenTAL-1, TRIMM-2, MonumenTAL-2, and RedirecTT-1 trials demonstrated that as a monotherapy and in combination with other drugs, TALVEY displayed strong responses in R/R patients. This includes patients who had been previously exposed to and progressed with bispecific T-cell engagers or CAR T-cell therapies targeting BCMA.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

Talquetamab is the only and first-in-class bispecific antibody targeting CD3 and GPRC5D, a seven transmembrane receptor protein expressed on plasma cells. Although it does not face immediate direct competition in today's market, several GPRC5D-directed drugs are in earlier phase development.

Drugs to Watch: Where are they now?

Zolbetuximab

IMAB362 | VYLOY®

What is the current status of this drug?

VYLOY in combination with fluoropyrimidine- and platinum-based chemotherapy is approved for the first-line treatment of locally advanced unresectable of metastatic HER2-negative, Claudin18.2-positive gastric and gastroesophageal junction (GEJ) adenocarcinoma across key G7 markets (United States, EU5, Japan) and China.

What happened to the drug in 2024 / early 2025?

- January 2024: The U.S. FDA issued a complete response letter due to third-party manufacturing issues.
- March 2024: VYLOY was approved in Japan
- September 2024: VYLOY was approved in Europe.
- October 2024: The U.S. FDA granted approval following resubmission that addressed manufacturing concerns.
- January 2025: Mainland Chinese regulators extended its global reach by granting approval.

Has this met your expectations?

Yes, but chemotherapy is still the main treatment for gastroesophageal cancer, where platinum/fluoropyrimidine-based agents remain the standard of care.

VYLOY in combination with chemotherapy (mFOLFOX6 or CAPOX) showed clinically meaningful improvements of PFS and OS compared to chemotherapy alone in two phase 3 trials SPOTLIGHT and GLOW. These results are significantly addressing a critical unmet need and supporting its rapid uptake in HER2-negative population.

Why did it succeed or fail to meet expectations?

The broad expression of Claudin18.2 represents a relevant market opportunity with approximately 38% of gastric cancer cases being eligible for the treatment.

The targeted mechanism of action has generated a strong clinical interest as it addresses a critical gap in the current treatment landscape for the HER2-negative gastric and GEJ adenocarcinoma.

VYLOY is largely benefiting from its first-in-class status. The lack of intra-class competition, together with relatively low expression overlap with other biomarkers (e.g. PD-L1), is driving its uptake in this patient population.

What other milestones or challenges does the drug face as it tries to build towards the forecast?

As the drug begins to be widely used in clinical practice, real-world data on long-term safety and effectiveness will be crucial to confirm clinical trial findings and guide future treatment protocols.

Several studies are ongoing to explore VYLOY's activity in other Cladudin18.2-expressing indications either alone or as part of combinations (e.g. immune-checkpoint inhibitors). If those trials are positive, they could secure label expansions to VYLOY further broadening its market.

VYLOY's adoption in E.U. countries will hinge on successful negotiations with local health authorities and the establishment of favorable reimbursement strategies.

Several other therapies targeting Claudin18.2 are in clinical development. Some of these candidates employ different mechanism of actions than mAbs, such as antibody-drug conjugates, bispecific agents and cell therapies. If approved, these agents would pose significant competition to VYLOY.

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