Clarivate™

Drugs to Watch 2023

Transformative intelligence for a healthier tomorrow

By Robert Poolman, Senior Vice President, Product Management, Clarivate

We are living in a time of incredible promise for patients – and not a little peril for the pharmaceutical industry. On one hand, the biomarker revolution is delivering targeted treatments. More than one in four United States Food and Drug Administration (FDA) new drug approvals has been for a personalized medicine over the past seven years.

On the other hand, pharmas and biotechs stand at the precipice of a steep patent cliff, with patent losses threatening to wipe out $92 billion a year in sales of blockbuster drugs by 2025. While innovative treatments could replenish these pipelines, the pace of approvals is slowing in key markets. The FDA approved just 37 new molecular entities and biologics license applications – well short of the 50 green-lighted in 2021 – and just 12 accelerated approvals amid Congressional scrutiny. More than half of pharma CEOs in a recent survey cited regulatory changes as a top trend disrupting their businesses.

As many companies continue to struggle with four key challenges, powerful new data and analytics tools hold potential to solve business challenges by speeding up development cycles.

- **Gaining an individualized view of the patient**
  We are no longer in a world where patient centricity is optional for life science companies. Due to a convergence of trends in technology, drug development, the regulatory landscape and the commercial market for medicines, developing a deep understanding of the individual and delivering patient-centric outcomes is now critical for biopharma and medtech.
- **Streamlining R&D**
  Pharma faces a steep patent cliff in the coming years. Many of the innovative therapeutics companies are betting on to replenish pipelines involve emerging technologies and therapeutic modalities, introducing complexity to the R&D process. Pharmas are leveraging bioinformatics, AI-powered tools and machine learning to streamline discovery, R&D and the integration of internal and external data sets.
- **Future-proofing regulatory affairs strategies**
  Adding to this complexity, companies are faced with a dense and fast-evolving raft of regulations that can vary widely, despite movement towards developing global standards. To speed innovative medicines to market, companies must future-proof their regulatory strategies by anticipating changes and understanding differences from market to market.
- **Understanding the burden of disease**
  In tandem with the movement toward patient centricity as well as cost-control efforts, regulators and payers are increasingly demanding that pharmas and medtechs explain how they are addressing the burden of disease, not just on patients but also on caregivers, families, employers and society as a whole. Addressing this question and indeed, considering the targets of UN Sustainable Development Goal 3 are key to resolving the burden of disease.

More than ever before, bringing the next generation of Drugs to Watch™ is a formidably complex task. We at Clarivate™ are proud to partner with global innovators large and small to help speed future medical breakthroughs to market – breakthroughs that can be delivered to patients faster, improve quality of life and shape the future of healthcare.

Personalized medicines to treat undruggable diseases – and a looming patent cliff

The business of developing and commercializing innovative prescription drugs is always a vital one, with patient lives and quality of life on the line. However, the precarity of the financial situation for the many companies facing steep patent cliffs over the next decade is making the task that much more urgent.

Over the next five years, ten of the top-selling drugs and biologics on the market, collectively worth $90 billion, will lose patent exclusivity and face competition from generics and biosimilars. HUMIRA®, set to see a key patent expire in the United States this year, realized $17 billion in U.S. sales for 2021 and has already seen significant erosion in earnings due to the launch of biosimilars in European markets.

Competition driving down the prices of medicines is great for patients and payers, of course, but in order to fund the next cycle of pharmacological advances, companies must replenish their pipelines. This year's Drugs to Watch list from Clarivate is made up almost entirely of personalized medicines, treatments targeted to a particular biomarker, ensuring greater efficacy and less precious time lost searching for a drug or biologic that will arrest or reverse the progress of disease.

A quarter-century after the launch of Herceptin®, the pioneering personalized medicine targeting the HER2 gene, these treatments have made up more than 25% of FDA approvals for each of the past seven years.

The rise of personalized medicine has facilitated treatments for rare diseases and previously untreatable conditions – Herceptin was a revolutionary treatment because it was indicated for the roughly one in five breast cancer cases that are HER2-positive. Before Herceptin, these patients had very poor prognoses. One of our Drugs to Watch for 2020, ENHERTU®, recently won FDA approval for treatment of HER2-low breast cancer, a newly defined subset affecting approximately 60% of HER2-negative metastatic breast cancer patients.

Of course, as companies target smaller patient populations with more targeted drugs, even some truly novel and highly successful treatments will garner less revenue. Accordingly, we've revised our methodology to recognize not just blockbuster drugs and biologics but also those with the potential to transform treatment paradigms, even if our forecasts show them coming up short of a billion dollars in annual sales. After all, while pharmas and biotechs must meet revenue targets in order to finance the development of future miracle drugs, their higher purpose is the advancement of human health.

To that end, this year's report also includes a brief look at the industry's progress in addressing the diseases highlighted in the United Nations Sustainable Development Goals, which include infectious diseases like HIV, tuberculosis, malaria, neglected tropical diseases and water-borne diseases, as well as maternal mortality and non-communicable diseases like mental illness and substance abuse. As the U.N. plan notes, there is a 31-year gap between the countries with the shortest and longest life expectancies and many populations are being left behind, particularly in the Global South. The pharmaceutical industry, focused on solving the difficult and expensive to treat conditions afflicting the wealthy world, such as cancer, has a critical role to play in addressing this disparity.

Having met the enormous challenge of quickly developing vaccines and treatments for COVID-19, we can be sure that pharmas and biotechs are up to the task.

We've revised our methodology to recognize not just blockbuster drugs and biologics but also those with the potential to transform treatment paradigms.

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Methodology

Drugs to Watch from Clarivate showcases drugs recently launched or likely to enter the market this year that are forecast to become blockbusters within five years and/or to transform treatment paradigms (blockbuster is defined by the common $1 billion annual sales milestone).

Drug selection criteria

01

Candidate drugs in phase 2 or phase 3 trials, at pre-registration or registration stage or already launched early in 2022 were selected for analysis, including drugs launched for a new indication that could be particularly impactful on the industry; drugs launched prior to 2022 were excluded.

02

The dataset was then filtered for drugs that had total forecast sales of $1 billion or more in 2026.

To identify this year's Drugs to Watch 2023 list, we drew from expertise from over 160 Clarivate analysts covering hundreds of diseases, drugs and markets and eleven integrated data sets that span the R&D and commercialization lifecycle.

Clarivate experts then manually evaluated each drug in its individual context, based on factors such as expected approval or launch dates, competitive landscape, regulatory status, trial results, market dynamics and other factors and added novel drugs that, while likely to fall short of blockbuster status, are poised to be therapeutic game-changers.

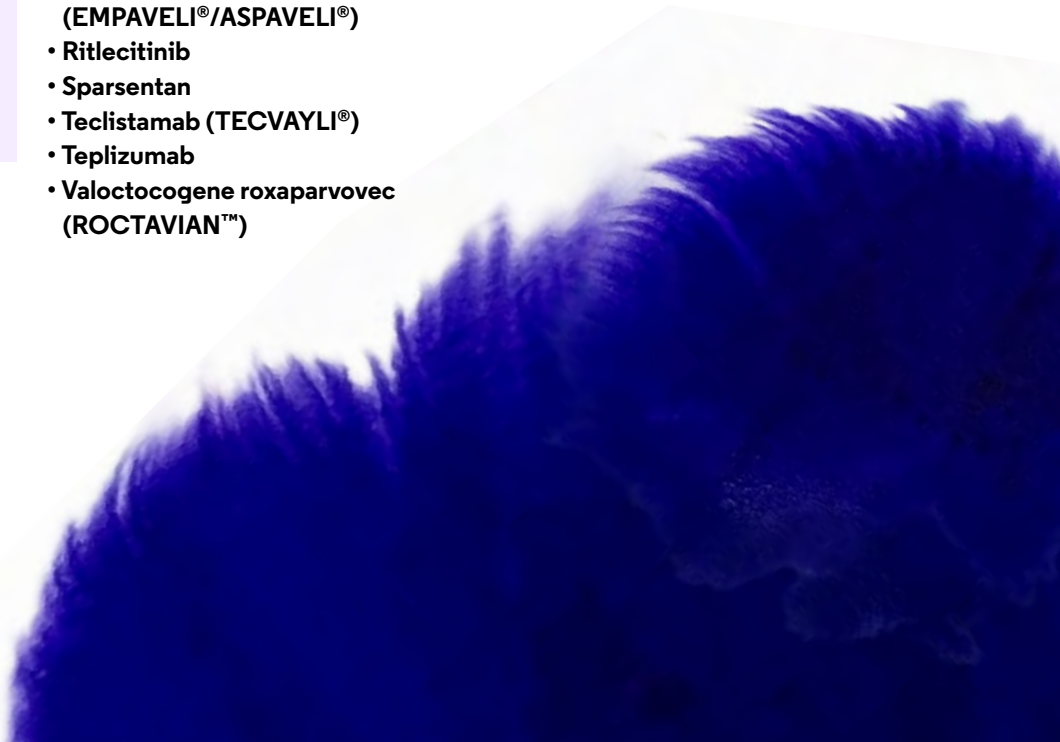
From there, we determined 15 Drugs to Watch in 2023:

- **Bimekizumab (BIMZELX®)**
- **Capivasertib**
- **Daprodustat (Duvroq)**
- **Deucravacitinib (SOTYKTU™)**
- **Foscarbidopa/foslevodopa**
- **Lecanemab (LEQEMBI™) and donanemab**
- **Lenacapavir (Sunlenca®)**
- **Mirikizumab**
- **Pegcetacoplan (EMPAVELI®/ASPAVELI®)**
- **Ritlecitinib**
- **Sparsentan**
- **Teclistamab (TECVAYLI®)**
- **Teplizumab**
- **Valoctocogene roxaparvovec (ROCTAVIAN™)**

The drug snapshots within the report draw from: interviews with therapy experts for the respective drug markets; Clarivate drug, disease landscape and forecast reports; Cortellis™ sales data (sourced from Refinitiv I/B/E/S); and other industry sources including biopharma company press releases and peer-reviewed publications.

This year's Drugs to Watch report includes an update on the COVID-19 vaccine and therapeutic landscape, which summarizes the vaccines and therapies that were granted emergency use authorizations/ conditional approvals as of October 2022, as well as sections looking at biosimilar competitors to HUMIRA, Drugs to Watch for the Mainland China market, progress towards personalized medicines and how pharmas are addressing sustainability issues through their R&D initiatives.

Please note that Clarivate analysts generated the data shown in this report on January 3, 2023.



Data sources and contributors

Since 2013, Clarivate has applied proprietary technologies, tools and techniques trusted by its global life sciences customers to produce the annual Drugs to Watch report.

Cortellis Competitive Intelligence™ provides access to data such as drug pipeline, deals, patents, global conferences and company content, along with the latest industry news and press releases. The Cortellis Competitive Intelligence Drug Timelines & Success Rates methodology is a patented analytic tool that applies statistical modeling and machine learning to more reliably and accurately forecast drug development milestones, timelines and probability of success.

Disease Landscape & Forecast provides comprehensive market intelligence and actionable insights across 180+ indications to help optimize long-term disease strategies.

BioWorld™ is an industry-leading suite of news services delivering actionable intelligence on the most innovative therapeutics and medical technologies in development.

Cortellis Clinical Trials Intelligence™ is a comprehensive source of detailed insights on clinical sites and trial protocols including biomarkers, targets and indications.

Cortellis Generics Intelligence™ provides access to reliable and integrated market performance, manufacturing and patent data in a single, easily searchable solution.

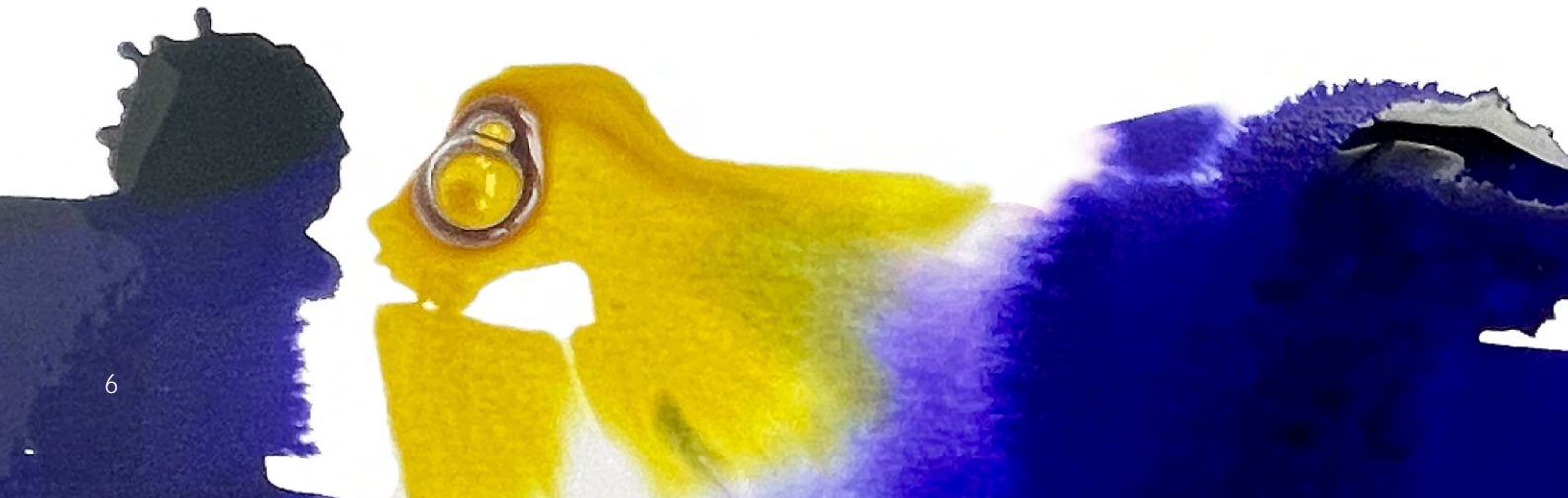
Cortellis Deals Intelligence™ combines a robust and comprehensive source of deals intelligence with enhanced visualizations of the highest quality data, to quickly find the optimal deal without compromising due diligence.

Access and reimbursement payer studies provide brand-level insight regarding the impact of payer policy on physician prescribing behavior so clients can optimize their market access strategy and determine how to best position their brand to specific stakeholders.

Real World Data Product and Analytics provides a comprehensive view of the market and a deep, impartial view of all stakeholders and sites of service through medical claims, EHR, Rx data and more.

Web of Science™ is the world's largest publisher-neutral citation index and research intelligence platform. It organizes the world's research information to enable academia, corporations, publishers and governments to accelerate the pace of research.

Derwent Innovation™ is a market-leading patent research and analytics platform delivering access to globally trusted patents and scientific literature. Enhanced content, proprietary search and data intelligence technology helps a global community of more than 40,000 innovators and legal professionals find answers to complex questions.



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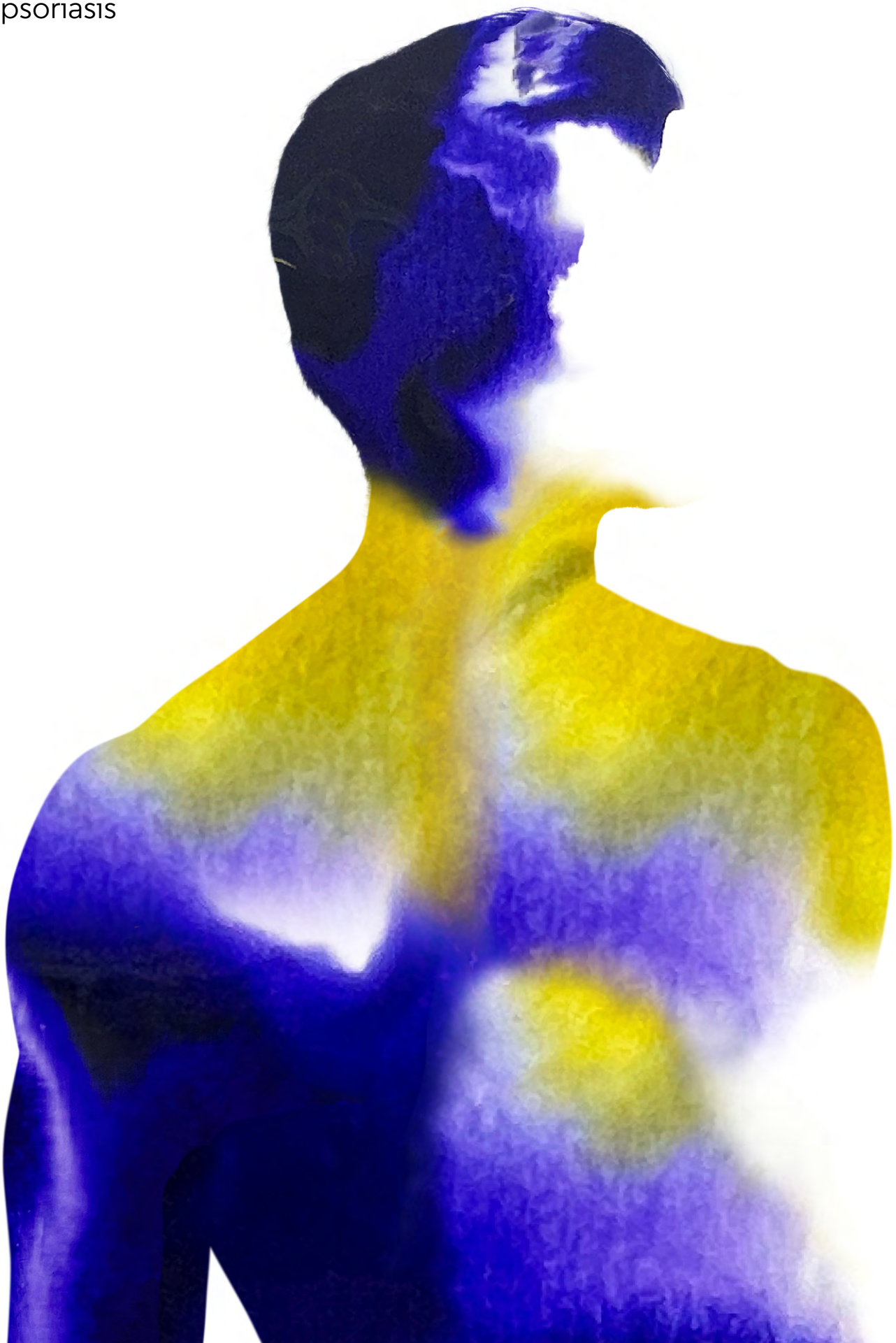
DOI 10.14322/drugs.to.watch.report.2023

1 Bimekizumab

Plaque psoriasis



Bimekizumab
BIMZELX®

About

Producer:
UCB

Type:
Humanized IgG1 monoclonal antibody (mAb)

Usage:
Subcutaneous injection every four weeks for the first five treatments, then every eight weeks to treat moderate to severe plaque psoriasis

Also being studied to treat axial spondyloarthritis, psoriatic arthritis and hidradenitis suppurativa

Impact:

~11.7m

symptomatic psoriasis cases in the G7 markets in 2021

80–90%

of patients with psoriasis have plaque psoriasis

As the first dual-specific IL-17 A/F inhibitor to treat plaque psoriasis, bimekizumab could be more effective than inhibitors of IL-17A only at reducing skin and joint inflammation as well as pathological bone formation, which are the primary contributors to the symptomatic burden of psoriasis and with fewer side effects than some current treatment options, including a pan-IL-17 inhibitor.

Prior approvals for the treatment of moderate to severe plaque psoriasis by the European Commission (EC), Japan's Ministry of Health, Labour and Welfare (MHLW), Health Canada and Australia's Therapeutic Goods Administration bode well for approval by the U.S. Food and Drug Administration (FDA).

Why is it a Drug to Watch?

Bimekizumab is the first dual IL-17 A/F inhibitor to treat moderate to severe plaque psoriasis. Phase 3 trial results showed superior skin clearance outcomes than existing treatments. Its less-frequent dosing schedule and good safety profile will likely be attractive to clinicians and patients.

EC and MHLW approvals were supported by results from three phase 3 trials, BE VIVID (bimekizumab vs ustekinumab/STELARA®), BE READY (bimekizumab vs placebo) and BE SURE (bimekizumab vs adalimumab/HUMIRA®):

- All three studies met co-primary endpoints.
- Bimekizumab showed statistically significant superior levels of skin clearance at week 16 (≥90% improvement on the Psoriasis Area Severity Index [PASI]).
- Responses at week 16 were maintained for up to one year in all studies.

The phase 3 BE RADIANT trial (bimekizumab vs the first-in-class IL-17 inhibitor, secukinumab/COSENTYX®) showed statistically significant superiority at skin clearance on the PASI 100 (100% reduction from baseline on the PASI).

Positive results for psoriatic arthritis, recently published in The Lancet, hold promise for its effectiveness in this patient population:

- BE OPTIMAL: biologic disease-modifying anti-rheumatic drug (bDMARD)-naïve adults with active psoriatic arthritis
- BE COMPLETE: adults with active psoriatic arthritis who were inadequate responders or intolerant to anti-TNF-alpha therapy

It was the first drug to receive NICE approval via its new fast-track approval scheme introduced in 2021; the decision was based on clinical trial evidence showing better effectiveness with bimekizumab than with three competitors previously approved by NICE. The cost-effectiveness estimates resulted in NICE recommendation for the estimated 18,000 people who will be eligible for the treatment.

Bimekizumab
BIMZELX®

Review and approval status

August 2021
For patients with moderate to severe plaque psoriasis who are candidates for systemic therapy: Marketing authorization: European Commission (EC)

January 2022
For patients with moderate to severe plaque psoriasis, generalized pustular psoriasis or psoriatic erythroderma: Marketing authorization: Japan's Ministry of Health, Labour and Welfare (MHLW)

February 2022
For patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy: Marketing authorization: Canada

September 2022
For patients with psoriatic arthritis (PsA): Marketing authorization application: EC

September 2022
For patients with active axial spondyloarthritis (axSpA): Marketing authorization application: EC

November 2022
For patients with moderate to severe plaque psoriasis: Biologics License Application resubmitted: United States

Actual and expected launch
2021: Europe
2022: Japan
2023: United States

Patents estimated to expire beginning in 2027

How will bimekizumab impact the market for plaque psoriasis?

- Its selective dual inhibition makes it stand apart from the already available IL-17 inhibitors, COSENTYX and ixekizumab (TALTZ®), as well as the IL-17 receptor antagonist, brodalumab (SILIQ®), which has a black box warning for suicidal ideation and behavior.
- Physicians report higher-than-expected primary failure with both COSENTEX and TALTZ and given the black box warning for SILIQ, there is opportunity for bimekizumab to fill both efficacy and safety gaps.

What gaps in treatment does bimekizumab fill?

The less frequent dosing of bimekizumab (every eight weeks) is more convenient than that of TNF-alpha inhibitors and other IL-17 inhibitors approved for this patient population. The chronicity and time requirement of clinic visits take a toll on patient quality of life, particularly those of working age. In addition, bimekizumab is among the few drugs approved for rare types of psoriasis, such as generalized pustular psoriasis and psoriatic erythroderma, in Japan. Further validation of its safety and efficacy for these conditions could expand its use to treat these patients in other countries and regions.

What hurdles might it need to overcome to reach blockbuster status?

As a fourth-in-class IL-17 entrant, bimekizumab will enter a competitive market in which new therapies, regardless of their improved clinical profiles, tend to be reserved for TNF-alpha and ustekinumab treatment-refractory patients with primary or secondary nonresponse until physicians are comfortable with the long-term safety of a new treatment. Increasing treatment choices will make treatment decisions more complex and bimekizumab will be competing with efficacious biologics, biosimilars and the targeted oral drugs Otezla® and SOTYKU. Entry in the U.S. market has been delayed first by COVID-19-related travel restrictions at the timing of its initial Prescription Drug User Fee Act (PDUFA) date of October 15, 2021 and second by the FDA's complete response letter (CRL) in May 2022 owing to gaps found during inspection of UCB's European manufacturing facilities. These delays could limit the sales potential in the United States and potentially negatively affect stakeholders' perceptions.

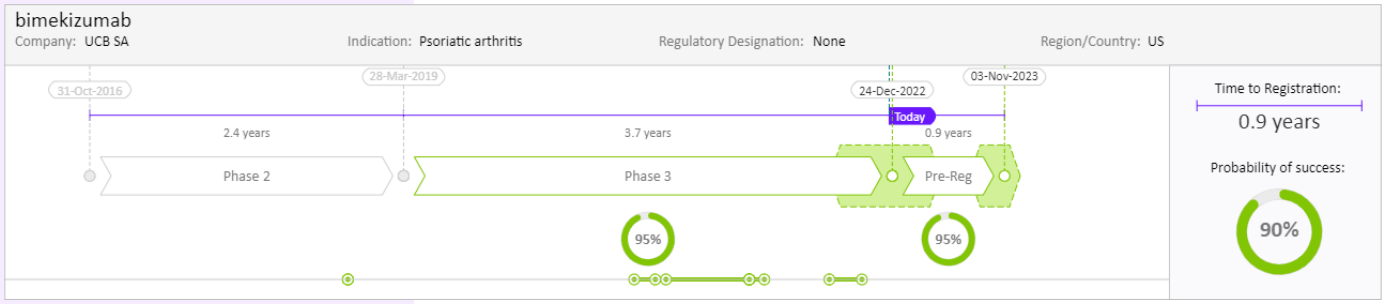
Bimekizumab
BIMZELX®

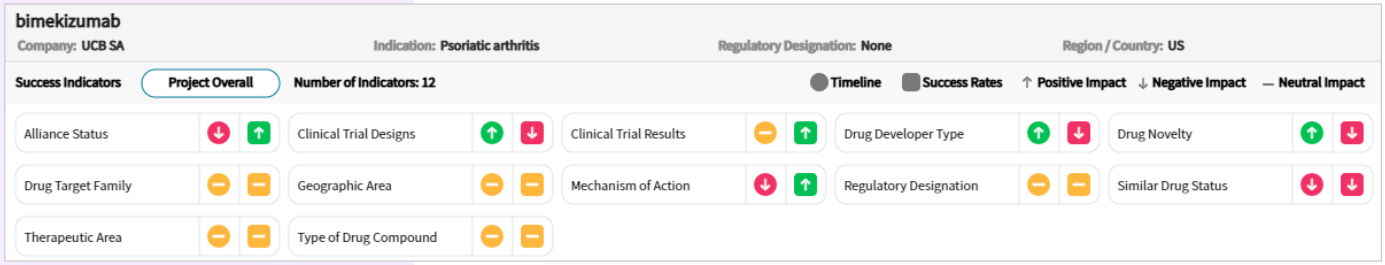
Market overview

$2.045B
expected sales in 2027

"The data look extremely impressive; it seems that dual inhibition of IL-17A and F is more effective than blocking only IL-17A. To me, it's an IL-17 antagonist with increased efficacy versus what we have. The expectation is that more patients will be cleared and more patients will remain on therapy. I think it will be a very useful drug."

Dermatologist, France





Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicates there is a 90% probability of success for bimekizumab in the United States for psoriatic arthritis.

2 **Capivasertib**

Breast cancer

Capivasertib
AZD5363

About

Producer:
AstraZeneca

Type:
ATP-competitive pan-AKT kinase inhibitor

Usage:
Oral administration to treat triple-negative and HR positive/HER2 negative breast cancer

Also in late-phase trials for prostate cancer

Impact:

~67k

diagnosed incident cases of triple-negative breast cancer in women in the G7 markets in 2021

~460k

diagnosed incident cases of HR-positive/HER-negative breast cancer in women in the G7 markets in 2021

Capivasertib is a novel, highly potent, selective ATP-competitive pan-AKT kinase inhibitor that exerts similar activity against the three isoforms AKT1, AKT2 and AKT3. Positive data have emerged from early-phase trials and several phase 3 trials are now underway.

These phase 3 trials could provide the basis for regulatory approval of capivasertib in combination with fulvestrant as second or later-line treatment for metastatic HR-positive/HER2-negative breast cancer and in combination with paclitaxel as first-line treatment for locally advanced or metastatic triple-negative breast cancer.

Why is it a Drug to Watch?

Originating from a collaboration between AstraZeneca, Astex Pharmaceuticals Inc, the Institute of Cancer Research and Cancer Research Technology, capivasertib has shown promising results in early-phase trials, with clinical benefit to patients irrespective of their PIK3CA/AKT1/PTEN mutational status:

- PAKT: phase 2 of capivasertib plus paclitaxel demonstrated impressive progression-free survival (PFS) and overall survival (OS) over paclitaxel alone, as first-line therapy for metastatic triple-negative breast cancer.
- FAKTION: phase 1/2 of capivasertib plus fulvestrant demonstrated significantly increased PFS and OS over fulvestrant alone in inoperable locally advanced or metastatic ER-positive/HER2-negative breast cancer patients who had relapsed or progressed on an aromatase inhibitor.

Multiple phase 3 trials are currently verifying and expanding on these results:

- CAPItello-290: capivasertib plus paclitaxel as first-line treatment for inoperable locally advanced or metastatic triple-negative breast cancer
- CAPItello-291: capivasertib plus fulvestrant in inoperable locally advanced or metastatic HR-positive/HER2-negative breast cancer patients who have relapsed or progressed on an aromatase inhibitor (i.e., second or later-line settings)

Primary results from the trial showed that the combination of capivasertib plus fulvestrant significantly improved PFS over placebo plus fulvestrant, translating to a 40% reduction in the risk of disease progression or death in this population.

- CAPItello-292: capivasertib, palbociclib (IBRANCE®) and fulvestrant to treat inoperable locally advanced or metastatic HR-positive/HER2-negative breast cancer in patients who have relapsed within 12 months of completing endocrine adjuvant therapy or who have disease progression during the initial 12 months of first-line endocrine therapy for locally advanced unresectable or metastatic breast cancer (i.e., first and second-line settings)

Capivasertib
AZD5363

Review and approval status

Expected launch
2023: United States and Europe
2024: Japan

Patents estimated to expire beginning in 2028

How will capivasertib impact the market for breast cancer?

Owing to the large number of incident and recurrent cases, high treatment rates across the many lines of treatment in some patient segments and typically long treatment durations, breast cancer is one of the largest therapy markets in oncology and is expected to grow from $22.6 billion in 2021 to $50.5 billion in 2031 in the G7 markets. Sales are expected to increase from $11.1 billion in 2021 to $27.7 billion in 2031 for HR-positive/HER2-negative breast cancer treatments and from $1.6 billion in 2021 to $6.8 billion in 2031 for triple-negative breast cancer treatments.

- Capivasertib is forecast to exceed sales of $1 billion in 2031 across the major G7 markets.
- Capivasertib is estimated to hold 5% of the first-line metastatic triple-negative breast cancer market and approximately 10% of the second, third and fourth-line metastatic HR-positive/HER2-negative breast cancer market in 2031 (across the G7 markets).
- Uptake of capivasertib will help sustain the growth of PI3K/AKT/mTOR pathway inhibitor sales in the midst of eroding everolimus sales due to generic options entering the market.

What gaps in treatment does capivasertib fill?

Triple-negative breast cancer is a particularly aggressive form of breast cancer characterized by a heterogeneous patient population with a lack of well-established predictive biomarkers. As such, targeted therapies are lacking as well as efficacious therapy options in general. For both metastatic HR-positive/HER-negative and triple-negative disease, capivasertib promises to advance and diversify treatment options for these difficult-to-treat patients.

What hurdles might it need to overcome to reach blockbuster status?

The market for triple-negative breast cancer treatments is expected to become increasingly competitive, with the booming drug development in this space owing to the high level of unmet need and lack of approved agents. Multiple drug classes are being investigated, including immune checkpoint inhibitors, antibody-drug conjugates, therapeutic vaccines, PARP inhibitors and CDK4/6 inhibitors. Since the majority of capivaserib's sales are forecast to be derived from the metastatic HR-positive/HER2-negative setting, major hurdles in uptake and thus sales potential include competition from established earlier-to-market therapies in this setting and emerging novel therapies (e.g., oral selective estrogen receptor degraders [SERDs] and TROP2 inhibitors).

Capivasertib
AZD5363

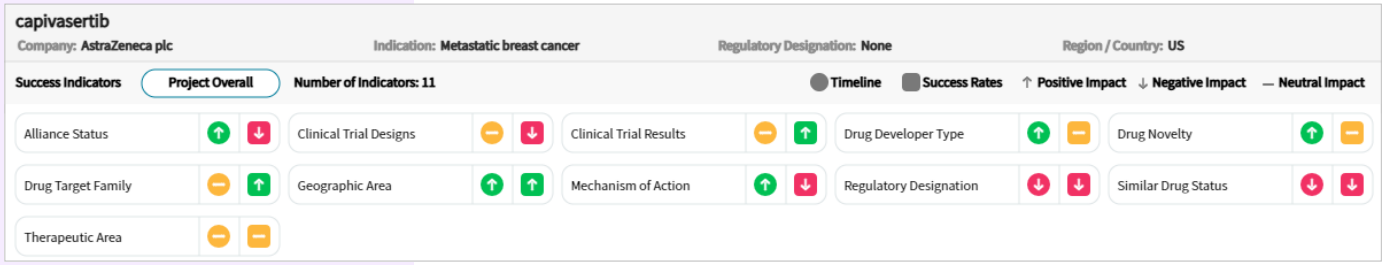
Market overview

$0.53B

expected sales in 2027

“The AKT inhibitors seem active, but they also have a lot of toxicity. The other issue is determining where these best sit in the treatment algorithm, given that breast cancer is becoming increasingly competitive as new agents are approved.”

Medical oncologist, Italy



Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate there is a 90% probability of success for capivasertib in the United States for metastatic breast cancer.

3 **Daprodustat**

Chronic kidney disease
(CKD)–related anemia

Daprodustat
GSK1278863/
Duvroq

About

Producer:
GlaxoSmithKline plc.

Type:
Hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI)

Usage:
Oral administration to treat CKD-related anemia, regardless of dialysis status

Impact:

~67m

cases of CKD in the G7 markets in 2021

Daprodustat belongs to a novel class of oral treatments for CKD-related anemia. Already available for CKD-related anemia in Japan, its uptake has been impressive. In other markets, upon approval, it is expected to differentiate itself from entrenched, injectable erythropoiesis-stimulating agents (ESAs) by its safety profile, efficacy and oral administration. As such, it will help fill the gap in safe treatments for this growing patient population.

Why is it a Drug to Watch?

Approved by the Ministry of Health, Labour and Welfare (MHLW) in Japan and under review by the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA), daprodustat is an HIF-PHI developed to treat anemia associated with CKD, which has a high incidence rate and few effective, safe treatment options.

The New Drug Application (NDA) submitted to the U.S. FDA was supported by results from the phase 3 ASCEND program, which included five studies investigating daprodustat across the spectrum of CKD:

- ASCEND-ND (non-dialysis), ASCEND-D (dialysis), ASCEND-ID (incident dialysis) and ASCEND-TD (dialysis): daprodustat versus the standard of care, ESAs, resulting in hemoglobin within target levels and non-inferiority of major adverse cardiovascular events (MACE)
- ASCEND-NHQ: daprodustat versus placebo, resulting in increased hemoglobin and similar adverse events with daprodustat.

In 2018, GSK plc and Kyowa Hakko Kirin entered into a strategic collaboration agreement for Kyowa Hakko Kirin to commercialize daprodustat in Japan.

Daprodustat
GSK1278863/
Duvroq

Review and approval status

June 2020
Marketing authorization: MHLW

March 2022
Marketing authorization application (MAA) validated: European Medicines Agency (EMA)

April 2022
NDA accepted: U.S. FDA

February 1, 2023
PDUFA

Actual and expected launches
2020: Japan
2023: United States and Europe

Patents estimated to expire beginning in 2027

How will daprodustat impact the market for CKD-related anemia?

In the face of competition, uptake of daprodustat might be fostered by its oral formulation (versus intravenous), effective hemoglobin-raising efficacy for patients that have failed ESA therapy, reduction in the need for iron supplementation and likelihood for competitive pricing in comparison with the market-leading ESA brands.

Given the complete response letters (CRLs) from the FDA for vadadustat and roxadustat, daprodustat has the opportunity to be first-in-class in the United States for this patient population.

In Japan, Duvroq is leading market share (at ~47%) within the HIF class against four other competitors, despite being the second to launch.

Many patients in Japan are switching from the current standard of care or starting their treatment with Duvroq.

What gaps in treatment does daprodustat fill?

Anemia is a common complication of CKD and worsens as kidney disease progresses. Current treatment involves injectable recombinant ESAs, which have associated serious adverse cardiac reactions and risk of sudden cardiac death in addition to inconsistent responses. Daprodustat could potentially be a game changer for these patients, providing a safer option that significantly improves outcomes regardless of dialysis status.

What hurdles might it need to overcome to reach blockbuster status?

Daprodustat will compete with Aranesp®, MIRCERA® and EPOGEN®/PROCRIT®, which currently dominate market sales, in addition to other well-established therapeutic approaches in CKD such as intravenous iron replacement products and blood transfusions that offer rapid increases in hemoglobin levels.

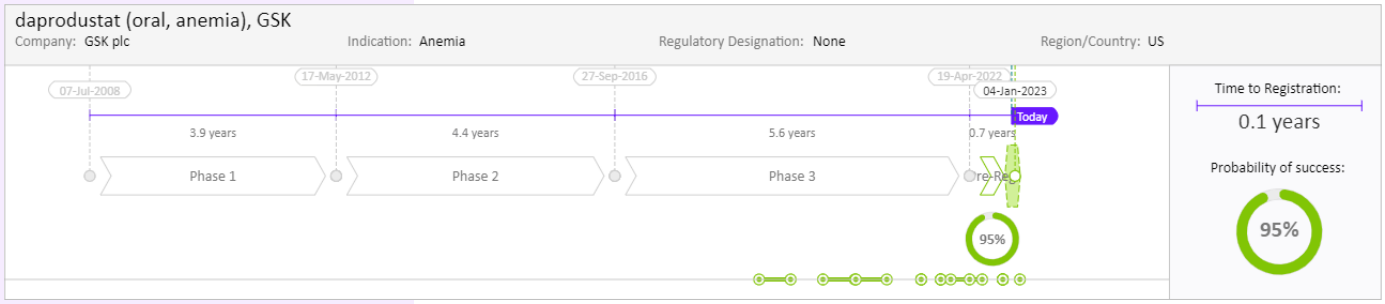
In October, the FDA's Cardiovascular and Renal Drugs Advisory Committee voted in favor of the drug's use in adult dialysis patients, but not in adult non-dialysis patients.

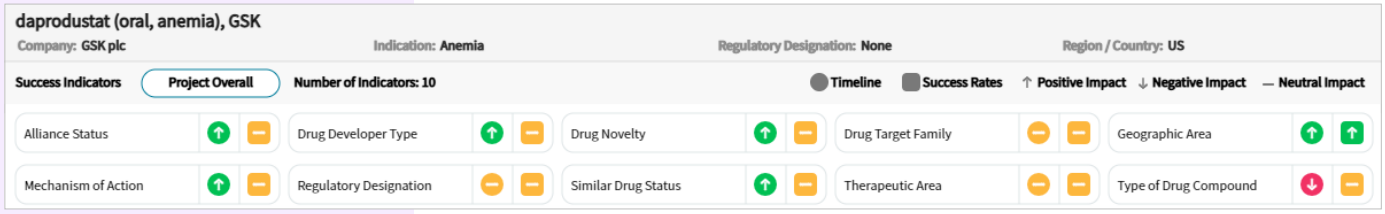
Daprodustat
GSK1278863/
Duvroq

Market overview

$0.53B

expected sales in 2027





Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate there is a 95% probability of success for daprodustat in the United States.

4 **Deucravacitinib**

Plaque psoriasis

Deucravacitinib
BMS-986165

About

Producer:
Bristol Myers Squibb

Type:
Allosteric TYK2 inhibitor

Usage:
Once-daily oral administration to treat moderate-to-severe plaque psoriasis

Also being investigated to treat pustular psoriasis, erythrodermic psoriasis, psoriatic arthritis, systemic lupus erythematosus and inflammatory bowel disease

Impact:

~11.7m

symptomatic psoriasis cases in the G7 markets in 2021

45 years

average age of symptomatic psoriasis cases

Approvals in Europe and Japan are expected to follow on the heels of the U.S. Food and Drug Administration (FDA) approval for deucravacitinib in September 2022. As a novel oral, targeted agent that selectively inhibits tyrosine kinase 2 (TYK2), a Janus kinase (JAK) family member that mediates cytokine-driven immune and inflammatory signals, it has the potential to fill a gap in the treatment armamentarium for plaque psoriasis.

In addition to its impact for these patients, it is being evaluated for other indications that could benefit more patient populations and boost overall sales.

Why is it a Drug to Watch?

Deucravacitinib is a first-in-class oral TYK2 inhibitor with a unique mechanism of action that inhibits signaling of IL-23, IL-12 and type 1 interferon (IFN), key cytokines involved in the pathogenesis of the multiple immune-mediated diseases for which deucravacitinib is being evaluated.

U.S. FDA approval was supported by results from two phase 3 trials, POETYK PSO-1 (deucravacitinib vs placebo) and POETYK PSO-2 (deucravacitinib vs twice-daily apremilast/Otezla®), with adults with moderate-to-severe plaque psoriasis in the United States, Europe and Japan, which showed:

- superior skin clearance of once-daily deucravacitinib at both 16 and 24 weeks, measured by Psoriasis Area Severity Index (PASI) 75 response and static Physician's Global Assessment (sPGA) 0/1;
- sustained response with deucravacitinib at 52 weeks; and
- a safety profile consistent with that noted in phase 2 trials.

Deucravacitinib
BMS-986165

Review and approval status

November 2021
NDA accepted: U.S. FDA

November 2021
Marketing authorization application (MAA) validated: European Medicines Agency (EMA)

December 2021
New Drug Application (NDA) submission: Japan's Ministry of Health, Labour and Welfare (MHLW)

September 2022
For patients with moderate-to-severe psoriasis who are candidates for systemic therapy or phototherapy: Approved: U.S. FDA, MHLW

Expected launches
2022: United States
2023: Europe

Actual launch
November 2022: Japan

Patents estimated to expire beginning in 2033

How will deucravacitinib impact the market for plaque psoriasis?

Uptake of deucravacitinib could be bolstered by its:

- oral administration with an efficacy that can compete with that of biologics, which might encourage use in patients who are failing on current oral agents and/or phototherapy and
- superior efficacy over apremliast, which could result in first-line use or for patients who are refractory or intolerant to apremilast, specially since physicians do not consider apremilast to be very efficacious.

Avoidance of a black box warning is positive for other TYK2 drugs currently in development.

What gaps in treatment does deucravacitinib fill?

For symptomatic patients with moderate-to-severe plaque psoriasis, safe, efficacious oral therapies remain an unmet need. Physicians and patients alike prefer the convenience of oral agents over the administration of subcutaneous therapies via injection pen. However, oral systemic drugs often have safety concerns such as renal impairment, hypertension, malignancy and teratogenicity that limit their long-term use. In addition, the currently available oral targeted therapy, apremilast, is not as effective as available biologics, a gap that could be filled by deucravacitinib.

What hurdles might it need to overcome to reach blockbuster status?

Although extra regulatory scrutiny on the safety profile of deucravacitinib was expected given that a previous oral therapy, tofacitinib, that targeted close parallel pathways (JAK1 and JAK3) was turned down by both the FDA and EMA based on its safety data, deucravacitinb avoided a black box label and was approved by the U.S. FDA. Despite some potential mild trepidation by prescribers initially, experts expect that deucravacitinib's efficacy and tolerability data will set it apart. It will compete with Otezla, which does not require the same level of monitoring as deucravacitinib, and the price point of deucravacitinib ($75,000 a year) is higher than that of Otezla ($55,000 per year). It remains to be seen if these will be barriers to uptake.

Deucravacitinib
BMS-986165

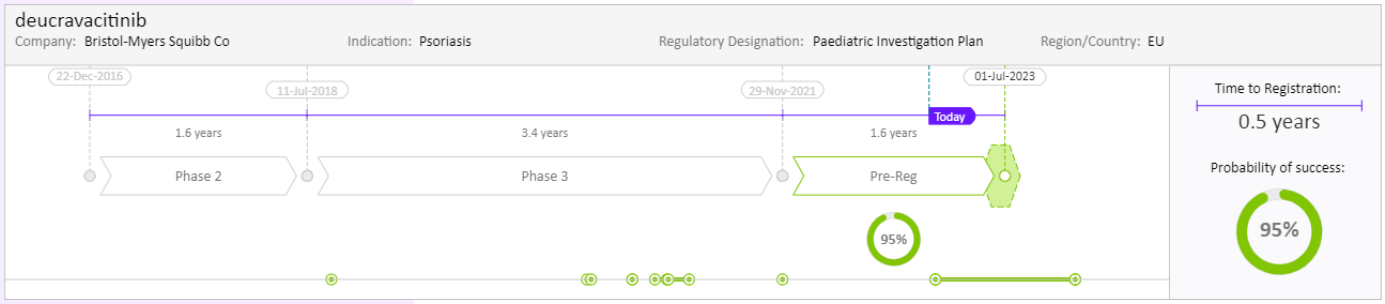
Market overview

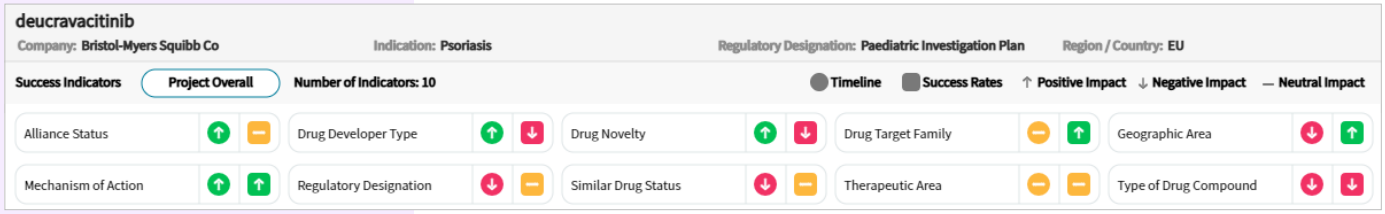
$2.12B

expected sales in 2027

"BMS-986165 is an oral agent and seems well tolerated. The data that I see are very encouraging, so it looks as though they have efficacy that is as good as biologics. If that's the case, then it's very exciting."

Dermatologist, United Kingdom





Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate there is a 95% probability of success for deucravacitinib in the European Union.

5 **Foscarbidopa/ foslevodopa**

Parkinson’s disease

Foscarbidopa/ foslevodopa
ABBV-951

About

Producer:
AbbVie

Type:
Carbidopa and levodopa prodrugs

Usage:
Continuous 24-hour subcutaneous infusion to treat motor fluctuations in patients with advanced Parkinson's disease

Impact:

2.8m

diagnosed prevalent cases of Parkinson's disease in the G7 markets in 2021

Foscarbidopa/foslevodopa, in development by AbbVie, is a novel reformulation of the gold-standard Parkinson's disease treatment (carbidopa/levodopa) delivered via a subcutaneous pump for the treatment of motor fluctuations in advanced Parkinson's disease.

In addition to serving a niche group of patients with high unmet need, it offers better efficacy than orally administered carbidopa-levodopa, dosing flexibility and a more convenient pump than existing and upcoming competitors and it is backed by AbbVie's experience in this space via its own DUOPA™/DUODOPA® (carbidopa/levodopa enteral suspension).

Why is it a Drug to Watch?

If launched when predicted, foscarbidopa/foslevodopa will be the first subcutaneous carbidopa/levodopa infusion to market, addressing noted shortcomings with DUOPA/DUODOPA (e.g., surgical requirements, complications).

Although many current treatment options manage motor fluctuations of Parkinson's disease, patients with advanced Parksinon's disease often achieve poor motor control, even with chronic polypharmacy. By stabilizing levodopa levels, AbbVie's pump will offer a more effective alternative for the right patients.

A randomized, controlled phase 3 trial showed:

- an increase in 'on' time of almost three hours compared with oral carbidopa-levodopa, as early as one week into the study and
- a decrease in 'off' time by a similar magnitude.

A single-arm, phase 3 trial showed:

- an increase in 'on' time of approximately three and a half hours and
- a decrease in participants with morning akinesia from 77.7% to 19.4%.

Ongoing phase 3 extension trials are further testing long-term safety and tolerability.

Foscarbidopa/ foslevodopa
ABBV-951

Review and approval status

May 2022
New Drug Application (NDA) submission: U.S. Food and Drug Administration (FDA)

Expected launch
2023: United States, Europe and Japan

Patents estimated to expire beginning in 2039

How will foscarbidopa/ foslevodopa impact the market for Parkinson's disease?

- Experts are enthusiastic about delivering levodopa-carbidopa via subcutaneous infusion.
- The ability to offer multiple dose strengths at one insertion site might prove a strong advantage for foscarbidopa/foslevodopa over the ND0612 pump by NeuroDerm Ltd (a wholly owned subsidiary of Mitsubishi Tanabe Pharma Corporation), which offers only one strength and requires two insertion sites.
- Foscarbidopa/foslevodopa will most likely be prescribed to intermediate and advanced-stage patients with motor fluctuations despite four or more daily doses of oral levodopa-carbidopa (plus one or more levodopa-adjunct therapies).
- It will compete primarily with other invasive therapies (i.e., DUOPA/ DUODOPA, ND0612, SPN-830 by Supernus Pharmaceutical Inc, Lecigon® by STADA and Lobsor Pharmaceutical, deep brain stimulation [DBS]) in advanced Parkinson's disease and may compete with longer-lasting oral levodopa reformulations and levodopa-adjunct therapies in uncontrolled intermediate-stage disease with a high pill burden.
- DBS is expected to remain a treatment of choice for advanced disease in younger patients, but foscarbidopa/ foslevodopa could be an alternative for patients ineligible for DBS or who do not want to undergo surgery.
- Efficacy, side effects and cost, as well as the convenience, size and dosing flexibility of competing pumps, will play important roles in treatment selection in advanced Parkinson's disease.
- Expected high pricing could drive blockbuster peak sales despite focused adoption.

What gaps in treatment does foscarbidopa/ foslevodopa fill?

Fluctuations in motor function ('on/off' periods) progressively worsen for most patients with Parkinson's disease until they are no longer effectively managed by available levodopa formulations and adjunctive therapies. These fluctuations impact the patient's ability to perform activities of daily living as well as quality of life for both patient and caregiver. With its continuous delivery, foscarbidopa/foslevodopa optimizes the pharmacokinetic/pharmacodynamic (PK/PD) profile of the standard of care, which may deliver profound relief for patients with Parkinson's disease, especially those in the later stages of the disease.

What hurdles might it need to overcome to reach blockbuster status?

Though it will be first to market, foscarbidopa/foslevodopa will compete with other subcutaneous pump options, most notably that by NeuroDerm Ltd expected to launch in mid-2024 and expected high pricing is likely to constrain access and uptake. Also of concern is the high rates of discontinuation of foscarbidopa/foslevodopa reported in completed phase 3 trials.

Foscarbidopa/ foslevodopa
ABBV-951

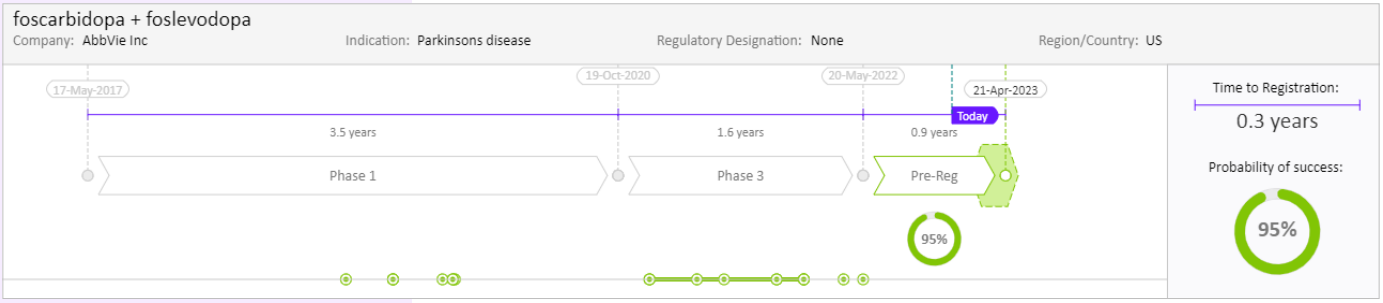
Market overview

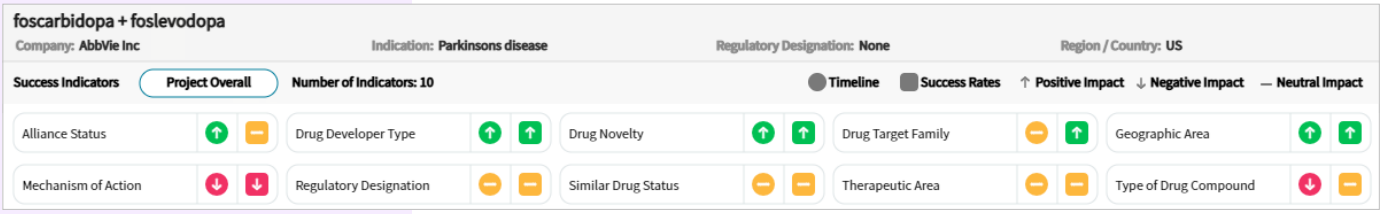
$0.88B

expected sales in 2027

"[ABBV-951] can be given continuously via pump subcutaneously. So, this means it will be much more helpful for patients and physicians than the classical Duodopa given in the small intestine. This will increase the number of patients to whom we propose this therapy, will increase the acceptability to the patient and will probably allow us to get rid of all the complications related to the intestinal device like infection."

Neurologist, Italy



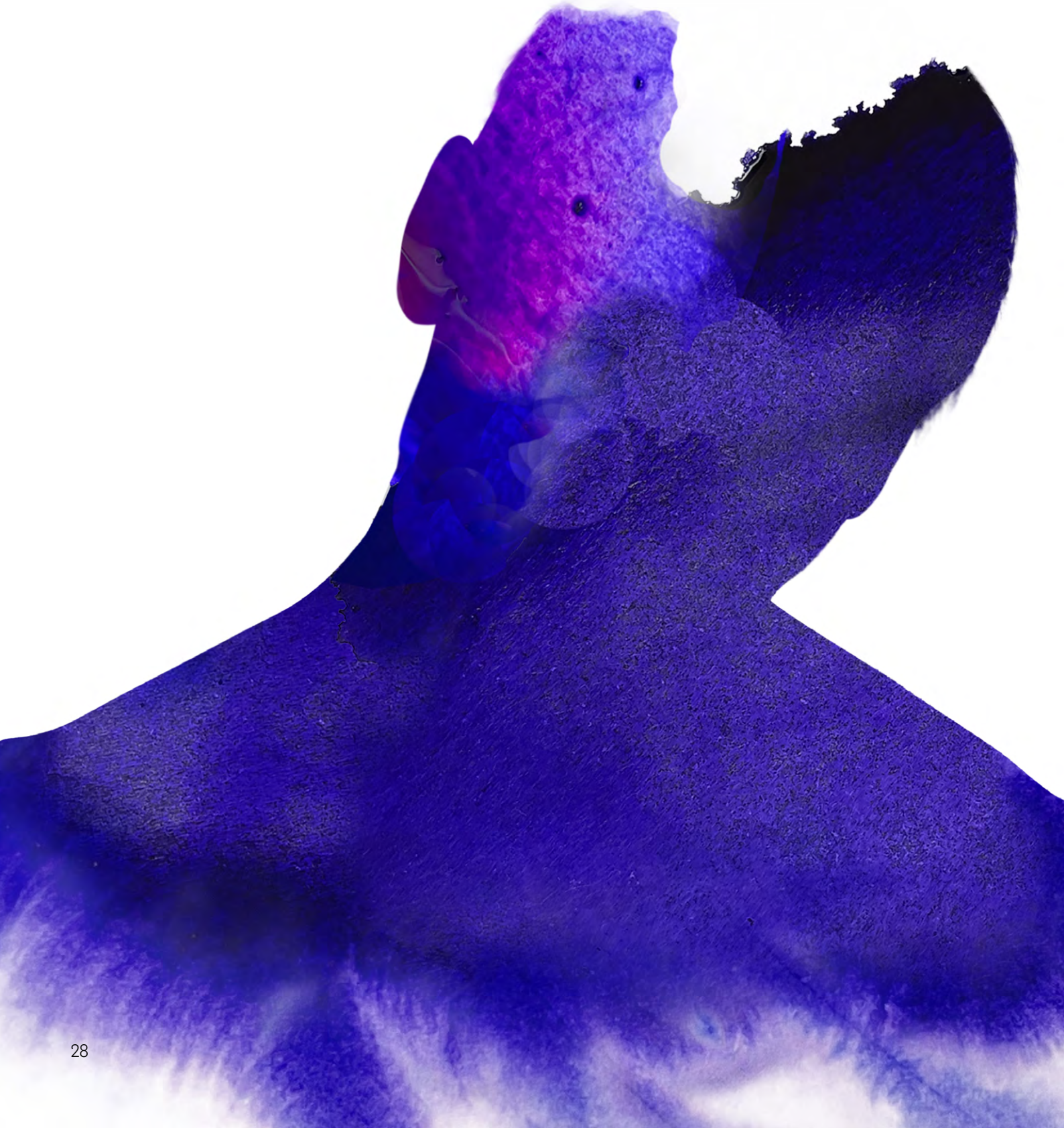


Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate there is a 95% probability of success for foscarbidopa/ foslevodopa in the United States.

6&7 **Lecanemab and Donanemab**

Alzheimer's disease



Lecanemab
LEQEMBI™
Donanemab
LY-3002813

About

Lecanemab

Producer:
Eisai Co Lt and Biogen Inc.

Type:
Anti-Aβ protofibril MAb

Usage:
Intravenous infusion every 2 weeks for the treatment of mild cognitive impairment (MCI) due to Alzheimer's disease and mild Alzheimer's disease

Less frequent maintenance dosing intervals and subcutaneous administration also being explored

Donanemab

Producer:
Eli Lilly and Company

Type:
Anti-Aβ N3pG MAb

Usage:
Intravenous infusion every 4 weeks for the treatment of MCI due to Alzheimer's disease and mild Alzheimer's disease

Impact:

~40m

people with Alzheimer's disease globally

>35%

expected increase in total prevalent cases of early Alzheimer's disease in the G7 markets by 2031 due to aging population

The U.S. Food and Drug Administration (FDA)'s accelerated approval of ADUHELM™ (aducanumab) for the treatment of early Alzheimer's disease in 2021 met with controversy and uptake was curtailed by a lack of clinician support and Medicare coverage.

Now, supported by landmark clinical data from a phase 3 trial, next-in-class anti-Aβ monoclonal antibody (MAb) lecanemab has been granted accelerated approval by FDA and appears poised for ex-U.S. launches, marketed under the brand name LEQEMBI™. Donanemab, and others in the class (e.g., Roche's gantenerumab), may follow suit pending the results of ongoing trials. If approved, differentiation in the areas of adverse events (AEs), convenience and clinical and biomarker efficacy will be key determinants of future uptake.

Why are they Drugs to Watch?

The U.S. FDA's accelerated approval of ADUHELM based on biomarker endpoints (i.e., decreased amyloid levels in the brain) opened the gate for U.S. regulatory submission based on similar data from other disease-modifying therapies (DMTs). The phase 3 trial readout for lecanemab validates the clinical efficacy of agents in this class, positions the drug for global regulatory approvals and bodes well for the phase 3 trial results for donanemab, which are still pending.

Lecanemab

- Both primary and secondary endpoints were met in the global confirmatory phase 3 CLARITY AD trial conducted with patients with early Alzheimer's disease: treatment led to significant changes in the global cognitive and functional scale (CDR-SB) starting at six months and reaching a 27% reduction in clinical decline at 18 months, compared with placebo. The incidence of amyloid-related imaging abnormalities-edema/effusion (ARIA-E) was 12.5% with lecanemab and 1.7% with placebo (35% with ADUHELM and 27% with donanemab, as reported in other studies).
- Phase 2 efficacy results showed a reduction in decline from baseline on the Alzheimer's Disease Composite Score (ADCOMS) and other metrics at 78 weeks and rapid, deep amyloid plaque clearance.
- The phase 3 AHEAD 3-45 and phase 2/3 DIAN-TU (in combination with E2814, an anti-tau MAb by Eisai Co Ltd) prevention studies are ongoing in patients with preclinical Alzheimer's disease and Alzheimer's disease– causing genetic mutations, respectively.

Donanemab

- Phase 3 studies (TRAILBLAZER-ALZ-2 and TRAILBLAZER-ALZ-3) are ongoing in patients with early Alzheimer's disease and preclinical Alzheimer's disease, respectively. Data from TRAILBLAZER-ALZ-2 are expected in the first half of 2023.
- Phase 2 efficacy results showed a reduction in decline from baseline on the Integrated AD Rating Scale (iADRS) and other metrics at week 76; rapid, deep reduction in amyloid plaques; and lower risk of ARIA-E (27%) than with ADUHELM (35%).
- A small phase 3 trial (TRAILBLAZER-ALZ-4) comparing donanemab with ADUHELM head-to-head on the superiority of amyloid plaque clearance in early Alzheimer's disease patients is ongoing, with data expected in late 2022.
- A global, placebo-controlled phase 3 trial (TRAILBLAZER-ALZ-5) evaluating the safety and efficacy of the drug in patients with early AD and tau pathology is ongoing, with completion expected in the first half of 2027.

Lecanemab
LEQEMBI™
Donanemab
LY-3002813

Review and approval status

Lecanemab

June 2021
Breakthrough Therapy designation: U.S. FDA

December 2021
Fast Track designation: U.S. FDA

March 2022
Submission under the 'prior assessment consultation': Pharmaceuticals and Medical Devices Agency (PMDA)

July 2022
Biologics License Application (BLA) accepted and priority review granted: U.S. FDA

January 6, 2023
Granted accelerated approval: U.S. FDA

Expected launch
2023: United States
2024: Japan and Europe

Patents estimated to expire beginning in 2025

Donanemab

June 2021
Breakthrough Therapy designation: U.S. FDA

August 2022
BLA accepted and priority review for accelerated approval granted: U.S. FDA

Expected launch
2023: United States
2025: Japan and Europe

Patents estimated to expire beginning in 2031

How will these drugs impact the treatment options for Alzheimer's disease?

Until the approval of ADUHELM, symptomatic therapy was the only treatment option for patients with Alzheimer's disease. Acetylcholinesterase inhibitors and memantine, now generic, have been and will continue to be the standard of care across mild, moderate and severe disease.

Other anti-Aβ DMTs are in late-phase development, including gantenerumab (Roche).

Many more drugs from a range of mechanisms of action (MOAs; e.g., tau-based therapies, sigma-1 receptor inhibitors, glucagon-like peptide 1 [GLP-1] analogues, SIGLEC3 and Trem2 antibodies) are in mid and late-phase trials, with potential for further differentiation (e.g., oral administration) and adjunctive use.

Regulatory success of anti-Aβ MAbs could infuse more investment dollars into dementia and influence companies' decisions about which drugs to develop; although this could lead to bypassing of other MOAs to develop next-gen anti-amyloid drugs, the existing pipeline is rich and modest clinical efficacy and AEs of near-to-market agents will sustain the opportunity for many future entrants.

Further trial results supporting the amyloid-beta hypothesis for Alzheimer's disease causality, as well as improved safety and delivery profiles, could facilitate uptake for lecanemab, donanemab and future anti-Aβ and non-Aβ–targeting drugs.

What gaps in treatment do donanemab and lecanemab fill?

The most critical need for patients with Alzheimer's disease has long been safe, effective DMTs that slow cognitive and functional decline. Uptake of ADUHELM is minimal for a multitude of reasons, limiting the patient benefit. Lecanemab and donanemab appear to offer improved risk/benefit profiles over ADUHELM, while additional therapies could eventually provide greater patient choice and the potential for synergistic combinations to maximize outcomes.

What hurdles might they need to overcome to reach blockbuster status?

Backed by positive phase 3 outcomes, blockbuster sales for lecenamab (and other putative DMTs) should easily be within reach based on population size, market demand and pricing. That said, the entry of ADUHELM accomplished little to prime health system preparedness and questions and challenges remain regarding access, reimbursement and affordability; early patient detection and presentation; seamless specialist referral and diagnosis pathways; infusion infrastructure; and healthcare provider perceptions about the risk/benefit of drugs in the class and their willingness to prescribe. Upcoming regulatory and payer decisions on lecanemab will likely set the precedent for others in the class and uptake is expected to be slow until reimbursement terms are set.

Lecanemab
LEQEMBI™

Market overview

$1.02B
expected sales in 2027

“Based on the data from the phase 2 trial, BAN-2401 could be more efficacious than aducanumab and looking at the numbers for ARIAs, I am just speculating that they are slightly less.”

Neurologist, Germany

Donanemab
LY-3002813

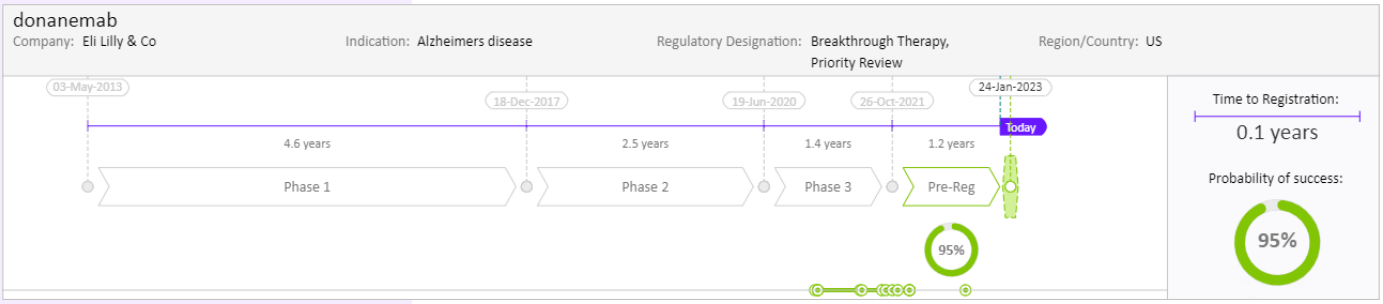
Market overview

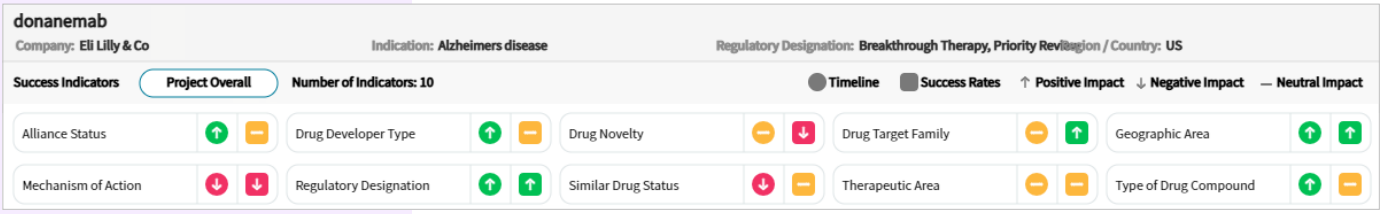
$1.34B

expected sales in 2027

"I think it's going to be better than aducanumab (due to the short treatment duration) because we can expect improvement in a shorter time. We can even compromise with the patients who would be not waiting so much to see if the drug works. We can take only maybe six months and, if it doesn't, we can stop the treatment."

Neurologist, Spain





Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate there is a 95% probability of success for donanemab in the United States.

8 Lenacapavir

HIV

Lenacapavir
Sunlenca®/GS-6207

About

Producer:
Gilead Sciences Inc.

Type:
Long-acting HIV-1 capsid inhibitor

Usage:
Twice yearly subcutaneous or oral administration to treat MDR HIV infection

Also being studied to treat HIV and as PrEP

Impact:

~38.4m

people had HIV globally in 2021

<10%

Only 6 countries globally have achieved <10% HIV drug resistance rates in long-term treated adults

Approved in Europe and the U.S., lenacapavir is a first-in-class, long-acting HIV-1 capsid inhibitor for the treatment of multi-drug resistant (MDR) HIV in people who have been heavily treated, a patient population with unmet medical need.

Also currently being investigated to treat HIV and for pre-exposure prophylaxis (PrEP), its infrequent dosing and self-administration will likely make it a favored choice in a population with treatment adherence challenges.

Why is it a Drug to Watch?

Lenacapavir inhibits HIV-1 at multiple stages during its lifecycle (capsid assembly, transport and disassembly), differentiating it from most other antivirals that target only one stage of viral replication and opening a new avenue for developing long-acting therapies for people living with or at risk of HIV.

It has no known cross resistance to other current drug classes.

Its multitarget inhibitory effect also presents a low risk of triggering drug resistance.

U.S. FDA and European Commission approvals were supported by data from the phase 2/3 CAPELLA study:

- Lenacapavir assessed in combination with an optimized background regimen in heavily treatment-experienced people with MDR HIV, a patient population with significant unmet need
- Undetectable viral load (<50 copies/mL) achieved by 83% of participants at week 52
- Mean increase in CD4 count of 83 cells/μL

Other phase 3 studies are ongoing and planned to assess lenacapavir for PrEP:

- PURPOSE 1: lenacapavir and emtricitabine/tenofovir alafenamide for PrEP in adolescent girls and young women at risk of HIV infection
- PURPOSE 2: lenacapavir for PrEP in cisgender men, transgender women, transgender men and gender non-binary individuals who have sex with partners assigned male at birth

In March 2021, Gilead Sciences Inc. and Merck entered an agreement to co-develop and co-commercialize lenacapavir and islatravir (nucleoside reverse transcriptase translocation inhibitor) into a two-drug regimen.

Lenacapavir
Sunlenca®/
GS-6207

Review and approval status

August 2022
For adult patients with MDR HIV infection: Marketing authorization: EC

December 2022
For heavily-treatment-experienced adult patients with MDR HIV-1 infection: Marketing authorization: U.S.

Actual and expected launch
2022: Europe
2023: United States
2028: Japan

Patents estimated to expire beginning in 2028

How will lenacapavir impact the market for HIV?

Lenacapavir is expected to have a competitive advantage given its convenient, twice-yearly administration that will help address treatment burden and social stigma. Rapid uptake is therefore anticipated and it is predicted that lenacapavir will account for more than one-half of yearly sales of long-acting regimens by 2031.

What gaps in treatment does lenacapavir fill?

MDR is a growing issue for people living with HIV, creating challenges with disease management for the patients themselves as well as in achieving global goals of ending the HIV epidemic. There is significant unmet medical need in particular for heavily treatment-experienced people with MDR HIV. With its convenient self-administration method and twice-yearly dosing, lenacapavir could overcome the lack of adherence to HIV therapies that can occur due to the burden of daily dosing (pill fatigue) and stigma related to HIV. The lower gastrointestinal toxicity, reduction in related side effects and fewer drug-drug interactions will also make lenacapavir more tolerable for many people living with HIV.

What hurdles might it need to overcome to reach blockbuster status?

Given the relatively small sample size and short length of the phase 2/3 CAPELLA study, long-term data are needed to convince health care providers to prescribe lenacapavir in patients with MDR, especially because of the robust, long-term data for RUKOBIA (ViiV Healthcare) in the same population. For development as a long-acting regimen for HIV treatment (not in the presence of MDR), a good partner agent is needed. The most advanced combination to date (lenacapavir + Merck's islatravir) was temporarily paused due to a dose-dependent decrease in white blood cell counts, but phase 2 trials are expected to resume. Although expected to be approved for HIV PrEP in 2025, lenacapavir will need to demonstrate better safety and efficacy than currently available long-action options. Pricing will also play a role in uptake as PrEP, since DESCOVY® will also go off patent in 2025 and pricing will likely become competitive.

Lenacapavir
Sunlenca®/
GS-6207

Market overview

$1.08B
expected sales in 2027

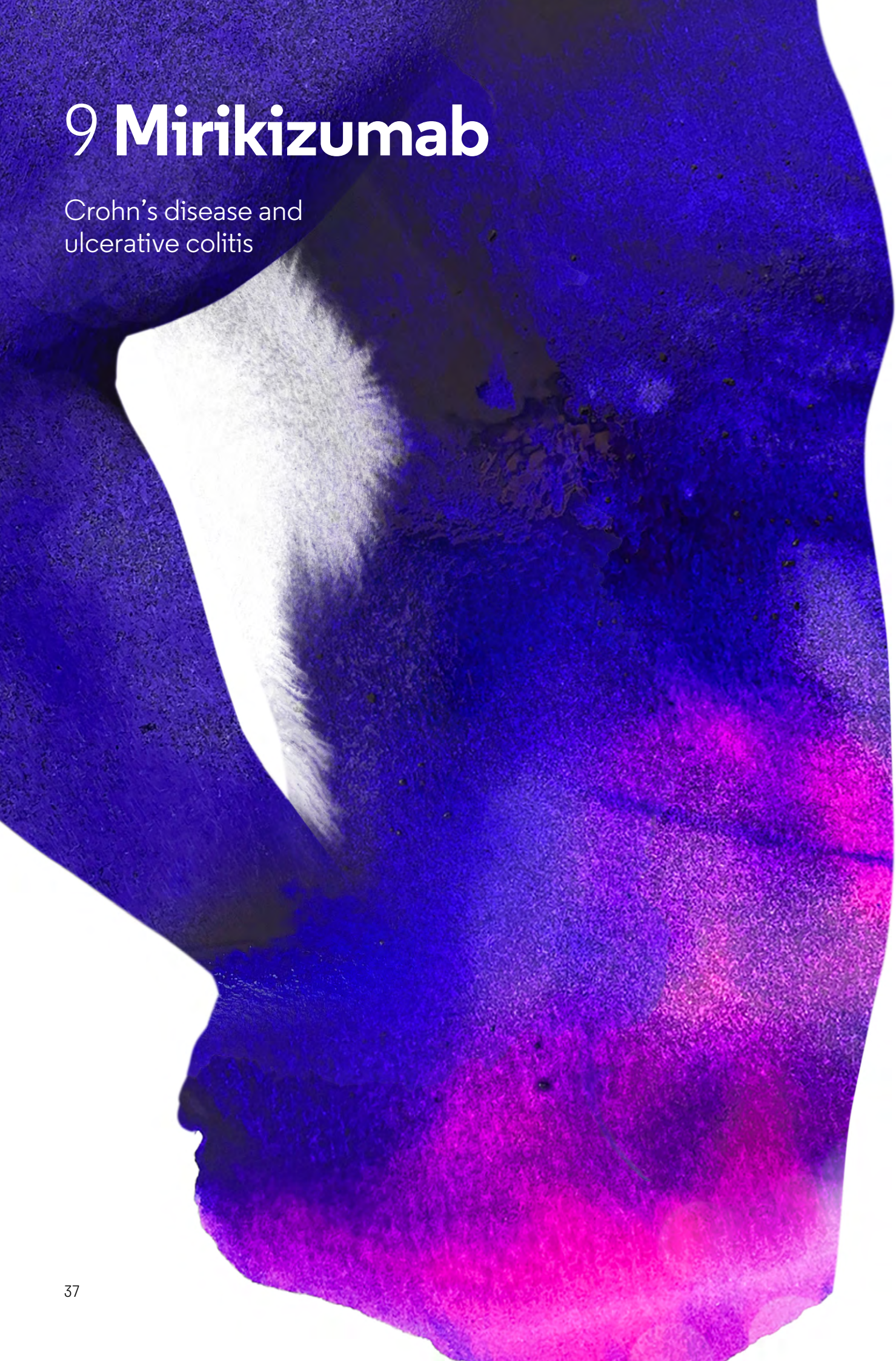
"Lenacapavir is quite promising. We need more data on both its efficacy and safety, but I think it's exceedingly promising because of the potential to be given subcutaneously every six months."

Infectious disease specialist, United States

Cortellis data indicate there is a 90% probability of success for lenacapavir in Japan.

9 Mirikizumab

Crohn's disease and
ulcerative colitis



Mirikizumab
LY-3074828

About

Producer:
Eli Lilly and Company

Type:
Humanized IgG4 monoclonal antibody

Usage:
Monthly intravenous or subcutaneous administration to treat Crohn's disease and moderately-to-severely active ulcerative colitis

Impact:

Crohn's disease:

~1.8m

diagnosed prevalent cases in the G7 markets in 2021

Ulcerative colitis:

~2.3m

diagnosed prevalent cases in the G7 markets in 2021

Mirikizumab, a monoclonal antibody targeting the p19 subunit of IL-23, will likely be first-in-class for ulcerative colitis and the third in the class approved for Crohn's disease.

Part of a set of emerging therapies with novel mechanisms of action, it will contribute to the growing market share held by these therapies and potentially more efficacious and long-lasting treatment options for patients.

Why is it a Drug to Watch?

Based on positive phase 2 results for patients with Crohn's disease (significant reductions in disease severity and increased rates of remission), mirikizumab advanced into the following phase 3 studies:

- VIVID-1: mirikizumab vs ustekinumab or placebo in patients 15 to 80 years old with moderate-to-severe disease; with a primary completion date in December 2023, expected to serve as the basis for regulatory filings in the United States, Europe and Japan
- VIVID-2: long-term extension study to evaluate efficacy and safety

Positive results from the phase 3 LUCENT 1 induction study (vs placebo) with patients with moderate-to-severe ulcerative colitis showed improvement as early as four weeks and, at 12 weeks, met its primary and all key secondary endpoints of:

- Clinical remission
- Endoscopic remission
- Symptomatic remission
- Reduced bowel urgency
- Clinical response
- Improvement in endoscopic histologic inflammation

The phase 3 LUCENT-2 study followed LUCENT-1 participants for one year and showed:

- nearly two-thirds of participants maintained clinical remission at one year and
- nearly all participants with clinical remission at one year were not taking corticosteroids for at least three months prior to the end of maintenance treatment.

These results were regardless of previous failure to TNF inhibitors, tofacitinib or other biologics.

Ongoing phase 3 studies include:

- LUCENT-3: long-term extension study to evaluate efficacy and safety
- SHINE-1: evaluating mirikizumab in pediatric participants (aged 2-17 years)

Mirikizumab
LY-3074828

Review and approval status

Ulcerative colitis

March 2022
Biologics License Application (BLA) submission: U.S. Food and Drug Administration (FDA)

March 2022
Marketing authorization application submission: European Medicines Agency (EMA)

Q2 2022
Marketing authorization submission: Japan's Ministry of Health, Labor and Welfare (MHLW)

Crohn's disease expected launch
2025: United States, Japan and Europe

Ulcerative colitis expected launch
2023: United States, Japan and Europe

Patents estimated to expire beginning in 2034

How will mirikizumab impact the market for Crohn's disease and ulcerative colitis?

- Because treatments for Crohn's disease and ulcerative colitis vary significantly in potency, onset of action, side effect profile and route of administration, symptom severity and remission status contribute to drug selection.
- Growth in the market for both diseases is most likely driven by increasing uptake of ENTYVIO® and STELARA® and approval and uptake of premium-priced emerging therapies, including mirikizumab.
- Entry of the biosimilar ustekinumab could temper sales of competing therapies.
- Several novel agents, including mirikizumab, are launching for both diseases within the next couple of years, making competition fierce and the market increasingly fragmented.

Crohn's disease

- Mirikizumab is the third IL-23 inhibitor launching for Crohn's disease.
- Emerging therapies, including mirikizumab, will most likely be used in patients refractory to TNF-α inhibitors or who have failed multiple biological agents.
- There is significant commercial opportunity to treat patients refractory to TNF-α inhibitors given they fail to achieve treatment goals in a large proportion of patients.

Ulcerative colitis

- Mirikizumab is expected to launch at the same time as two other IL-23 inhibitors.
- Targeted therapies, such as mirikizumab, are typically used to treat moderate-to-severe disease.
- There is potential for approval in the pediatric population: expanded patient population, differentiation from other in-class competitors, filling the gap in limited targeted therapies for this population.

What gaps in treatment does mirikizumab fill?

Both Crohn's disease and ulcerative colitis are characterized by intermittent disease courses, with acute flares followed by periods of remission. Patients risk hospitalization and the need for surgical intervention, in addition to experiencing poorer quality of life. Neither disease has a cure, so pharmacotherapy aims to induce remission of acute flairs, maintain remission (without corticosteroids) and improve quality of life. Treatment gaps that mirikizumab could help fill include sustainable long-term remission (many patients lose response to biologics) and therapies with alternative mechanisms of action for patients intolerant or resistant to TNF-α inhibitors.

What hurdles might it need to overcome to reach blockbuster status?

The later market entry of mirikizumab, after STELARA and other IL-23 inhibitors, for both Crohn's disease and ulcerative colitis, will likely restrain its uptake. Regarding STELARA, gastroenterologists will have had 6-8 years of clinical experience prescribing it and, at least initially, new IL-23 inhibitors are unlikely to steal significant patient share and could be used primarily as later-line therapies. In addition, the launch of biosimilar ustekinumab, which is expected in 2023, could encroach on the use of all IL-23 inhibitors. Unless it shows significantly greater safety and efficacy, mirikizumab will be one of many therapeutic options in an increasingly crowded space.

Mirikizumab
LY-3074828

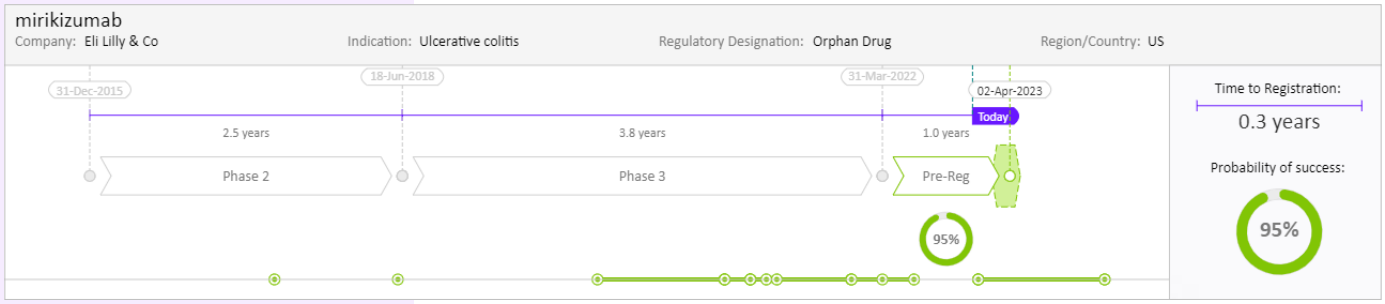
Market overview

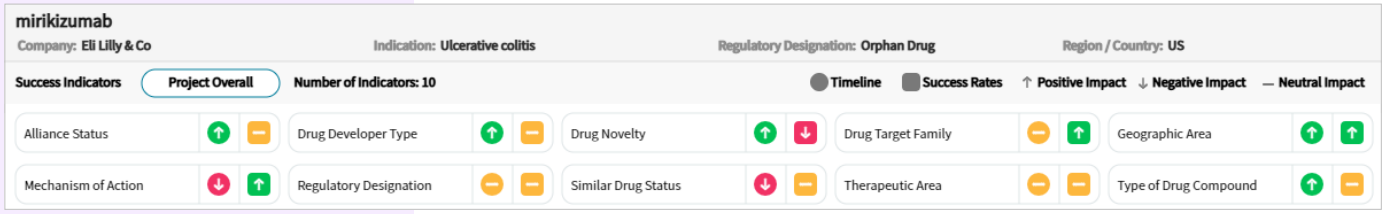
$0.595B

expected sales in 2027

“I feel that the data for mirikizumab are very good. Also, I would say that we still need overall data. I do not have a preference among all interleukin inhibitors; however, there is preference for ustekinumab because it is already in the clinical practice system.”

Gastroenterologist, Italy



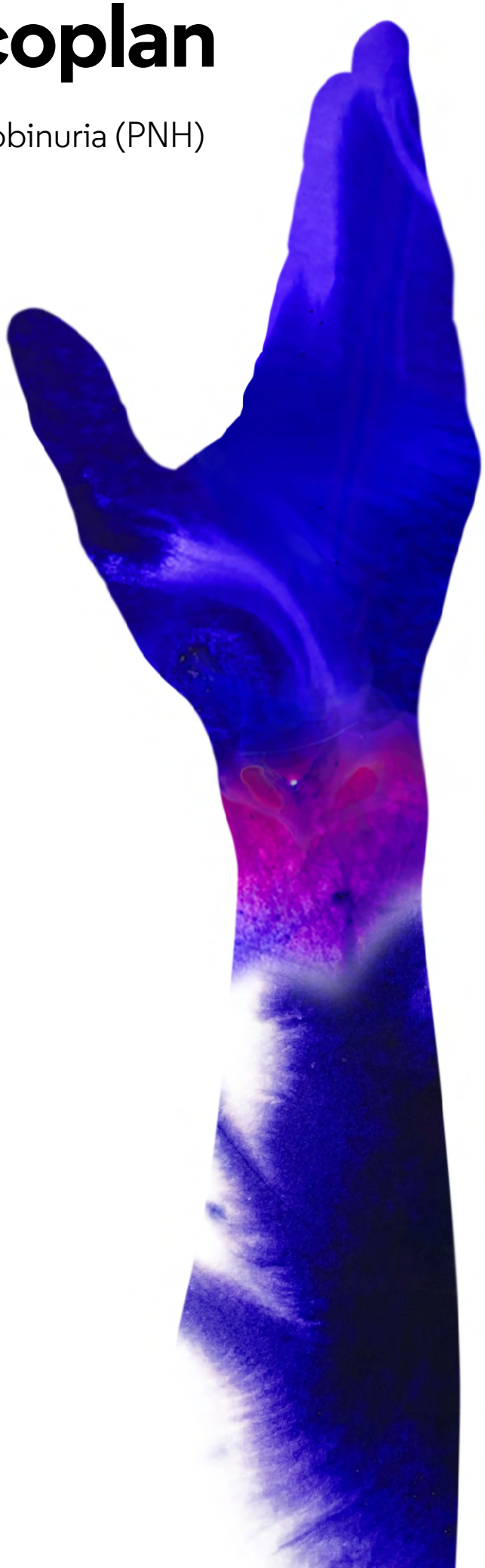


Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate there is a 95% probability of success for mirikizumab for ulcerative colitis in the United States.

10 **Pegcetacoplan**

Paroxysmal nocturnal hemoglobinuria (PNH)
and geographic atrophy (GA)



Pegcetacoplan
EMPAVELI®/
ASPAVELI®/APL-2

About

Producer:
Apellis Pharmaceuticals Inc.

Type:
Complement C3 inhibitor

Usage:
Twice-weekly subcutaneous infusion via pump to treat PNH

Monthly or every-other-month intravitreal administration to treat GA secondary to AMD

Also being investigated for immune complex membranoproliferative glomerulonephritis (IC-MPGN), C3 glomerulopathy (C3G), amyotrophic lateral sclerosis (ALS), cold agglutinin disease (CAD) and hematopoietic stem cell transplantation-associated thrombotic microangiopathy (HSCT-TMA)

Impact:

2.0

cases per 100,000 people: prevalence of PNH in the G7 markets in 2021

~2.3m

cases of GA in the G7 markets in 2021

Pegcetacoplan has launched already in the United States and Europe for PNH, a rare hematological disease. As one of the few drugs to have completed phase 3 trials for GA, pegcetacoplan is anticipated to be the first drug to launch for GA or 'dry late age-related macular degeneration (AMD)', which has no approved pharmacotherapy.

The U.S. Food and Drug Administration (FDA)'s granting of fast track status and priority review designation underscores the unmet need in this underserved patient population and the potential for pegcetacoplan to experience commercial success upon launch.

Why is it a Drug to Watch?

Subcutaneous pegcetacoplan generated $15.1 million in sales in 2021 following its launch in the United States in May 2021 to treat PNH. Additional global approvals for PNH will likely contribute to greater sales over the coming years and the contribution of sales for PNH is likely to be smaller than that for GA.

If launched when expected, pegcetacoplan will be the first GA therapy to market. Its novel mechanism of action targets complement C3, which has been detected in drusen in the retina of GA patients and shown to induce VEGF expression. It has demonstrated the ability to delay GA progression and its potential bimonthly dosing could prove to be an advantage over other competitors with monthly dosing only.

The New Drug Application (NDA) submitted to the U.S. FDA for GA was supported by results from phase 2 and 3 trials.

Phase 2 FILLY: significantly slowed GA progression at 18 months

Phase 3 OAKS and DERBY trials:

- Monthly and bimonthly administrations reduced lesion growth from baseline (OAKS: 22% and 18%; DERBY: 19% and 16%, respectively) at 24 months compared with sham treatment, suggesting an accelerated effect over the treatment duration, which could encourage treatment adherence in the absence of visual acuity improvements
- Reduction in GA lesion growth regardless of distance from the fovea, which could lead to a more inclusive label than Zimura (Iveric Bio; tested only in extrafoveal lesions)
- Favorable safety for 11,757 injections over 24 months (0.034% rate of endophthalmitis/injection; 0.24% rate of intraocular inflammation/injection), with no reported cases of occlusive vasculitis or retinitis

Pending data from the three-year open label extension study, GALE, may demonstrate long-term safety, an improved treatment effect and favorable functional data.

Pegcetacoplan
EMPAVELI®/
ASPAVELI®/APL-2

Review and approval status

May 2021
For adults with PNH:
Approval: U.S. FDA

December 2021
For adults with PNH who are anemic after treatment with a C5 inhibitor for at least three months: Marketing authorization: European Commission (EC)

For GA secondary to AMD:

July 2018
Priority Review designation:
U.S. FDA

July 2022
Fast track designation:
U.S. FDA

December 2022
Anticipated submission for marketing authorization:
European Medicines Agency (EMA)

February 2023
PDUFA date (FDA)

PNH Actual and expected launch
2021: United States
2022: Europe

GA Actual and expected launch
2023: United States
2024: Europe

Patents estimated to expire beginning in 2033

How will pegcetacoplan impact the market for PNH and GA?

- With the aging population across the major markets, the prevalence of GA is expected to continue increasing and the launch of pegcetacoplan and of Zimura could lead to increased GA diagnoses.
- The promising results from the phase 3 trials bode well for the mechanism of action and could pave the way for other complement system inhibitors to make it to market.
- There are no therapies currently approved for the treatment of GA and there is substantial unmet need.
- The majority of sales will likely result from the intravitreal formulation for GA.
- Moderate uptake is expected upon launch, balanced between the approval based on slowing of GA progression and the lack of efficacy for visual acuity improvement, a more meaningful endpoint for quality of life.
- Pegcetacoplan is poised to be the first therapy approved for GA, providing a first-to-market advantage over Zimura, which is expected to launch a full year after pegcetacoplan.
- Pegcetacoplan is forecasted to have 76% of overall complement system inhibitor market share in the United States and Europe in 2027.

What gaps in treatment does pegcetacoplan fill?

PNH is a rare, acquired, life-threatening blood disease that has historically required either frequent intravenous infusions or a bone marrow transplant in more severe cases, both related with high treatment burden. More convenient, longer-lasting treatments have only recently begun to be available and could improve both adherence and outcomes.

The largest unmet need for patients with GA has been an efficacious and safe therapy. Over time, patients with GA experience severe vision impairment and blindness, resulting in loss of independence and decreased quality of life. There are currently no approved treatments for GA. Therefore, pegcetacoplan has the potential to fulfill this unmet need, slow the progression of GA and maintain sight for millions of patients.

What hurdles might it need to overcome to reach blockbuster status?

Despite its potential first-to-market launch into an area of high unmet need, the uptake of pegcetacoplan might be tempered by the need for monthly or bimonthly intravitreal administration, especially since many patients with GA are asymptomatic and not experiencing notable vision loss. This dosing interval in addition to the lack of therapeutic benefit on patients' visual acuity likely contributed to the relatively high treatment discontinuation rates seen in phase 2 and 3 trials for GA. It also remains to be seen if targeting the complement cascade in GA is efficacious and safe in the long term, following the failure of lampalizumab, a complement D factor inhibitor, in phase 3 trials and its discontinuation for GA. Pegcetacoplan will need to demonstrate long-term efficacy and safety to drive its uptake among retinal specialists and ophthalmologists. The complement inhibitor pipeline is crowded and pegcetacoplan could face competition from numerous other competitors, including Zimura (complement C5 inhibitor, Iveric Bio, phase 3 for GA in the United States and Europe), danicopan (complement D factor inhibitor, Alexion Pharmaceuticals Inc and AstraZeneca, phase 2 for PNH and GA) and iptacoplan (oral complement B factor inhibitor, Novartis, phase 2 for PNH and GA).

Pegcetacoplan
EMPAVELI®/
ASPAVELI®/APL-2

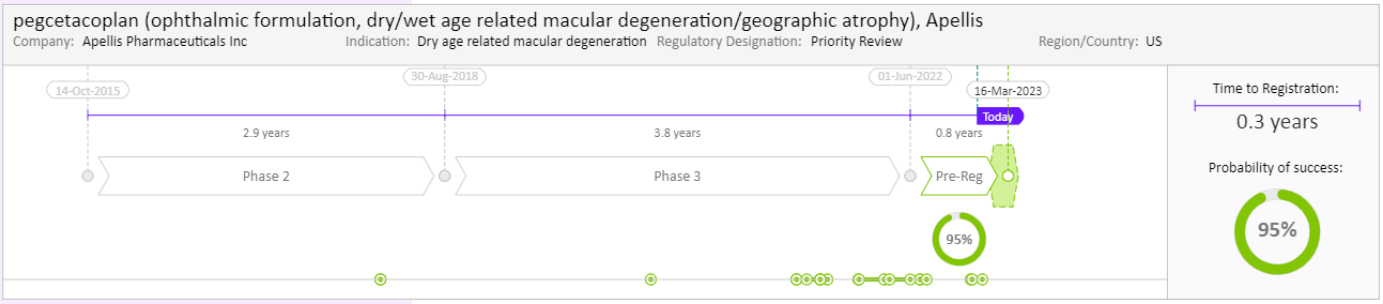
Market overview

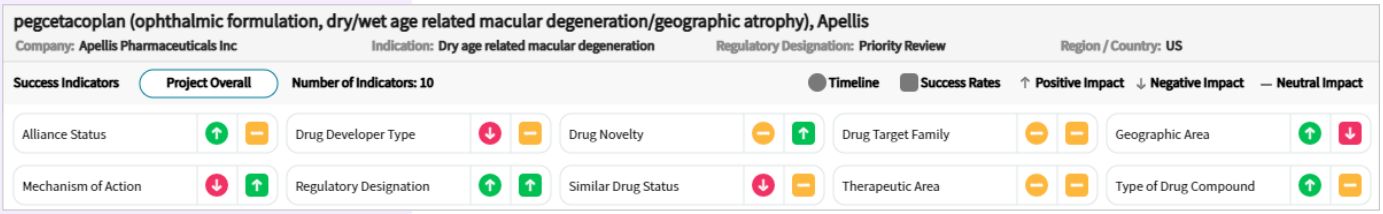
$1.312

expected sales in 2027 for GA

"Pegcetacoplan and Zimura both seem to slow down the growth of lesions. It sounds very promising because we have nothing to offer these patients. I'm not sure which of the two will be the first to get to market, but the one to do so will have a huge advantage."

Retinal specialist, United States





Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate there is a 95% probability of success for pegcetacoplan for GA in the United States.

ll Ritlecitinib

Alopecia

Ritlecitinib
PF-06651600

About

Producer:
Pfizer Inc

Type:
Janus kinase 3 (JAK3)/ TEC inhibitor

Usage:
Daily oral administration to treat alopecia areata

Also being evaluated for vitiligo, Crohn's disease, ulcerative colitis and, in combination with either tofacitinib or zimlovisertib, rheumatoid arthritis

Impact:

~4.7m

people with alopecia areata in the United States and top five European markets in 2020

Ritlecitinib will likely benefit from its first-in-class status, rapid onset of action and expected label for both adults and adolescents, potentially providing an effective option to stimulate hair growth in a stigmatizing disease.

It is currently the only JAK inhibitor being evaluated for adolescent patients who are the most likely to aggressively seek care for a disorder that profoundly affects their physical appearance.

Why is it a Drug to Watch?

Ritlecitinib is the first in a new class of oral, highly selective kinase inhibitors. It is a dual inhibitor of the TEC family of tyrosine kinases and of Janus kinase 3 (JAK3).

The New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) and marketing authorization application (MAA) to the European Medicines Agency (EMA) were supported by data from the phase 2B/3, dose-ranging ALLEGRO study in patients 12 years and older with at least 50% scalp hair loss:

- The 30 mg and 50 mg doses resulted in significantly greater proportions of patients with no more than 20% hair loss after six months compared with placebo.
- Ritlecitinib was tolerated well by adults and adolescents.

The phase 3 ALLEGRO-LT study is investigating the drug's long-term safety and efficacy at the 50 mg dose.

Ritlecitinib
PF-06651600

Review and approval status

September 2018
Breakthrough Therapy Designation: U.S. FDA

September 2022
NDA accepted: U.S. FDA
MAA accepted: EMA

Expected launch
2023: United States
2024: Europe

Patents estimated to expire beginning in 2039

How will ritlecitinib impact the market for alopecia areata?

This large and under-served market is expected to grow to as much as $2.5 billion by 2030 in the United States and the top five European markets (Germany, France, the U.K., Spain and Italy), largely driven by JAK inhibitors. Ritlecitinib's broad target population and first-in-class status are expected to help it achieve a 2.0% and 1.4% share of drug-treated patients in the United States and the top five European markets, respectively, by 2030.

- First-line therapy for nearly all treated, newly diagnosed patients involves topical corticosteroids; when those are insufficient, systemic corticosteroids are used.
- Only one therapy is currently approved to treat alopecia areata—Olumiant®, which received U.S. FDA approval and a positive Committee for Medicinal Products for Human Use (CHMP) opinion in 2022—but JAK inhibitors have been used off-label for years.
- Despite the class-wide black box warning for serious infections, mortality, malignancy, major adverse cardiovascular events (MACE) and thrombosis, the long history of JAK inhibitor use for other indications has contributed to their use in alopecia areata.
- The safety risks outlined in the black box warning have particularly constrained off-label use of JAK inhibitors in pediatric and adolescent patients.
- Entrenched, inexpensive, off-label treatment options such as corticosteroids could mean new therapies are used as later-line therapies or in more severe cases.
- Numerous studies showing the efficacy of JAK inhibitors for hair regrowth has garnered interest in their use.

What gaps in treatment does ritlecitinib fill?

Alopecia areata often causes hair loss at the scalp but can also affect eyebrows, eyelashes, facial hair and other areas, leading to a potentially negative impact on patients' daily lives and a significant emotional burden. First-line therapy for new diagnoses are topical corticosteroids, which vary in their effectiveness at hair regrowth.

What hurdles might it need to overcome to reach blockbuster status?

Given the existing concerns about safety issues associated with JAK inhibitors, adoption will likely depend on the safety data from the phase 3 ALLEGRO-LT trial. This is especially true given alopecia is primarily a cosmetic disease, for which the benefit will need to outweigh the risk. Competition from other JAK inhibitors in the market or in late-stage development could also limit uptake.

Ritlecitinib
PF-06651600

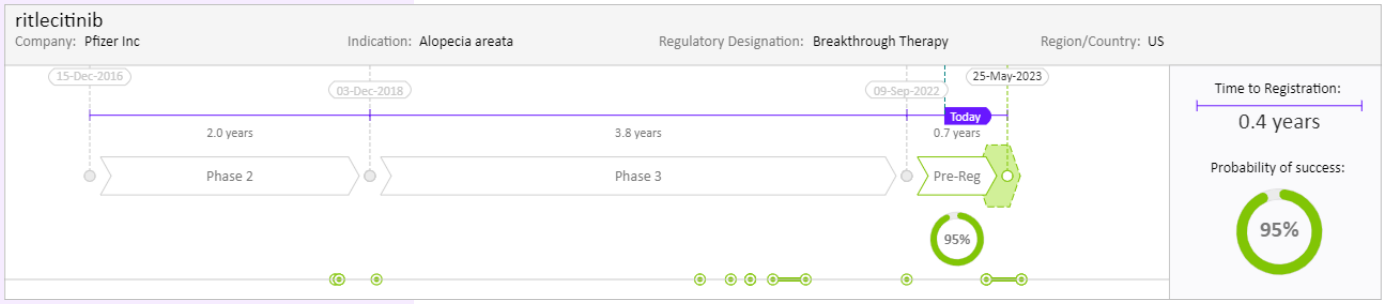
Market overview

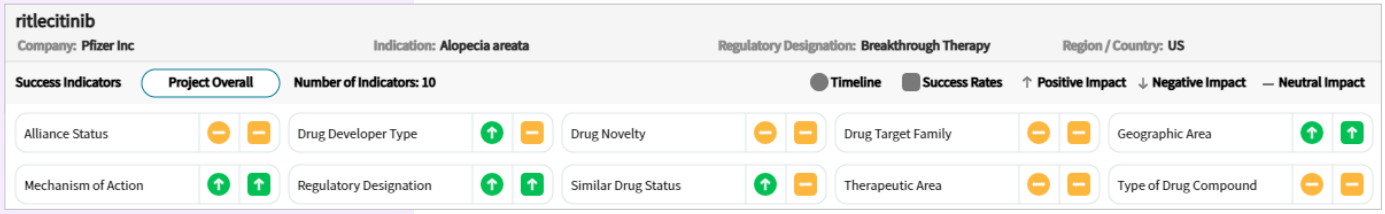
$0.20B

expected sales in 2027

“It is important that adolescent patients are being included in pivotal trials because adolescents are often the patients most profoundly affected by alopecia areata.”

Several interviewed physicians, United States





Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate there is a 95% probability of success for ritlecitinib in the United States.

12 Sparsentan

Rare kidney disorders

Sparsentan

About

Producer:
Travere Therapeutics Inc

Type:
Dual endothelin angiotensin receptor antagonist (DEARA)

Usage:
Daily oral administration to treat IgA nephropathy and FSGS

Impact:

~200–350k

people with IgA nephropathy globally

FSGS:

~1/7m

Affects approximately seven in one million individuals

Sparsentan is a first-in-class, orally active, single molecule that functions as a high-affinity, dual-acting antagonist of both endothelin type A (ETA) and angiotensin II subtype 1 (AT1) receptors, which are associated with progression of kidney disease.

Its development for IgA nephropathy and FSGS promises to halt that progression for many patients and fills a gap in the treatment armamentarium.

Why is it a Drug to Watch?

- Preclinical data have shown that blockades of both ETA and AT1 pathways can reduce proteinuria, protect podocytes and prevent glomerulosclerosis in rare chronic kidney diseases such as IgA neuropathy and FSGS.
- Data from the phase 3 PROTECT trial supported the submission to the FDA for IgA nephropathy. The study showed a greater than threefold reduction in proteinuria from baseline after 3 weeks compared with the active control irbesartan (angiotensin II receptor binder).
- The phase 3 DUPLEX trial for FSGS is ongoing. Interim data showed significantly more people in the sparsentan arm (42%) achieved FSGS partial remission endpoint (FPRE) than in the irbesartan comparator arm (26%).
- If approved for both indications, it could be the first treatment on the market to address both populations.
- In September 2021, Travere Therapeutics Inc and Vifor Pharma AG entered a collaboration and licensing agreement for the commercialization of sparsentan in Europe, Australia and New Zealand.

Sparsentan

Review and approval status

IgA nephropathy

January 2021
Orphan drug designation: U.S. Food and Drug Administration (FDA)

February 2021
Orphan drug designation: European Commission (EC)

May 2022
Priority review of New Drug Application (NDA) accepted: U.S. FDA

August 2022
Conditional marketing authorization accepted: European Medicines Agency (EMA)

February 17, 2023
PDUFA date

Expected approval for IgAN
2023: the United States and the European Union

Patents estimated to expire beginning in 2030

How will sparsentan impact the market for IgA nephropathy and FSGS?

- The first commercially available treatment specifically for IgA nephropathy is TARPEYO™, which was approved by the U.S. FDA via the accelerated approval pathway and launched in Q1 2022.
- If trial data from sparsentan provide evidence that it protects kidney function, it could have a competitive advantage over TARPEYO, which is awaiting additional data to determine if it slows the decline of kidney function.
- Because of different mechanisms of action, it remains to be seen if sparsentan and TARPEYO will vie for the same IgA nephropathy market.

What gaps in treatment does sparsentan fill?

Both IgA nephropathy and FSGS are rare kidney disorders that can lead to end-stage renal disease requiring dialysis or a kidney transplant. IgA nephropathy generally progresses slowly, while FSGS can follow an aggressive clinical course. Treatment is primarily directed at managing symptoms. Corticosteroids or other immunosuppressive drugs are routinely combined with renin-angiotensin-aldosterone system inhibitors (RAASIs), but these are limited by serious side effects. Therefore, effective, safe and well-tolerated drugs that protect kidney function or slow the progressive decline in glomerular filtration rate (GFR) are needed.

What hurdles might it need to overcome to reach blockbuster status?

Sparsentan will not be the first treatment specifically for IgA nephropathy after the launch of TARPEYO in early 2022. Other potential competitors in what could become a competitive market are currently in late-stage development.

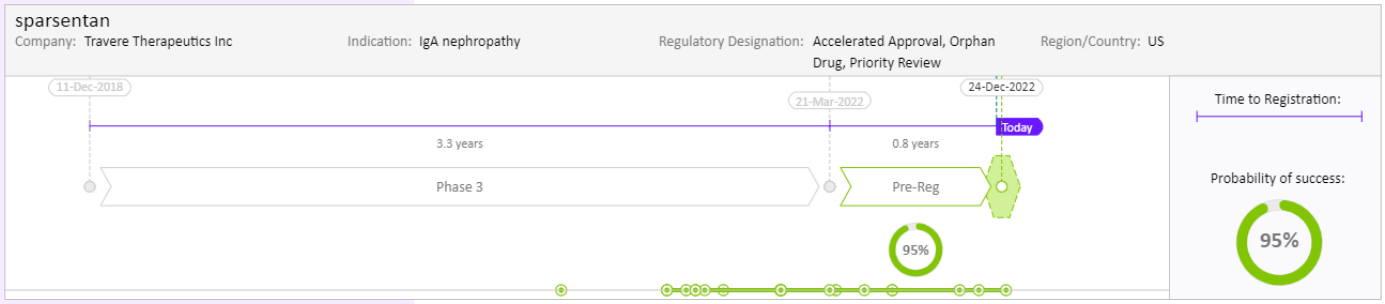
Sparsentan

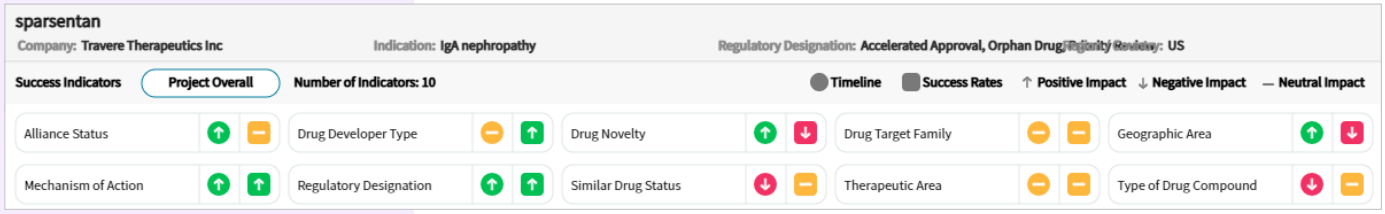
Market overview

$0.81B

expected sales in 2027

Cortellis data indicate there is a 95% probability of success for sparsentan in the United States.





Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

13 Teclistamab

Multiple myeloma

Teclistamab
TECVAYLI®/
JNJ-64007957

About

Producer:
Janssen Pharmaceutical Companies of Johnson & Johnson

Type:
Bispecific antibody targeted at BCMA and CD3

Usage:
Weekly subcutaneous injection to treat R/R multiple myeloma

Impact:

~72k

diagnosed incident cases of multiple myeloma in the G7 markets in 2021

After receiving conditional and accelerated approval from the EC and FDA, respectively, teclistamab is the first-in-class bispecific antibody targeted to B-cell maturation antigen (BCMA) to treat multiple myeloma.

It has been investigated and approved based on a pivotal phase 1/2 trial for relapsed or refractory (R/R) multiple myeloma patients who have received at least three prior lines of therapy and experienced disease progression on their last therapy. Ongoing phase 3 trials are expected to provide confirmation of clinical benefit in teclistamab's approved setting and lead to label expansions in other multiple myeloma patient populations, including in combination with other approved agents. Teclistamab is poised as an important addition to the treatment armamentarium for this uncurable, often-relapsing disease.

Why is it a Drug to Watch?

Teclistamab is an off-the-shelf, first-in-class, T-cell redirecting, bispecific antibody targeted to BCMA and CD3; it is being investigated to treat multiple myeloma.

The European Commission (EC)'s conditional marketing authorization (CMA) supported by the European Medicine Agency (EMA)'s Priority Medicines (PRIME) designation and accelerated approval by the U.S. Food and Drug Administration (FDA) were based on positive results from the multi-cohort pivotal phase 2 (part 3) MajesTEC-1 study, which showed:

- 63.0% overall response rate (ORR) after a median five lines of prior therapy, 58.8% very good partial response (VGPR) rate and 39.4% complete response (CR) rate with 46% of patients who achieved a CR or better being minimal residual disease (MRD) negative (10-5);
- median PFS duration of 11.3 months and median OS duration of 18.3 months; and
- occurrence of adverse events at a level consistent for this patient population and with other therapies such as BCMA-targeted CAR T-cell therapy.

Ongoing phase 3 clinical trials are investigating the use of teclistamab in combination with other drugs:

- MajesTEC-3: phase 3 of teclistamab plus daratumumab in R/R multiple myeloma after one to three prior line(s) of therapy (i.e., second to fourth-line settings)
- MajesTEC-4: phase 3 of teclistamab plus lenalidomide as maintenance treatment in newly diagnosed multiple myeloma following autologous stem cell transplant (ASCT)
- MajesTEC-7: phase 3 of teclistamab plus daratumumab and lenalidomide in newly diagnosed multiple myeloma ineligible or not intended for ASCT as initial therapy
- MajesTEC-9: phase 3 of teclistamab plus pomalidomide, bortezomib and dexamethasone (PVd) or carfilzomib and dexamethasone (Kd) in R/R multiple myeloma after one to three prior line(s) of therapy (i.e., second to fourth-line settings)

An application to the Medicare new technology add-on (NTAP) program was submitted for fiscal year 2023, based on the argument that teclistamab is dissimilar to other bispecific antibodies for this indication, satisfying the requirement for newness.

Teclistamab
TECVAYLI®/
JNJ-64007957

Review and approval status

June 2021
Breakthrough Therapy Designation:
U.S. FDA

December 2021
BLA submission, priority review granted:
U.S. FDA

January 2022
MAA submission: EMA

August 2022
For patients with R/R multiple myeloma who have received at least three prior therapies (immunomodulatory agent, proteasome inhibitor and a CD38-targeted antibody) and demonstrated disease progression on the last therapy
CMA: EC

October 2022
For patients with R/R multiple myeloma who have received at least four prior therapies (immunomodulatory agent, proteasome inhibitor and a CD38-targeted antibody)
Accelerated approval: U.S. FDA

Expected and actual launch
2022: Europe and United States
2023: Japan

Patents estimated to expire beginning in 2036

How will teclistamab impact the market for multiple myeloma?

Multiple myeloma is one of the largest therapy markets in oncology owing to treatment being dominated by combination regimens comprising premium-priced small molecule and biologic drugs. High treatment rates, many potential lines of treatment for R/R disease and long treatment durations for some therapies drive the large size of this market. The multiple myeloma market is expected to grow from $23.6 billion in 2021 to $35.3 billion in 2031.

- Teclistamab is forecast to achieve sales of $1.8 billion in 2031, across the major G7 markets.
- Teclistamab is expected to hold approximately 4% of the first-line ASCT market and 5% of the R/R (second to seventh-line) multiple myeloma market in 2031 (across the G7 markets).
- As a subcutaneous-administered, off-the-shelf product that can be combined with currently approved drugs and regimens to improve their efficacy, teclistamab is positioned at a competitive advantage to some other current and emerging therapies in the R/R setting.

What gaps in treatment does teclistamab fill?

Teclistamab has demonstrated deep and durable responses in patients with R/R disease, which indicates its potential to provide sizeable clinical benefit without significant adverse events. It has the potential to extend remissions and delay disease progression.

Given that a large proportion of multiple myeloma patients relapse and require subsequent therapy and remissions become shorter as the disease progresses with each new line of therapy, teclistamab partially fulfills the need for more effective therapies. As an off-the-shelf product, teclistamab is at a significant competitive advantage over patient-specific CAR T-cell therapies; as such, a larger number of patients may be eligible to receive teclistamab versus CAR T-cell therapies. These include older patients who do not meet the current FDA criteria for CAR T-cell therapies and patients who rapidly progress and are unable to wait for CAR T-cell therapies to be manufactured.

What hurdles might it need to overcome to reach blockbuster status?

Although teclistamab has the advantage of being the first of its class to market, it will likely face stiff competition from other BCMA-targeted therapies (e.g., antibody-drug conjugates and CAR T-cell therapies) and bispecific therapies (including bispecifics targeted to BCMA). The latter will be teclistamab's main hurdle. However, bispecific therapies, including teclistamab, are associated with infections, which could hamper uptake (and sales); heavily pretreated R/R multiple myeloma patients are at risk of infections owing to (often) low immunoglobin levels. Given there are several BCMA-targeted therapies marketed for multiple myeloma and others in the pipeline, significant questions remain about BCMA-targeted therapies, such as whether patients can be retreated with them and where they are best positioned in the treatment algorithm. Uncertainty over the optimal treatment sequences for some patients could prove to be a barrier to teclistamab's uptake.

Teclistamab
TECVAYLI®/
JNJ-64007957

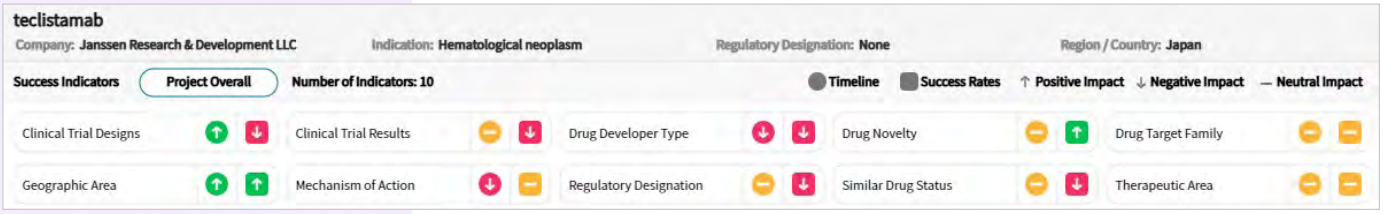
Market overview

$1.8B

expected sales in 2031

"The expression of BCMA is restricted to plasma cells and it's universally expressed in multiple myeloma. BCMA is definitely a great target for multiple myeloma. One way to exploit it is as antibody constructs, which typically have BCMA and CD3."

Hematologist-oncologist, Germany

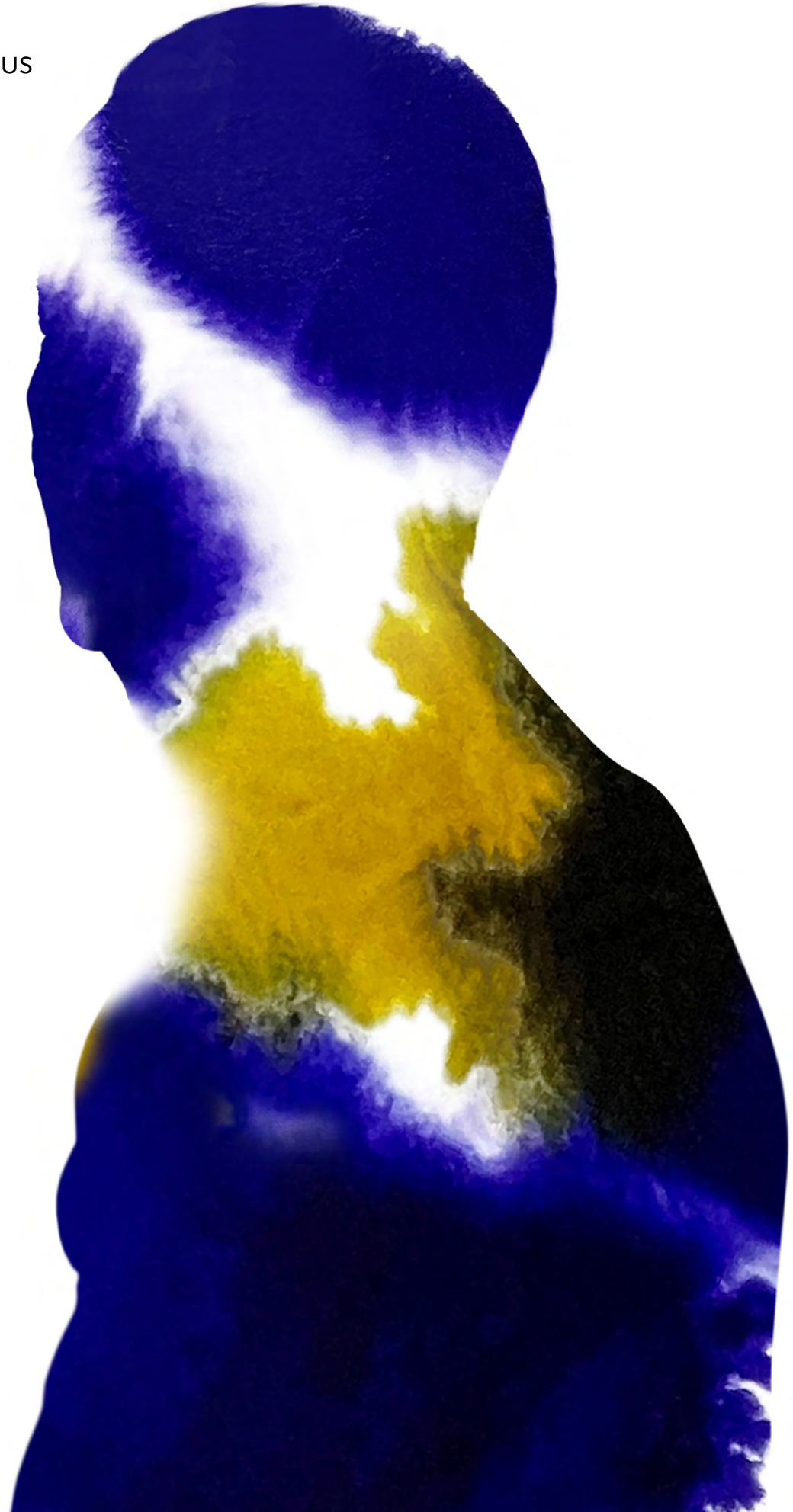


Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate that there is a 67% probability of success for teclistamab in Japan.

14 **Teplizumab**

Type 1 diabetes mellitus



Teplizumab
PRV-031

Teplizumab is the first immunotherapy to launch for T1DM and is a landmark drug given its potential ability to preserve beta cell function and delay the need for insulin treatment.

About

Producer:
Provention Bio Inc

Type:
Anti-CD3 monoclonal antibody

Usage:
Daily intravenous administration for 12-14 days to delay progression to clinical T1DM in at-risk people

Impact:

~1.8m

cases of T1DM in the G7 markets in 2021

Why is it a Drug to Watch?

Teplizumab is an Fc receptor–nonbinding anti-CD3 monoclonal antibody that was granted Breakthrough Therapy Designation by the U.S. Food and Drug Administration (FDA) based on results from the phase 2 At-Risk trial in at-risk children and adolescents aged 8 years to 17 years without a diagnosis of T1DM but with a relative with T1DM.

In the study, the onset of T1DM was delayed or prevented. The phase 3 PROTECT is assessing the efficacy and safety of teplizumab in children and adolescents aged 8 years to 17 years with a diagnosis in the previous six weeks. Findings from this study will also support the request for additional pharmacokinetic/pharmacodynamic (PK/PD) data in the complete response letter (CRL) from the U.S. FDA in 2021.

Provention Bio has partnered with Sanofi SA to launch teplizumab for T1DM. Sanofi will co-promote the drug and has exclusive right of first negotiation to in-license the drug.

Teplizumab
PRV-031

Review and approval status

August 2019
Breakthrough Therapy Designation: U.S. FDA

October 2019
Priority Medicines (PRIME) designation: European Medicines Agency (EMA)

February 2022
Biologics License Application (BLA) resubmitted: U.S. FD

November 17, 2022
Approved: U.S. FDA

Actual and expected launch
December 2022: United States
2024: Europe

Patents estimated to expire beginning in 2026

How will teplizumab impact the market for T1DM?

- Mainstay of treatment remains insulin for glycemic control.
- Few immunotherapies have made it to late-stage clinical development.
- Specialists are optimistic about immunotherapies that can prevent or slow beta cell deterioration, which they feel could shift the treatment paradigm.
- If approved when expected, teplizumab will have the advantage of being the first immunotherapy to market.

What gaps in treatment does teplizumab fill?

Insulin is the cornerstone of T1DM treatment to maintain glycemic control and avoid glucose-related complications such as retinopathy, nephropathy and neuropathy that present a significant disease burden. However, many patients with T1DM struggle to maintain recommended glycemic levels due to high treatment costs and complicated disease management (e.g., dose calculations, devices, sensors, pens, multiple daily injections). Disease-modifying drugs such as teplizumab have the potential to prolong disease progression and improve quality of life.

What hurdles might it need to overcome to reach blockbuster status?

Identification of the eligible population might prove to be challenging in practice, given the need for large-scale screening for high-risk individuals especially when testing for early T1DM antibodies is not routinely conducted. Another consideration is that not all individuals with the relevant antibodies progress to T1DM, which might indicate the need for an additional screening stage to determine eligibility. Physicians also view the daily infusion for 12-14 days as burdensome and expect it to be a barrier to uptake.

Teplizumab
PRV-031

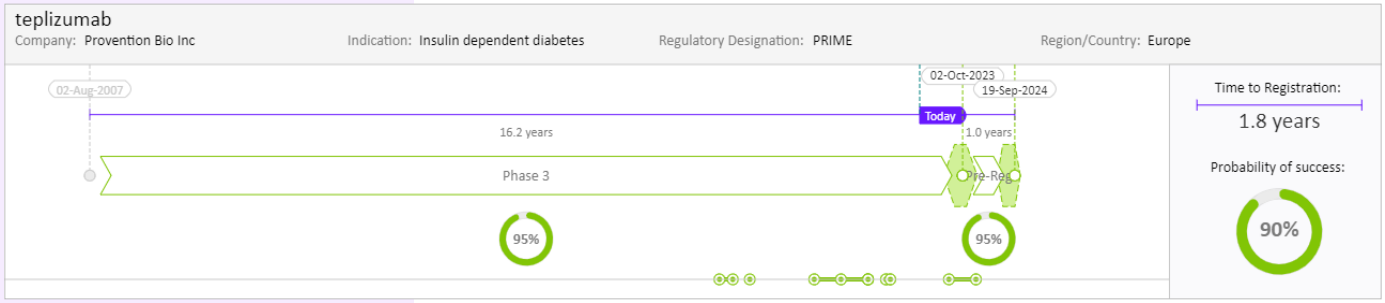
Market overview

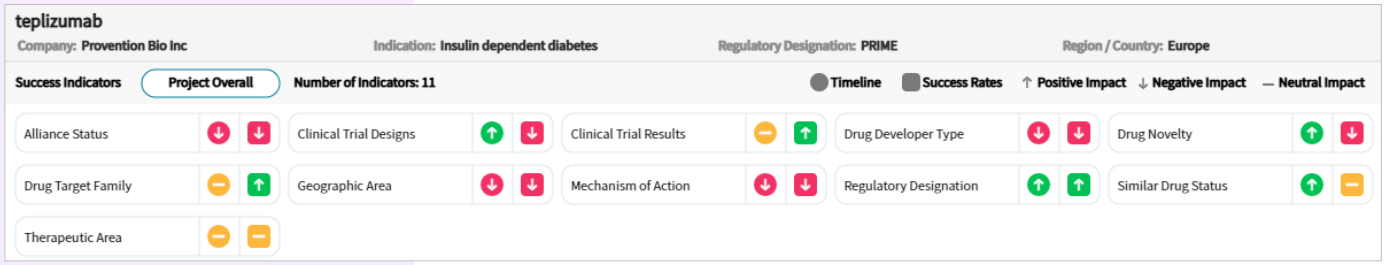
$0.39B

expected sales in 2027

"We are still far from immunotherapy being SOC, but teplizumab has shown some potential. If approved, we will see more patients being screened for autoantibodies and picked up prior to their clinical need for insulin.The challenges are going to be the cost and access. It is not an easy infusion because it takes 12 days—there are lots of other factors that will have to play out in terms of how realistic the drug is on the overall market."

Physician, United States



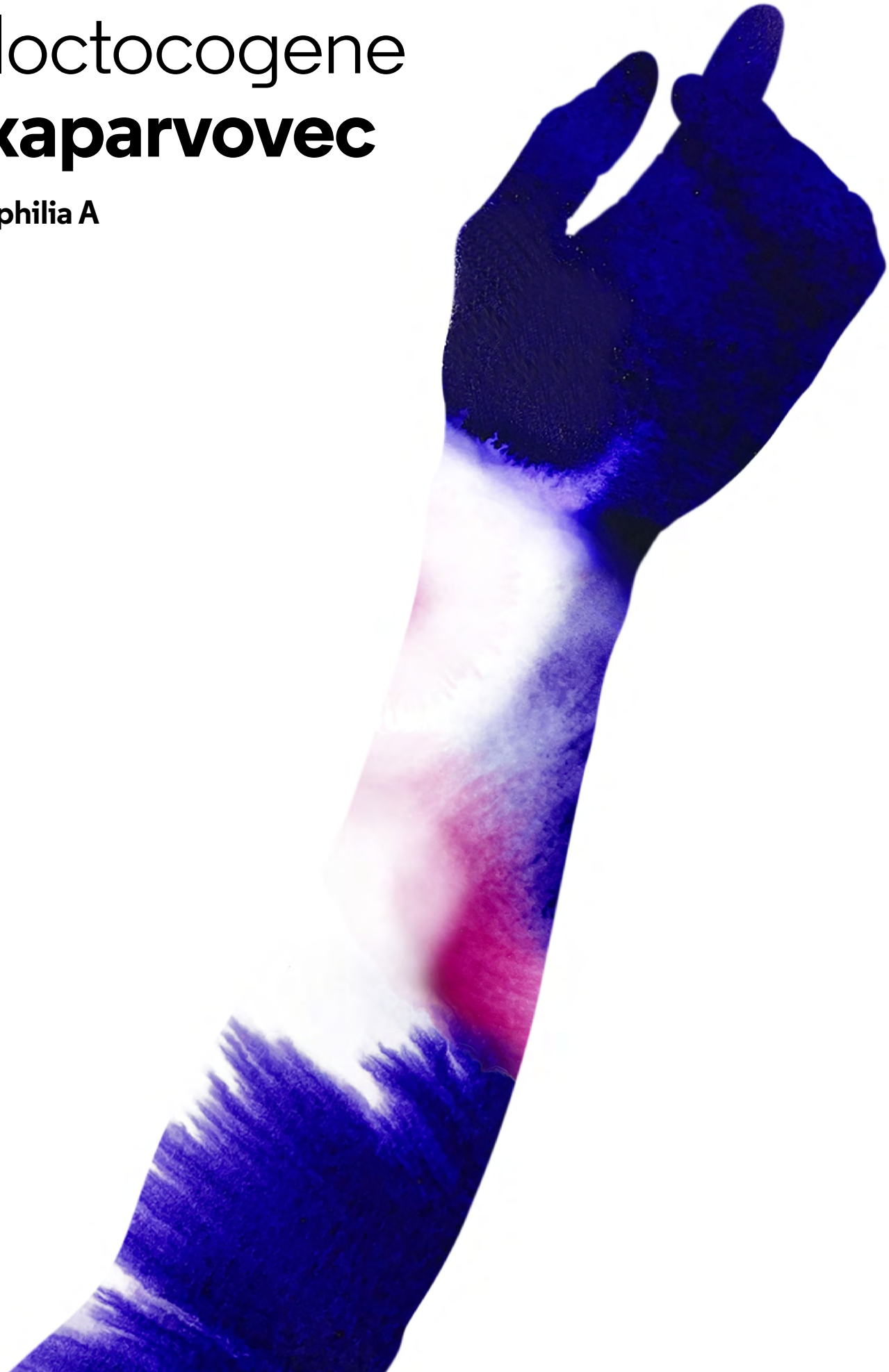


Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate there is an 90% probability of success for teplizumab in Europe.

15 Valoctocogene **roxaparvovec**

Hemophilia A



Valoctocogene roxaparvovec
ROCTAVIAN™/
BMN-270

About

Producer:
BioMarin Pharmaceutical Inc.

Type:
AAV5-based gene transfer therapy

Usage:
Single intravenous infusion to treat severe hemophilia A

Impact:

~16,500

cases of severe hemophilia A in the G7 markets in 2021

Approved by the European Commission (EC) in August 2022, valoctocogene roxaparvovec is also poised to be the first gene therapy to launch in the United States for severe hemophilia A.

Treatment benefit is expected to last for years, reduce the number of bleeding events, minimize the need for replacement factor VIII (FVIII) and negate the use of otherwise burdensome prophylaxis treatment.

Why is it a Drug to Watch?

By restoring the expression of endogenous FVIII, valoctocogene roxaparvovec reduces the number of bleeding events experienced by people with hemophilia A, converting the patient from having severe hemophilia to mild disease.

The EC approval and resubmission to the U.S. Food and Drug Administration (FDA) were supported by data from a phase 1/2 trial and the phase 3 GENEr8-1 trial, including additional long-term follow-up data to confirm the duration of effect, as requested in the complete response letter (CRL) from the FDA.

In the GENEr8-1 trial, valoctocogene roxaparvovec decreased the annualized bleeding rate and improved the annualized FVIII infusion rate.

BioMarin Pharmaceutical Inc has constructed, commissioned and validated a gene therapy manufacturing facility that will produce the therapy.

BioMarin Pharmaceutical Inc is developing a companion diagnostic with ARUP Laboratories Inc.

Valoctocogene roxaparvovec
ROCTAVIAN™/
BMN-270

Review and approval status

March 2021
Regenerative medicine advanced therapy (RMAT) designation: U.S. FDA

August 2022
Marketing authorization: EC

September 2022
Marketing authorization for AAV5 DetectCDx™ Kit c ompanion diagnostic: EC

September 2022
Biologics License Application (BLA) resubmitted: U.S. FDA

March 31, 2023
PDUFA date

Actual and expected launch
2022: Europe
2023: United States

Patents estimated to expire beginning in 2033

How will valoctocogene roxaparvovec impact the market for hemophilia A?

- Gene therapies potentially offer curative treatment, but FVIII levels do not appear to be sustained with the first generation of gene transfer therapies.
- Initial uptake will be very slow but gradually increase as more safety data, postmarketing real world data and data on the pretreatment parameters that determine individual responses become available.
- By the time these data are available, the hemophilia A competitive landscape is likely to change drastically and FVIII gene therapy may be a much less attractive alternative.
- Payer decisions for valoctocogene roxaparvovec could set the tone for future gene therapies, with many key opinion leaders and payers stating that pay-for-performance is the only viable, ethical way for society to afford an expensive, potentially ineffective treatment when other safe, efficacious therapies already exist.
- Payers also suggest that the cost of valoctocogene roxaparvovec could result in coverage for only patients most likely to benefit (young without joint damage vs an older person who already has severe joint damage).

What gaps in treatment does valoctocogene roxaparvovec fill?

Approximately 43% of people with hemophilia A experience painful, spontaneous bleeds into their muscles and joints that contribute to progressive, debilitating joint damage that can have a major impact on quality of life. Standard of care consists of 100 to 150 intravenous infusions (two to three times a week) of replacement FVIII a year and does not always prevent joint damage. Correction of the coagulation system can be life-changing and valoctocogene roxaparvovec could potentially be the first treatment to accomplish this with a single infusion, eliminating the need for blood transfusions and FVIII replacement therapy.

What hurdles might it need to overcome to reach blockbuster status?

There are a number of factors that could influence whether valoctocogene roxaparvovec will be broadly adopted within the target population including the presence of safe, efficacious therapies; use restricted to patients older than 18 years; and loss of FVIII expression over time, as observed in clinical trials. In addition, the combination of this loss of efficacy, unpredictable and variable individual responses to the treatment and a lack of long-term safety data might make both patients and physicians hesitant to use, and payers hesitant to cover, a novel gene therapy. Coverage could depend on a set of predetermined conditions and the patient copay might be high.

Valoctocogene roxaparvovec
ROCTAVIAN™/
BMN-270

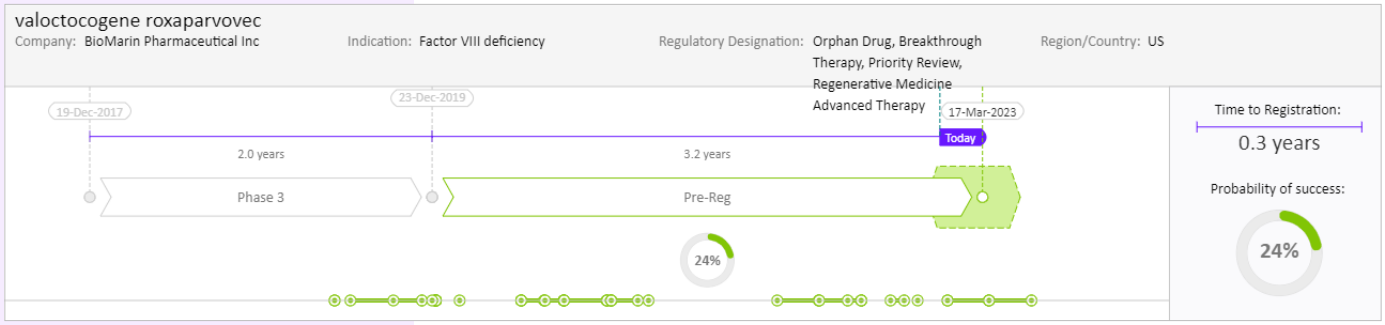
Market overview

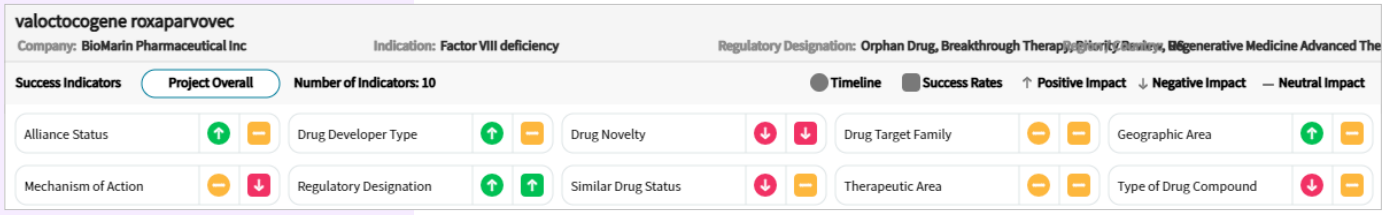
$1.09B

expected sales in 2027

"We put the $2–3 million in the context of how much uncertainty exists around how much we're currently paying in factor. If the return on investment takes two to three years (that is, BMN 270 really works) and we don't need any factor VIII over at least a two to three year period, hopefully longer and if I can recoup those costs over a two-year period, I think that would be seen as very positive."

Payer, United States



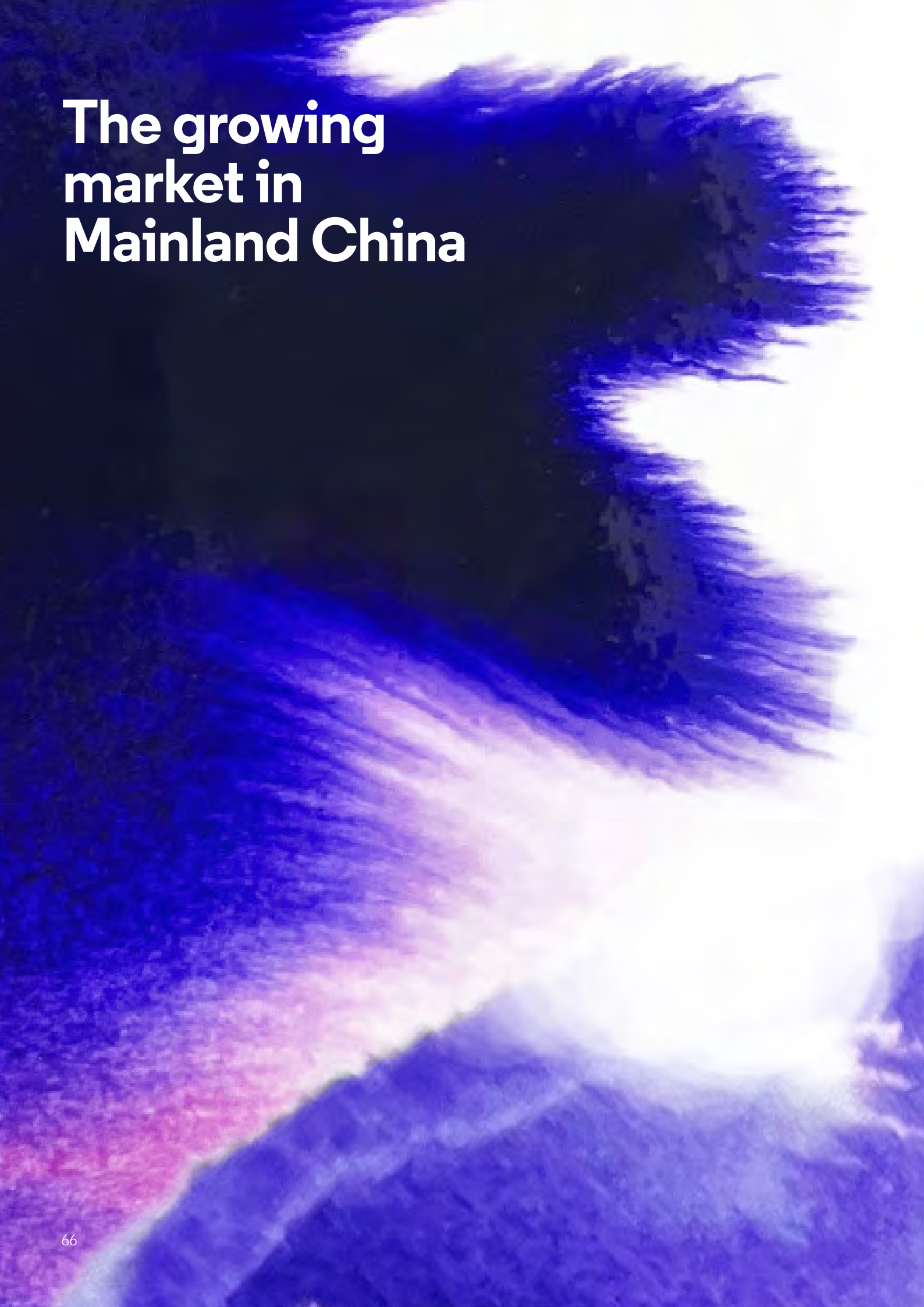


Source: Cortellis Competitive Intelligence, Drug Timeline & Success Rate Prediction current as of December 15, 2022

Cortellis data indicate there is an 24% probability of success for valoctocogene roxaparvovec in United States.

Trends to watch in 2023

The growing market in Mainland China



The growing market in Mainland China

~3m

cancer-related deaths would occur in Mainland China in 2022

We identified nine drugs that are likely to achieve the traditional $1 billion blockbuster status in Mainland China by 2030, including both global and domestically manufactured assets.

Including a Mainland China approach within the market plan can extend the revenue-generating life of these drugs beyond the expected patent expiry in the United States and Europe.

Of the nine selected, eight are oncology drugs, which is likely driven by healthcare reforms under Healthy China 2030 that have placed a focus on addressing the increasing cancer burden in Mainland China. It was estimated that 4,820,000 new cancer cases and 3,210,000 cancer related deaths would occur in Mainland China in 2022.

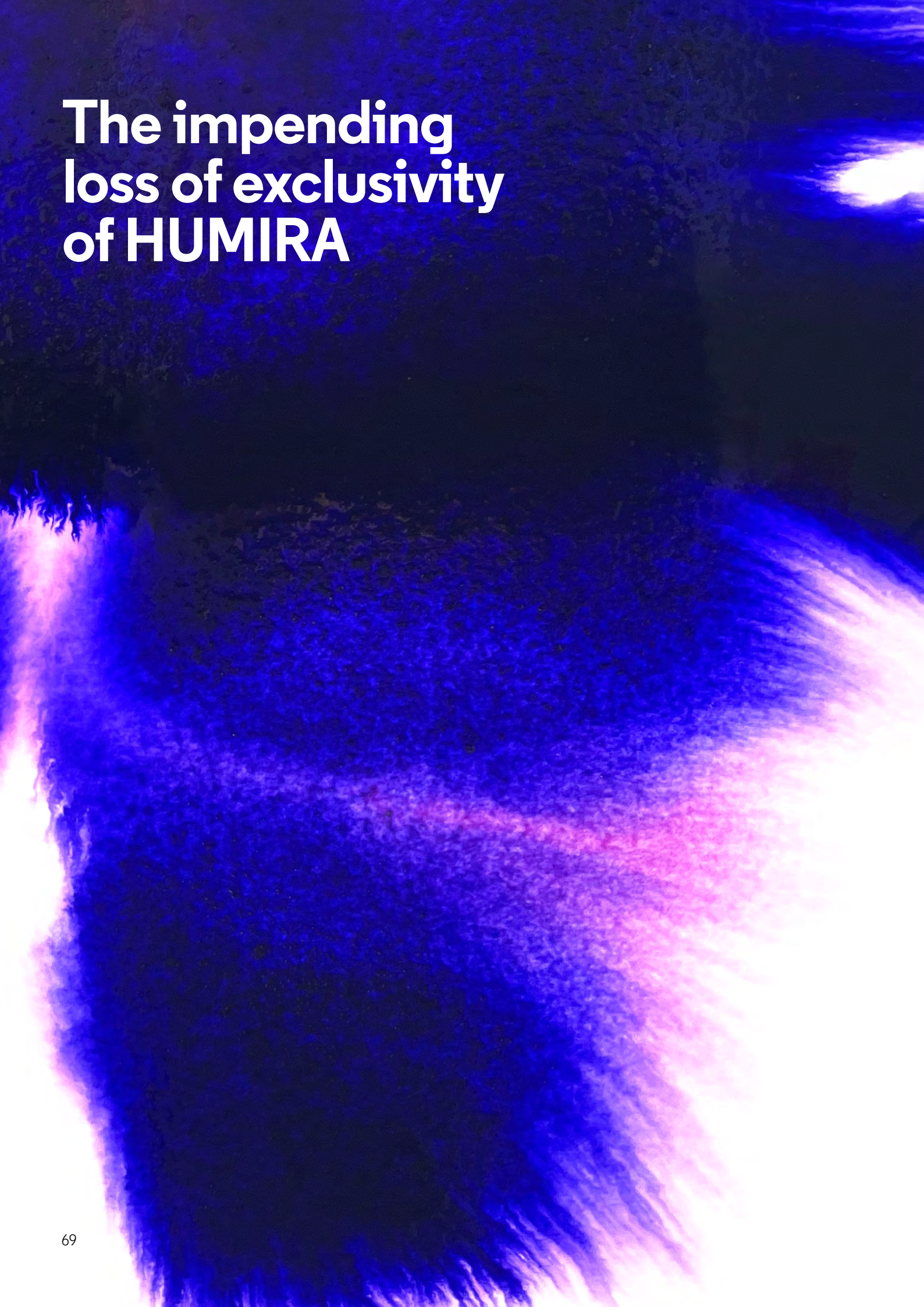
Game-changers in Mainland China

Drug	Company(s)	Initial U.S. approval	Initial European approval	Initial approval in Mainland China	2021 global sales ($M)	Expected patent expiry in Mainland China	Why it's a Drug to Watch
Anlotinib (Focus V®)	Chia Tai Tianqing Pharmaceutical (CTTQ)	N/A	N/A	2018	620	2028	Approved in Mainland China for a range of indications including non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC) and soft tissue carcinoma; received approval for advanced or metastatic thyroid cancer in 2022 in Mainland China; currently investigated in multiple phase 2 and 3 clinical trials in combination with several chemotherapy and targeted agents in Mainland China
Atezolizumab (TECENTRIQ®)	Genentech	2016	2017	2020	3,300	2029	First approved for extensive-stage SCLC in Mainland China; also approved for first-line hepatocellular carcinoma (HCC) and NSCLC in Mainland China
Camrelizumab (AiRuiKa™)	Jiangsu Hengrui Medicine Co Ltd	N/A	N/A	2019	600	2036	Leading immune checkpoint inhibitor (ICI) in Mainland China, with no biosimilar entry expected within the 10-year forecast period

Nivolumab (OPDIVO®)	Bristol Myers Squibb	2014	2015	2018	7,523	2026	First-ever ICI to receive approval in Mainland China; approved to treat epidermal growth factor receptor (EGFR)-negative and anaplastic lymphoma kinase (ALK)-negative NSCLC, squamous cell carcinoma of head and neck (SCCHN) with PD-L1 expression and advanced gastroesophageal junction (GEJ) carcinoma; approved as first-line treatment of advanced esophageal cancer
Pembrolizumab (KEYTRUDA®)	Merck	2014	2016	2018	17,200	2028	Second ICI to launch in Mainland China; received nine label approvals so far since first approval in 2018, including NSCLC, SCCHN, colorectal cancer, esophageal cancer, HCC and gastric cancer
Sacubitril valsartan (ENTRESTO®)	Novartis	2015	2015	2017	3,548	2027	Mainland China the second-largest market in 2021, making up 25% of sales outside the U.S.; expected to continue its strong uptake in chronic heart failure (CHF) following a second National Reimbursement Drugs List (NRDL) price discount in 2022 (~68%); in June 2021, first new therapy approved for essential hypertension in over 10 years, also reimbursable
Sintilimab (TYVYT®)	Innovent Biologics Inc and Eli Lilly and Company	N/A	2020	2018	418	2036	Strongly positioned to receive further label expansions in the next one to two years
Tislelizumab (Baize'an)	BeiGene	N/A	N/A	2019	255	2033	Currently placed as the third-best selling domestic PD-1 inhibitor and approved for a range of indications; further label expansions anticipated in the coming few years
Trastuzumab (HERCEPTIN®)	Roche	1998	2000	2002	2,700	Biosimilars available	Approved in Mainland China to treat HER2-positive breast cancer and gastric cancer; first biosimilar of trastuzumab launched in 2020 by Shanghai Henlius Biotech

Sources: BioWorld, Novartis Annual Report 2021, Eli Lilly and Company Annual Report 2021, BeiGene Annual Report 2021,Roche Annual Report 2021, Bristol Myers Squibb press release, Merck press release.

The impending loss of exclusivity of HUMIRA



The impending loss of exclusivity of HUMIRA

All eyes will be on the expiry of a key U.S. patent covering AbbVie's HUMIRA® (adalimumab) in 2023, which could see HUMIRA biosimilars launching in the United States throughout the year.

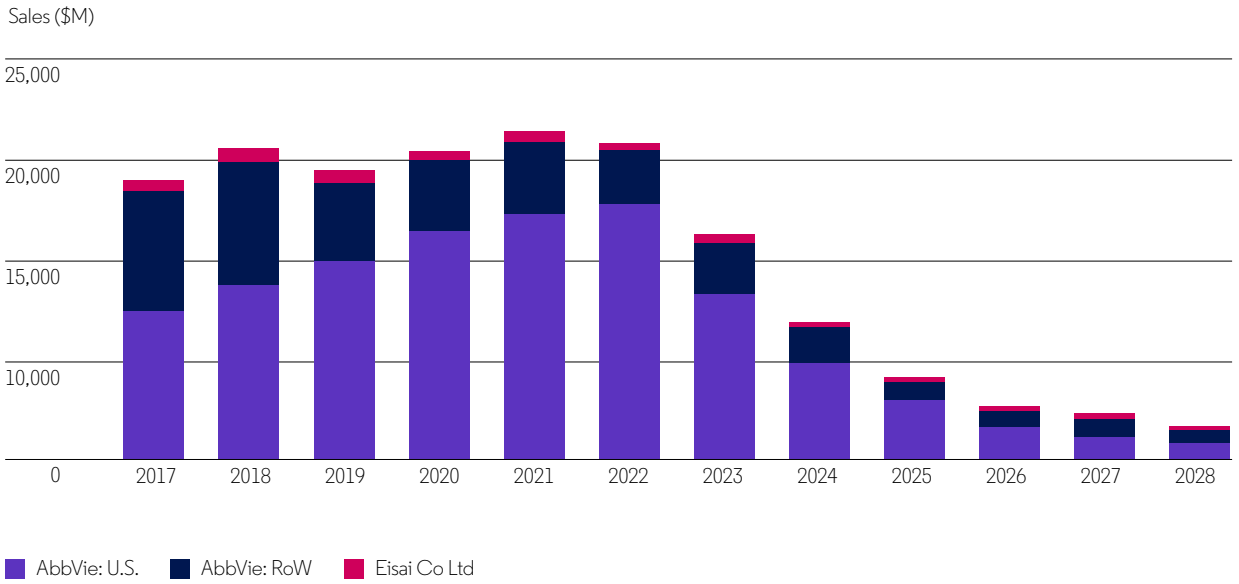
Although the company still holds some essential manufacturing patents that are not due to expire until 2034, with HUMIRA accounting for around 37% of AbbVie's 2021 sales, the entry of adalimumab biosimilars is expected to have an impact on the company's financials. It is estimated that HUMIRA sales in the United States could decline from $17.3 billion in 2021 to $13.9 billion in 2023 and $1.4 billion in 2028.

In the international markets, AbbVie has already faced direct biosimilar competition for HUMIRA in Europe and other regions and countries.

In the European Union, HUMIRA biosimilars were launched in October 2018 and had an immediate impact on international sales, which declined 31.1% in 2019, 7% in 2020 and 9.6% in 2021. This was due to AbbVie heavily discounting HUMIRA in response to the biosimilar competition, prompting many companies to delay or abandon plans to launch adalimumab biosimilars in European markets.

HUMIRA sales could also feel the impact of competition from biosimilar versions of other products such as REMICADE® (infliximab) and Enbrel® (etanercept).

Actual and forecast sales of HUMIRA globally, 2017-2028



Source: Cortellis

The impending loss of exclusivity of HUMIRA

Adalimumab biosimilars approved by the European Commission, by date of E.U. approval

Biosimilar	EU approval	Authorization holder	U.S. product name	Status
AMGEVITA™	March 21, 2017	Amgen Europe BV	AMJEVITA™	Launched October 16, 2018
SOLYMBIC	March 22, 2017	Amgen Europe BV	—	Withdrawn June 15, 2018
IMRALDI™	August 24, 2017	Samsung Bioepis	HADLIMA™	Launched October 17, 2018
Cyltezo®	November 10, 2017	Boehringer Ingelheim	Cytelzo	Withdrawn January 15, 2019
Hyrimoz®	July 26, 2018	Sandoz	Hyrimoz	Launched October 16, 2018
Hefiya	July 26, 2018	Sandoz	—	Launched October 16, 2018
Halimatoz	July 26, 2018	Sandoz	—	Withdrawn December 18, 2020
HULIO™	September 17, 2018	Viatris Inc	Hulio	Launched October 19, 2018
IDACIO®	April 02, 2019	Fresenius Kabi	—	Launched May 03, 2019
Kromeya	April 02, 2019	Fresenius Kabi	—	Withdrawn December 17, 2019
Amsparity	February 13, 2020	Pfizer Inc	Abrilada	Launch delayed
Yuflyma®	February 11, 2021	Celltrion	—	Launched June 23, 2022
LIBMYRIS	November 12, 2021	STADA Arzneimittel AG	—	Launched June 09, 2022
HUKYNDRA	November 15, 2021	STADA Arzneimittel AG	—	Launched June 09, 2022

Source: BioWorld

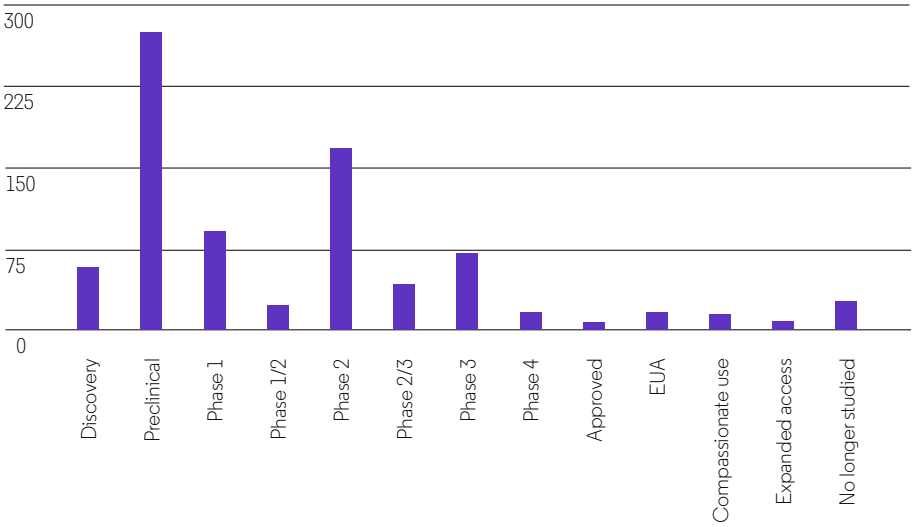
COVID-19 vaccines and therapies

COVID-19 vaccines and therapies

Although attention on COVID-19 vaccine and therapeutic development has waned since the height of the pandemic, research activity remains steady as the industry tries to stay ahead of new variants, continue to reduce COVID-19-related hospitalizations and mortality and grapple with long COVID.

Not all will make it to market, but the lessons continue to be folded into programs for other therapeutic areas and have accelerated advancement in areas such as mRNA.

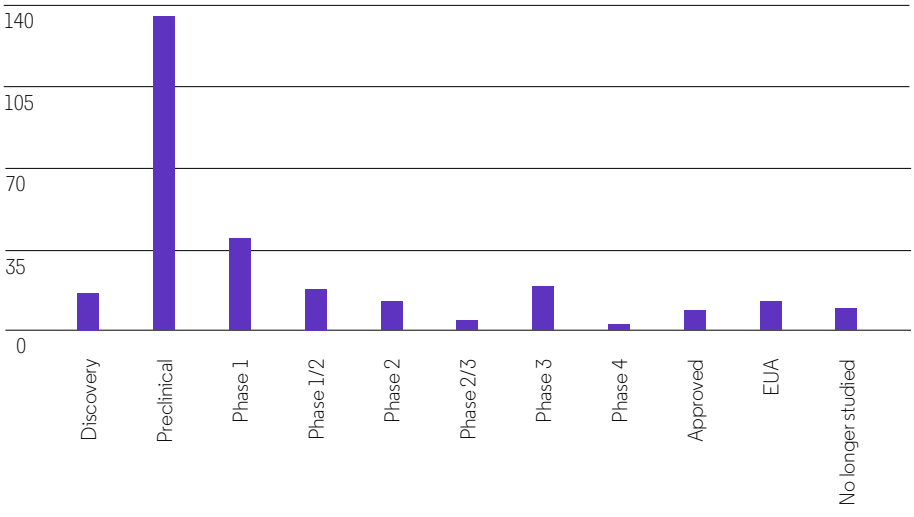
791 therapies are in development for COVID-19, and another 27 are no longer being studied.



Source: Source: BioWorld, based on company/institution reports of trial status

Hundreds of treatments and vaccines are still in the pipeline.

260 vaccines are in development for COVID-19, and another 9 are no longer being studied.



Source: Source: BioWorld, based on company/institution reports of trial status

COVID-19 vaccines and therapies
P1/8

Approved	DRUG
Approved	Avifavir (favipiravir)
Approved	Azvudine
Approved	BRII-196 (amubarvimab) and BRII-198 (romlusevimab)
Approved	Casirivimab and imdevimab (REGEN-CoV; Ronapreve; REGN-10933 plus REGN-10987; REGN-CoV2
Approved	Dexamethasone; Dexavan (dexamethasone phosphate)
Approved	Regkirona (regdanvimab; CT-P59)
Approved	Remdesivir (Veklury)
EUA	**DRUG**
EUA	AZD-7442 (combination of AZD-8895 and AZD-1061; tixagevimab and cilgavimab; Evusheld
EUA	Baricitinib (Olumiant)
EUA	Bebtelovimab (LY-CoV1404)
EUA	Convalescent plasma
EUA	EIDD-2801 (molnupiravir; MK-4482; Lagevrio)
EUA	Generic remdesivir; Bemsivir
EUA	Itolizumab
EUA	LY-3819253 (LY-CoV555, bamlanivimab)
EUA	LY-CoV016 (etesevimab)
EUA	MSCs
EUA	PF-07321332 (Paxlovid)
EUA	Proxalutamide (GT-0918)
EUA	Proxalutamide (GT-0918)
EUA	Reeqonus (favipiravir; Avigan)
EUA	SARS-CoV-2 targeting human monoclonal antibodies (MAbs); VIR-7831 (sotrovimab, Xevudy) and VIR-7832
EUA	Tocilizumab (Actemra; Roactemra)
Registered	Vivagel; Viraleze (SPL-7013)
EUA	Zyesami (aviptadil; RLF-100, inhaled)

Compassionate use	DRUG
Compassionate use	Allorx stem cells
Compassionate use	Bucillamine
Compassionate use	CER-001
Compassionate use	DAS-181 (recombinant sialidase)
Compassionate use	Giapreza
Compassionate use	IC-14
Compassionate use	Lenzilumab
Compassionate use	Mavrilimumab
Compassionate use	Namilumab (IZN-101)
Compassionate use	Narsoplimab
Compassionate use	Piclidenoson
Compassionate use	PLX cell product candidates (PLX-PAD)
Compassionate use	Ruconest (conestat alfa)
Compassionate use	Siltuximab (Sylvant)
Compassionate use	Allorx stem cells
Compassionate use	Zofin
Expanded access	**DRUG**
Expanded access	CAP-1002
Expanded access	Eculizumab (Soliris)
Expanded access	Exebacase
Expanded access	Exoflo
Expanded access	Genosyl DS
Expanded access	Inopulse
Expanded access	Jakafi (ruxolitinib)
Expanded access	Opaganib (Yeliva)
Expanded access	Remestemcel-L
Phase IV	**DRUG**
Phase IV	Baloxavir marboxil (Xofluza)
Phase IV	Berberine
Phase IV	Bivalirudin
Phase IV	Carragelose inhalation therapy (Inhaleen)
Phase IV	Carrimycin

COVID-19 vaccines and therapies
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Phase IV	Cyclosporine
Phase IV	Danoprevir (Ganovo) + ritonavir
Phase IV	Fluoxetine (Prozac)
Phase IV	Interferon-beta-1a (intravenous; also Traumakine}
Phase IV	N-acetylcysteine
Phase IV	OT-101 (trabedersen); artemisinin; Pulmoheal (Artiveda)
Phase IV	Quercetin, bromelain, zinc and vitamin C
Phase IV	Rebif (interferon beta-1a)
Phase IV	Umifenovir (Arbidol)
Phase IV	Valsartan
Phase III	**DRUG**
Phase III	Abatacept
Phase III	Almitrine
Phase III	Alvesco (ciclesonide)
Phase III	Anakinra (Kineret)
Phase III	Apabetalone (RVX-208)
Phase III	Aplidin (plitidepsin)
Phase III	ASC-09 + ritonavir (oral tablet)
Phase III	Asunercept
Phase III	AT-527 (bemnifosbuvir)
Phase III	Auxora (CM-4620-IE)
Phase III	Bacmune (MV-130)
Phase III	BCDA-04 (NK1R+ MSC)
Phase III	C-21
Phase III	Chloroquine and interferon beta-1b
Phase III	Colchicine
Phase III	COVID-HIG and COVID-EIG
Phase III	CPI-006
Phase III	Darunavir/cobicistat (Prezcobix)
Phase III	Dipyridamole
Phase III	DMX-200
Phase III	Dornase alfa (Pulmozyme)
Phase III	Doxycycline
Phase III	EB-05
Phase III	Emtricitabine/tenofovir (Truvada
Phase III	ENU-200
Phase III	Famotidine
Phase III	Farxiga (dapagliflozin)
Phase III	Fenretinide (LAU-7b)
Phase III	Hydroxychloroquine
Phase III	Hydroxychloroquine and other lupus therapies
Phase III	IFX-1 (vilobelimab)
Phase III	IMM-101
Phase III	Inhaled budesonide
Phase III	Jadicells
Phase III	Levilimab
Phase III	Lopinavir/ritonavir (Kaletra/Aluvia)
Phase III	Losmapimod
Phase III	Lovenox (enoxaparin)
Phase III	Methylprednisolone/corticosteroids
Phase III	MP-0420 (ensovibep)
Phase III	N-115
Phase III	Nitric oxide nasal spray (NONS) (Fabispray)
Phase III	Nomacopan
Phase III	NT-300 (nitazoxanide)
Phase III	Octagam 10%
Phase III	Peginterferon lambda
Phase III	Pulm-001
Phase III	QazVac
Phase III	Radiation therapy
Phase III	Recombinant alkaline phosphatase
Phase III	Rivaroxaban
Phase III	RTB-101
Phase III	S-217622 (ensitrelvir)
Phase III	SAB-185
Phase III	SNG-001 (interferon-beta-1a)
Phase III	Tacrolimus
Phase III	TAK-888; hyperimmune globulin; Covig-19
Phase III	Tamiflu (oseltamivir)

COVID-19 vaccines and therapies
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Phase III	Tavalisse (fostamatinib)
Phase III	Tigerase (dornase alfa biosimilar)
Phase III	Tissue plasminogen activator (Alteplase)
Phase III	TXA-127
Phase III	TY-027 (bifunctional peptide derivative)
Phase III	Ultomiris (ravulizumab-cwvz)
Phase III	Vascepa (icosapent ethyl)
Phase III	VERU-111 (sabizabulin)
Phase III	VV-116
Phase III	Vyrologix (leronlimab; PRO-140)
Phase III	XAV-19
Phase III	XC221
Phase III	Zithromax (azithromycin)
Phase II/III	**DRUG**
Phase II/III	ABP-300
Phase II/III	ABX-464
Phase II/III	ADG-20
Phase II/III	Ambrisentan
Phase II/III	ANA-001 (niclosamide)
Phase II/III	Atazanavir; daclatasvir; sofusbuvir; favipiravir
Phase II/III	BC-007
Phase II/III	BDB-001
Phase II/III	Bevacizumab
Phase II/III	Candesartan
Phase II/III	Cannabidiol-loaded exosomes
Phase II/III	CardiolRx
Phase II/III	Dociparstat sodium
Phase II/III	EDP-1815
Phase II/III	Emapalumab (Gamifant)
Phase II/III	Generic hydroxychloroquine
Phase II/III	Immunofree and Reginmune
Phase II/III	Ivermectin
Phase II/III	Lactoferrin
Phase II/III	Levamisole
Phase II/III	Losartan
Phase II/III	Monoclonal antibody duo treatment (BMS-986413/BMS-986414)
Phase II/III	Multistem
Phase II/III	NA-831, atazanavir and dexamethasone
Phase II/III	Nafamostat mesylate
Phase II/III	Nangibotide
Phase II/III	Noviricid
Phase II/III	Olokizumab and RPH-104
Phase II/III	Pamrevlumab
Phase II/III	Previfenon
Phase II/III	PTC-299
Phase II/III	Reparixin
Phase II/III	RESP-301
Phase II/III	Rnapc2 (AB-201)
Phase II/III	Sarconeos (BIO-101)
Phase II/III	SFX-01
Phase II/III	Sofosbuvir, daclatasvir, hydroxychloroquine; sofosbuvir, ribavirin
Phase II/III	STI-5656 (abivertinib maleate)
Phase II/III	Tempol (MBM-02)
Phase II/III	TRV-027
Phase II/III	Upamostat (RHB-107)
Phase II/III	Zavegepant (formerly vazegepant)
Phase II	**DRUG**
Phase II	Adrecizumab
Phase II	ADX-629 and reproxalap
Phase II	Alisporivir (Debio-025)
Phase II	Allocetra
Phase II	Allogeneic bone marrow-derived mesenchymal stem cells (itMSC)
Phase II	Alsitek (masitinib)
Phase II	AMY-101
Phase II	Anti-PD-1 antibody
Phase II	Apilimod (LAM-002A)
Phase II	APN-01
Phase II	Aprepitant (Cinvanti)
Phase II	Arakoda (tafenoquine)

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Phase II	ARD-301
Phase II	Artemic
Phase II	Artesunate
Phase II	AT-001
Phase II	ATI-450
Phase II	ATR-002 (zapnometinib)
Phase II	Phase II ATYR-1923
Phase II	Avasopasem manganese (GC-4419)
Phase II	AXA-1125
Phase II	Axatilimab (SNDX-6352)
Phase II	AZD-1656
Phase II	Azeliragon
Phase II	Bardoxolone
Phase II	Bemcentinib
Phase II	BGE-175 (asapiprant)
Phase II	BIO-11006 inhalation solution
Phase II	BIO-300 (Genistein)
Phase II	BLD-2660
Phase II	Brequinar
Phase II	Brilacidin
Phase II	Brukinsa (zanubrutinib)
Phase II	Camostat mesylate
Phase II	Cannabidiol-steroid formulation
Phase II	Centhaquine (PMZ-2010)
Phase II	CERC-002
Phase II	Cimetra
Phase II	Clazakizumab
Phase II	Clevudine
Phase II	CNM-ZnAg
Phase II	Codivir
Phase II	Combination of umbilical cord mesenchymal stem cell and umbilical cord mesenchymal stem cell exosomes
Phase II	Co-trimoxazole
Phase II	Covidrops
Phase II	COVI-MSC (adipose-derived mesenchymal stem cells)

Phase II	COVI-MSC (STI-8282)
Phase II	CP-COV03
Phase II	Crizanlizumab
Phase II	CSL-312 (garadacimab)
Phase II	CYTO-201 (metenkefalin)
Phase II	CYTO-205
Phase II	Dalcetrapib
Phase II	Dapansutrile
Phase II	Decitabine
Phase II t	Desidusta
Phase II	Duvelisib
Phase II	EC-18
Phase II	Eftilagimod alpha (IMP-321)
Phase II	EG-009A
Phase II	Elsufavirine (Elpida)
Phase II	ENA-001
Phase II	Ensifentrine
Phase II	Epoprostenol (Ventoprost)
Phase II	Estradiol patch
Phase II	Fingolimod (Gilenya)
Phase II	Fisetin
Phase II	Fluvoxamine
Phase II	Foralumab (TZLS-401)
Phase II	FW-1022
Phase II	FX-06
Phase II	GAMUNEX-C (intravenous immune globulin)
Phase II	GB-0139
Phase II	Gemoral (antiviral) with Veldona (low-dose oral interferon)
Phase II	Gimsilumab
Phase II	Glenzocimab
Phase II	GLS-1027
Phase II	GLS-1200
Phase II	HB-adMSCs
Phase II	Hexagen
Phase II	HLCM-051

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Phase II	Hocena (antroquinonol)
Phase II	Hydroxychloroquine and azithromycin
Phase II	Ibrutinib
Phase II	Iloprost
Phase II	Imatinib
Phase II	MC-2
Phase II	Infliximab
Phase II	INNA-051
Phase II	Interferon beta-1b and clofazimine
Phase II	Interleukin-2
Phase II	Interleukin-7 (CYT-107)
Phase II	IONIS-PKK-LRx
Phase II	KAND-567
Phase II	KB-109
Phase II	KIN-001
Phase II	KT-PC-301
Phase II	LAU-7b
Phase II	LB-1148
Phase II	LY-3127804
Phase II	Lyo lucinactant
Phase II	LYT-100 (deupirfenidone)
Phase II	M-5049
Phase II	Maraviroc
Phase II	MEDI-3506
Phase II	Mesenchymal stem cells (MSCs)
Phase II	Mesencure
Phase II	Metablok
Phase II	MN-166 (ibudilast)
Phase II	Monalizumab
Phase II	MPH-966
Phase II	MYMD-1
Phase II	NanO2
Phase II	Niclosamide (oral - FW-COV)
Phase II	NSAID and antihistamine
Phase II	OP-101
Phase II	Ozanimod
Phase II	PD-001
Phase II	Pegylated Interferon -a2b
Phase II	Pentarlandir
Phase II	PH-94B
Phase II	PLN-74809
Phase II	Prothione capsules
Phase II	Psilocybin
Phase II	PSJ-539
Phase II	PUL-042
Phase II	Quellor
Phase II	Rabeximod
Phase II	Ramelteon
Phase II	Rayaldee (calcifediol)
Phase II	Razuprotafib
Phase II	RBT-9
Phase II	Rejuveinix
Phase II	Reloxifene
Phase II	rhu-pGSN
Phase II	Rintatolimod (Ampligen)
Phase II	RSLV-132
Phase II	Ryanodex
Phase II	Secukinumab
Phase II	Selinexor (KPT-330, Xpovio)
Phase II	Silmitasertib
Phase II	Sirolimus (rapamycin)
Phase II	Skyrizi (risankizumab)
Phase II	SPI-1005 (ebselen)
Phase II	TD-0903 (nezulcitinib)
Phase II	Tecfarin
Phase II	Telmisartan
Phase II	Temelimab
Phase II	Thalidomide
Phase II	Thymalfasin (thymosin alpha 1)
Phase II	Tinzaparin or unfractionated heparin
Phase II	TJM-2 (plonmarlimab; TJ-003234)
Phase II	TNX-102 SL

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Phase II	Tocilizumab biosimilar
Phase II	Tofacitinib (Xeljanz)
Phase II	Tolimidone
Phase II	Tollovir (NLC-V-01)
Phase II	TQ Formula
Phase II	Tranexamic acid
Phase II	UNI-911 (niclosamide; UNI-91103)
Phase II	Vadadustat
Phase II	Vafidemstat
Phase II	VB-201
Phase II	Veyonda (idronoxil)
Phase II	Virazole (ribavirin inhalation solution)
Phase II	Xpro-1595
Phase II	Zilucoplan
Phase I/II	**DRUG**
Phase I/II	Anticovir (AP-003)
Phase I/II	BX-U001
Phase I/II	CAStem
Phase I/II	COR-101
Phase I/II	Cymerus
Phase I/II	CYNK-001
Phase I/II	EOM-613
Phase I/II	Immunistim (gamma-delta T)
Phase I/II	IN-006
Phase I/II	INO-4802
Phase I/II	Lanadelumab
Phase I/II	Meplazumab
Phase I/II	NKG2D-ACE2 CAR-NK cells
Phase I/II	Pentoxifylline
Phase I/II	Pulmostem
Phase I/II	RAPA-501-ALLO off-the-shelf cells
Phase I/II	SBI-101
Phase I/II	Sildenafil (Viagra)
Phase I/II	TL-895
Phase I/II	Tramadol
Phase I/II	TS-020
Phase I/II	Ulinastatin
Phase I	**DRUG**
Phase I	Adalimumab
Phase I	DM-03820
Phase I	Agent-797
Phase I	AIC-649
Phase I	Alvelestat
Phase I	AM-301 (Bentrio)
Phase I	Amnioboost
Phase I	Aptoll
Phase I	AT-100
Phase I	AT-301
Phase I	AT-H201
Phase I	AV-001
Phase I	Bacteriotherapy
Phase I	BAT-2020; BAT-2022
Phase I	Bempegaldesleukin
Phase I	BI-767551
Phase I	BZ-371B
Phase I	CD-16; N-803; BM-Allo.MSC (mesenchymal stem cells)
Phase I	CDI-45205
Phase I	Centi-B9
Phase I	CK-0802
Phase I	Convalescent Plasma; SARS-CoV-2 specific T cells
Phase I	Covishield (STI-9199)
Phase I	CT-P63
Phase I	Decidual stromal cells
Phase I	DNL-758 (SAR-443122)
Phase I	DXP-593; DXP-604
Phase I	EDP-235
Phase I	Emricasan
Phase I	Escozine (scorpion venom)
Phase I	FB-2001
Phase I	Fluvid

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Phase I	FT-516
Phase I	HFB-30132A
Phase I	Hypothalamus stem cell exosomes
Phase I	IBIO-123
Phase I	IDB-003
Phase I	IMM-BCP-01 (biosynthetic convalescent plasma; IMM-20253 and IMM-20184)
Phase I	ISA-106
Phase I	JMB-2002
Phase I	JS-016 (etesevimab)
Phase I	Larazotide
Phase I	Leflunomide
Phase I	Lomecel-B
Phase I	MK-5475
Phase I	Motixafortide
Phase I	MTX-COVAB; COVAB-36
Phase I	Nebulized platelet lysate
Phase I	Neumifil
Phase I	Niagen (nicotinamide riboside)
Phase I	Novaferon
Phase I	NT-I7 (efineptakin alfa)
Phase I	Ofev (nintedanib)
Phase I	PAX-101
Phase I	PBI-0451
Phase I	PL-8177
Phase I	Product-118
Phase I	Quadramune and metformin
Phase I	rCIG; GIGA-2050
Phase I	REVTx-99
Phase I	RGCA-CV01
Phase I	RLS-0071
Phase I	RP-7214
Phase I	SDC-1801
Phase I	SJP-002C
Phase I	SLV-213
Phase I	Solnatide
Phase I	ST-266
Phase I	STAT-205
Phase I	STI-1499 (Coviguard)
Phase I	STI-1558 (MPI-8)
Phase I	STI-2020dna (Covi-Amg)
Phase I	STI-4398 (Covidtrap)
Phase I	STSA-1002 and STSA-1005
Phase I	T-89
Phase I	Tadios
Phase I	Taffix
Phase I	TAK-671
Phase I	TAK-981
Phase I	TD-213
Phase I	Temporary Immunity Agent for COVID-19
Phase I	TLC-19
Phase I	Trans sodium crocetinate
Phase I	TVGN-489
Phase I	Umbilical cord-derived mesenchymal stem cells (intravenous)
Phase I	VHH72-Fc (XVR-011)
Phase I	Vibativ (telavancin)
Phase I	Voclosporin
Phase I	WP-1122
Phase I	Ziverdox
Phase I	Zotatifin
Observational	**DRUG**
Observational	Aspirin
Preclinical	**DRUG**
Preclinical	Aug-87
Preclinical	010DS-Zn
Preclinical	2B11
Preclinical	2-DG
Preclinical	3M-052 nanoparticle compound
Preclinical	47D-11
Preclinical	7HP-349
Preclinical	AB00-1

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Preclinical	Abiprot antibodies
Preclinical	ACE2 protein
Preclinical	ACE2.v2.4
Preclinical	ACE2-Fc
Preclinical	ACE-MAB fusion protein
Preclinical	ADX-1612 (ganetespib)
Preclinical	Affimer reagents
Preclinical	AKL-T01
Preclinical	ALD-R491
Preclinical	Alfacyte
Preclinical	ALG-097111
Preclinical	ALG-097558
Preclinical	Alphabody-based therapeutics
Preclinical	ALT-100
Preclinical	ALVR-109
Preclinical	ALX-009
Preclinical	Androgens (dutasteride)
Preclinical	Antibodies
Preclinical	Antibodies
Preclinical	Antibodies
Preclinical	Antibodies
Preclinical	Antibody
Preclinical	Antibody therapeutics
Preclinical	Antibody therapeutics
Preclinical	Anti-COVID-19 spike protein VNARs
Preclinical	Anti-IL-1R7 antibody
Preclinical	Antiviral
Preclinical	Antiviral
Preclinical	Antiviral
Preclinical	Antiviral
Preclinical	Antiviral
Preclinical	Antiviral agents
Preclinical	Antiviral compounds
Preclinical	Apograft-treated stem cells
Preclinical	AR-701 (AR-711, AR-712 and AR-713)
Preclinical	ARM/NK therapy
Preclinical	ARMS-I
Preclinical	ASC-10
Preclinical	ASC-11
Preclinical	Azelastine
Preclinical	AZM-0703
Preclinical	Balixafortide
Preclinical	BHV-1200
Preclinical	BOLD-100
Preclinical	BPI-002
Preclinical	Brensocatib (INS-1007)
Preclinical	BVX-0320; BVX-1021
Preclinical	BXT-25
Preclinical	CAL-02
Preclinical	Camrelizumab (Airuka); camrelizumab plus thymosin
Preclinical	Cannabigerol and quercetin
Preclinical	Cannabinoid containing complex mixtures
Preclinical	Cannabinoids
Preclinical	Cannabis sativa
Preclinical	Capton product
Preclinical	CB1 antagonist, antiviral and radiotherapeutic
Preclinical	CB-5064
Preclinical	CDI-988 and CDI-873
Preclinical	COR-803
Preclinical	COVID-19 antiviral oral therapy
Preclinical	COVID-19 compounds
Preclinical	COVID-19 compounds
Preclinical	COVID-19 Immunoglobulin
Preclinical	COVID-19 therapeutic
Preclinical	COVID-19 therapeutic
Preclinical	COVID-19 therapies
Preclinical	COVID-19 treatments
Preclinical	COVID-19 treatments
Preclinical	Crofelemer (Mytesi)
Preclinical	CRV-431
Preclinical	Cynarine
Preclinical	Dehydratech antiviral formulation
Preclinical	DHODH inhibitors

Progress towards personalized medicines

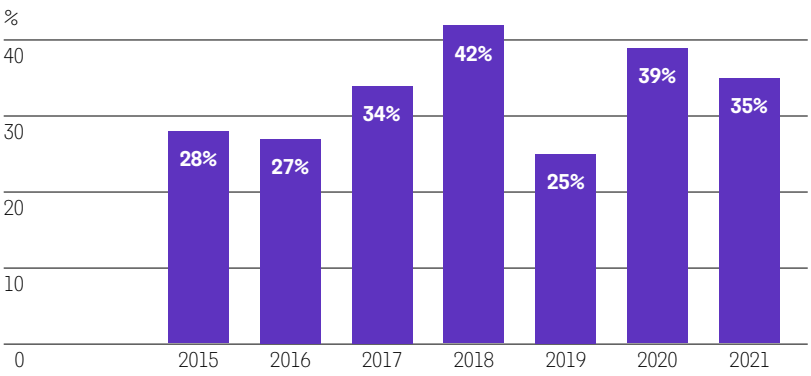
Progress towards personalized medicines

2023 marks the 25-year anniversary of the approval of Herceptin®, which changed the diagnosis of HER2+ breast cancer from a death sentence to one of hope thanks to Herceptin's ability to target HER2.

This monumental advancement also paved the path for future targeted drug development and approval. Fast forward to the last decade and personalized medicine has evolved from promise to reality, accounting for more than 25% of FDA approvals for the last seven years, momentum that is here to stay and is beginning to reach beyond oncology and rare diseases.

Shifting from the traditional 'one-size-fits-all' approach

Personalized medicines accounted for more than 25% of FDA approvals for each of the last seven years.

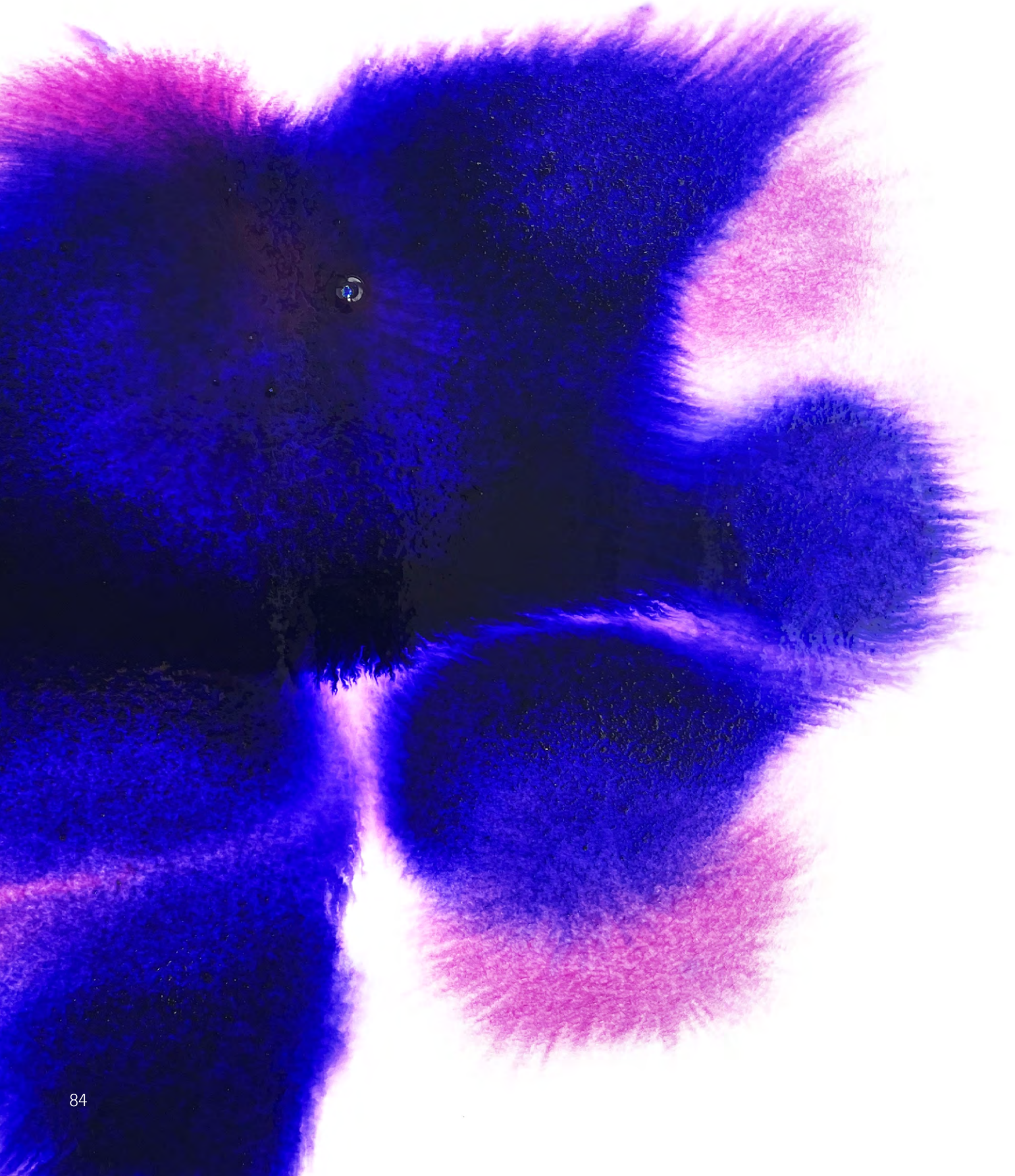


Source: Personalized Medicines Coalition

Shifting from the traditional 'one-size-fits-all' approach of developing and prescribing therapies has benefits not only for patients but also for clinicians, who often resort to trial and error to find the best treatment for a given patient, and clinical trials, leading to new and adaptive designs. Trial protocols can focus on the patients most likely to respond and least likely to experience serious adverse events, contributing to faster times to market and greater success rates.

Challenges yet to be overcome include regulatory harmonization, cost-effectiveness and reimbursement and the widespread infrastructure to identify eligible patients and ensure they have access to the treatments they need.

Global equity and sustainability



Sustainable Development Goals encourage innovative solutions for global epidemics

Since their introduction in 2015, the United Nations Sustainable Development Goals (SDGs) have achieved global adoption across industries, with many life sciences companies, such as Novo Nordisk, GSK plc, Pfizer and AstraZeneca, incorporating them into their environmental, social and governance plans. SDG 3 aims to "ensure healthy lives and promote well-being for all at all ages."

Of particular relevance to pharma and biotech are the targets of SDG 3.3, which focuses on ending the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combatting hepatitis, waterborne diseases and communicable diseases; and SDG 3.4, which encourages reducing premature mortality from noncommunicable diseases by one-third through prevention and treatment and promoting mental health and well-being.

The chart below contrasts several of these conditions with NASH, a recent hotspot of R&D activity due in part to its substantial commercial potential in the wealthy world.

Drugs in development (all phases) for diseases of concern in United Nations Sustainable Development Goal 3

Tubercolosis	44
Malaria	67
Hepatitises	153
HIV 1 and 2	195
Heart disease	757
Nonalcoholic steatohepatitis (NASH)[1]	148

Source: Cortellis Competitive Intelligence

[1] Included for comparison only, as NASH is not addressed in UN SDG 3.

Key takeaways for industry executives

- **Pharma companies continue to churn out innovative targeted treatments.**
  Bringing these novel treatments to market increasingly requires sophisticated use of real world evidence (RWE) to validate their efficacy and impact on patient lives for regulators and payers. Furthermore, with policymakers under pressure to control drug spending as economies slog through post-pandemic hangovers, pharmas will need up-to-date market access intelligence in order to navigate shifting policy and regulatory regimes.
- **Biotechs are operating in a much more austere financing environment than they were a year ago**
  and, with easy capital drying up, have lost some of the leverage they once enjoyed to commercialize their own products.With more of these companies contemplating deal-making, partnerships and acquisitions to bring their innovations to market, ensuring accurate valuation of their products and platforms will prove essential.
- **IP law firms with life science and healthcare practices will want to keep an eye on the patent disputes around emerging platforms,**
  such as the ongoing legal battle over gene editing techniques. Understanding the competitive landscape around developing modalities such as RNA therapeutics, antibody drug conjugates and machine learning/artificial intelligence can help firms identify opportunities and anticipate challenges.
- **Payers and providers seeking to manage the cost of these innovative medicines will need a clear view of pipelines and accurate forecasts**
  of potential pricing and earnings, as well as trustworthy analytics on their potential impact on patient outcomes.

Many life science companies will face urgent challenges in the year 2023, from patent cliffs to capital investment.

However, with the industry on the cusp of unlocking revolutionary technologies that could greatly advance human health, the opportunities have never been greater.

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Navigating the global healthcare landscape is increasingly complex and discovering, developing and commercializing successful treatments that change patient lives is a monumental task. **Learn how Clarivate can help with** experts, connected data and solutions across the product lifecycle.

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