Drugs to Watch & Key Trends - 2023

Mr. Mike Ward, Dr. Reena V Gupta, Dr. Hozana Castillo | March 15, 2023

Agenda

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MR. MIKE WARD

Global Head of Life Sciences and Healthcare Thought Leadership
Clarivate

Mike Ward joined Clarivate in 2020, as global head of Life Sciences and Healthcare thought leadership.

Mike has been analyzing and commenting on the global healthcare for more than 37 years. He was formerly an award-winning business journalist and has managed editorial teams covering all aspects of the global healthcare industry.

DR. REENA V. GUPTA
Senior Business Solution Consultant
Clarivate

Dr. Reena V. Gupta is a Senior Business Solution Consultant at Clarivate for Lifesciences and Healthcare Intelligence Solutions.

She has a doctorate in Organic Chemistry and around 16 years of unique comprehensive experience in pharmaceutical industry holding multiple senior roles. Dr. Reena has broad and rich knowledge of R&D, quality, regulatory, manufacturing, portfolio optimization and business aspects of the pharma industry.

Her objective is to get data and information driven quality intelligence accessible across the industry, enabling rapid access to life saving affordable medicines across the globe.

Introduction

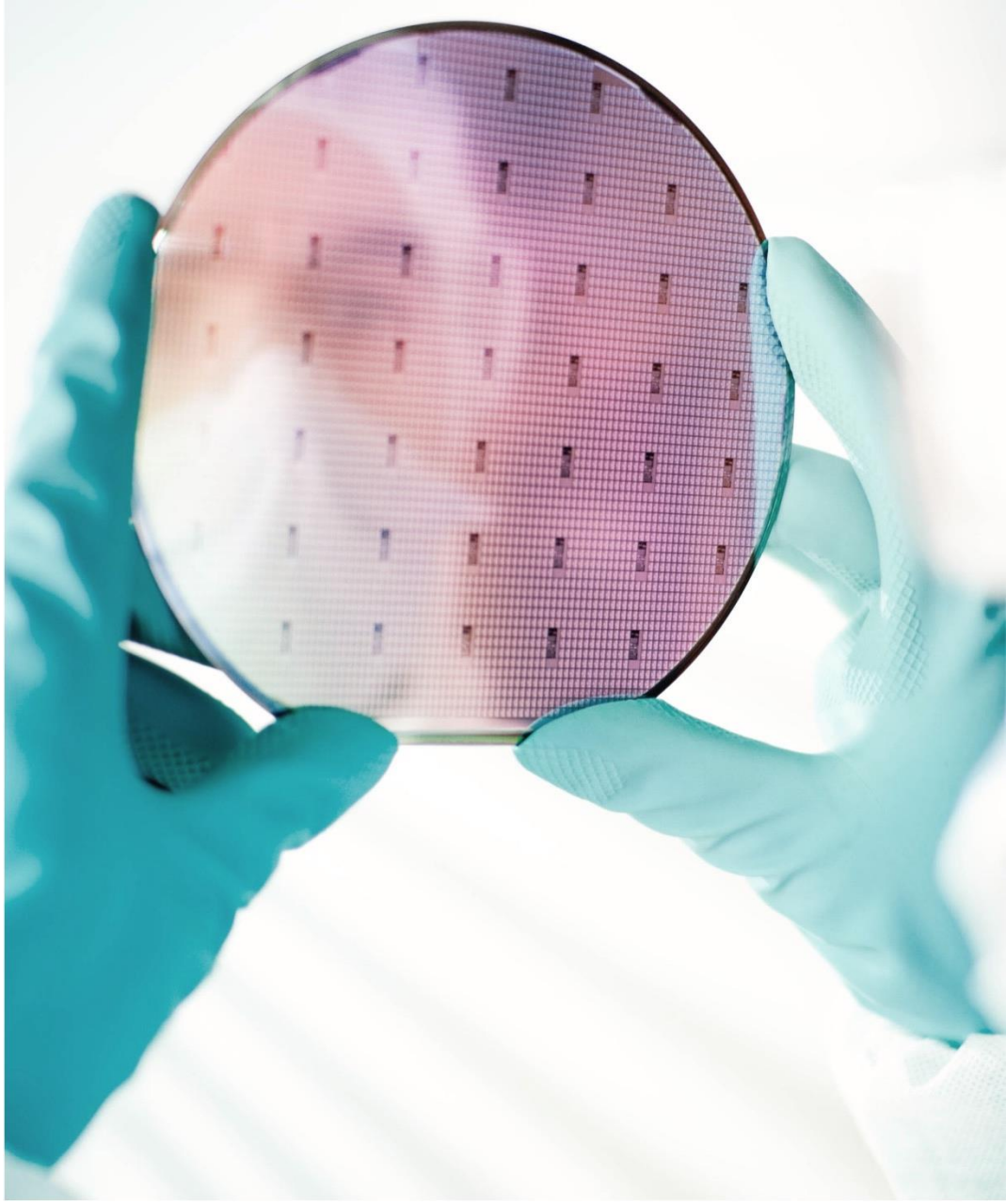
1. Top trends in pharma and biopharma
2. Shift towards value based health care
3. Key challenges –need for powerful data and analytics
    i. Gaining individualised view of patients
    ii. Streamlining R&D
    iii. Future proofing reg. affairs strategy
    iv. Understanding Burden of disease

01

Bimekizumab

BIMZELX®

*Product pack launched in Europe



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Bimekizumab

BIMZELX®

Innovator: UCB

Type/MoA (Mechanism of Action): Humanized IgG1 monoclonal antibody (mAb)

Indications

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

Why is it a drug to watch

- 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.
- Less-frequent dosing schedule and good safety profile will likely be attractive to clinicians and patients.
- the first drug to receive NICE approval (The National Institute for Health and Care Excellence) in UK via its new fast track approval; NICE recommendation

Impact on market

- ~11.7M symptomatic psoriasis cases in the G7 markets in 2021. 80–90% of patients with psoriasis have plaque psoriasis the G7 markets in 2021.

Treatment gaps addressed

- COSENTEX and TALTZ -Efficacy gap
- SILIQ-Safety gap-black box warning
- Less-frequent dosing schedule and good safety profile will likely be attractive to clinicians and patients.
- Approved for rare types of psoriasis-JP.

Hurdles might it need to overcome to reach blockbuster status

- Fourth-in-class IL-17 entrant- competitive market
- Increasing treatment choices- competing with efficacious biologics, biosimilars and the targeted oral drugs Otezla® and SOTYKTU.
- Delayed entry US market- Covid restrictions and complete response letter to UCB

DTSR prediction

Review and Approval status

August 2021-EC - For patients with moderate to severe plaque psoriasis who are candidates for systemic therapy.
January 2022-MHLW- For patients with moderate to severe plaque psoriasis, generalized pustular psoriasis or psoriatic erythroderma.
February 2022-Canada- For patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.
September 2022- Marketing authorization application: EC: For patients with psoriatic arthritis (PsA)
Marketing authorization application: EC: For patients with active axial spondyloarthritis (axSpA)
November 2022-US- Biologics License Application resubmitted: For patients with moderate to severe plaque psoriasis
Actual and expected launch 2021: Europe 2022: Japan 2023: United States

Market overview and Patent expiry

- Patents estimated to expire beginning in 2027
- $2.045B expected sales in 2027

02

Capivasertib

AZD5363

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Capivasertib

AZD5363

Innovator: AstraZeneca

Type/MoA (Mechanism of Action): ATP-competitive pan-AKT kinase inhibitor

Indications

- Oral administration to treat triple negative and HR positive/HER2 negative breast cancer.
- In late-phase trials for prostate cancer.

Why is it a drug to watch

- Promising results in early-phase trials, with clinical benefit to patients irrespective of their PIK3CA/AKT1/PTEN mutational status

Impact on market

- ~ 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 breast cancer in women in the G7 markets in 2021
- Breast cancer is one of the largest therapy markets in oncology –
  - 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.

Treatment gaps addressed

- Triple-negative breast cancer characterized by a heterogeneous patient population with a lack of well-established predictive biomarkers- lacking targeted therapies - lacking 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.

DTSR prediction

Hurdles might it need to overcome to reach blockbuster status

- Increasingly competitive- booming drug development- high level of unmet need and lack of approved agents
- Multiple drug classes being investigated- including immune checkpoint inhibitors, antibody-drug conjugates, therapeutic vaccines, PARP inhibitors and CDK4/6 inhibitors
- Capivasertib sales forecast - metastatic HR-positive/HER2-negative setting- 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

Review and Approval status

Expected launch

- 2023: United States and Europe
- 2024: Japan

Market overview and Patent expiry

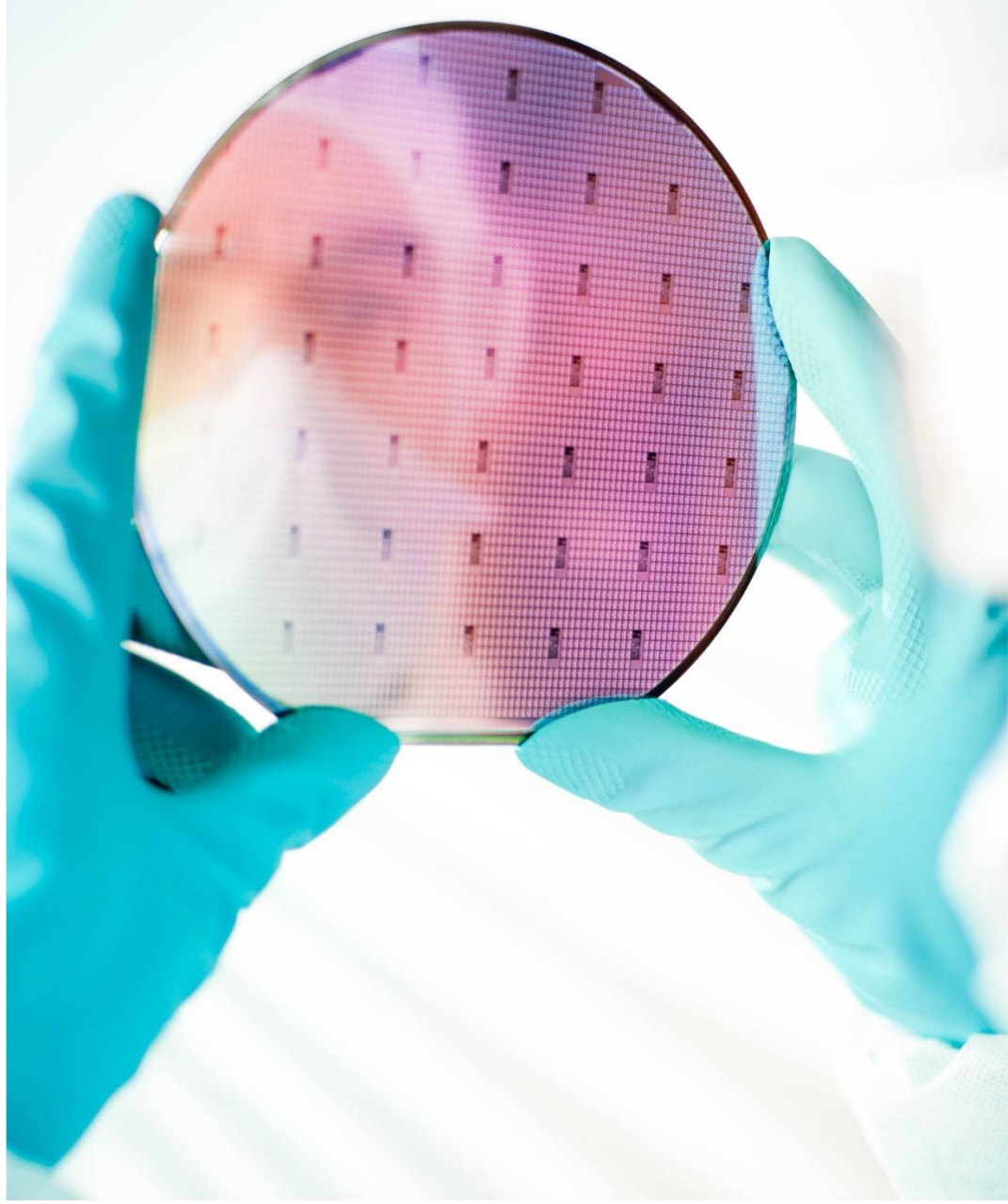
- Patents estimated to expire beginning in 2028.
- Forecast to exceed sales of $ 0.53bn in 2027, $1 billion in 2031 across the major G7 markets.
- Capivasertib is estimated to hold 5% of the first-line metastatic triple negative breast cancer market and approximately 10% of the second, third and fourth-line metastatic HR-positive/HER2-negative breast cancer market in 2031 (across the G7 markets).

03

Daprodustat

GSK1278863/Duvroq

Product pack launched in Japan



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Daprodustat

GSK1278863/Duvroq

Innovator: GlaxoSmithKline plc.

Type/MoA (Mechanism of Action): Hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI)

Indications

Chronic kidney disease (CKD)–related anemia

Why is it a drug to watch

- HIF-PHI developed to treat anemia associated with CKD, which has a high incidence rate and few effective, safe treatment options.
- 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)

Impact on market

- ~67m cases of CKD in the G7 markets in 2021
- Fostered by its oral formulation (versus intravenous), effective haemoglobin-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.
- Opportunity to be first-in-class in the United States for this patient population- CRLs from the FDA for vadadustat and Roxadustat
- In Japan, Duvroq is leading market share (at ~47%) within the HIF class against four other competitors, despite being the second to launch-switch from current treatment to Duvroq.

Treatment gaps addressed

- Anemia is a common complication of CKD.
- Current treatment involves injectable recombinant ESA- serious adverse cardiac reactions and risk of sudden cardiac death in addition to inconsistent responses.
- Safer option that significantly improves outcomes regardless of dialysis status.

DTSR prediction

Hurdles might it need to overcome to reach blockbuster status

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

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

Market overview and Patent expiry

- Patents estimated to expire beginning in 2027
- $0.53B expected sales in 2027

04

Deucravacitinib

BMS-986165

Product pack launched in Japan

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Deucravacitinib

BMS-986165

Innovator: Bristol Myers Squibb

Type/MoA (Mechanism of Action): Allosteric TYK2 inhibitor

Indications

- To treat moderate-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

Why is it a drug to watch

- First-in-class oral TYK2 inhibitor with unique mechanism of action that inhibits signalling of IL-23, IL-12 and type 1 interferon (IFN), key cytokines involved in the pathogenesis of the multiple immune-mediated diseases.
- Superior skin clearance, sustained response, safety profile.

Impact on market

- ~11.7m symptomatic psoriasis cases in the G7 markets in 2021
- ~ 45 years average age of symptomatic psoriasis cases
- Bolstered b'cos- oral administration with an efficacy that can compete with that of biologics
- superior efficacy over apremliast, which could result in first-line use for patients who are refractory or intolerant to apremilast, specially since physicians do not consider apremilast to be very efficacious.

Treatment gaps addressed

- For symptomatic patients with moderate to severe plaque psoriasis, safe, efficacious oral therapies remain an unmet need.
- currently available oral targeted therapy, apremilast, is not as effective as available biologics

DTSR prediction

Hurdles might it need to overcome to reach blockbuster status

- 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.
- 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).

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

Market overview and Patent expiry

- Patents estimated to expire beginning in 2033
- $2.12B expected sales in 2027

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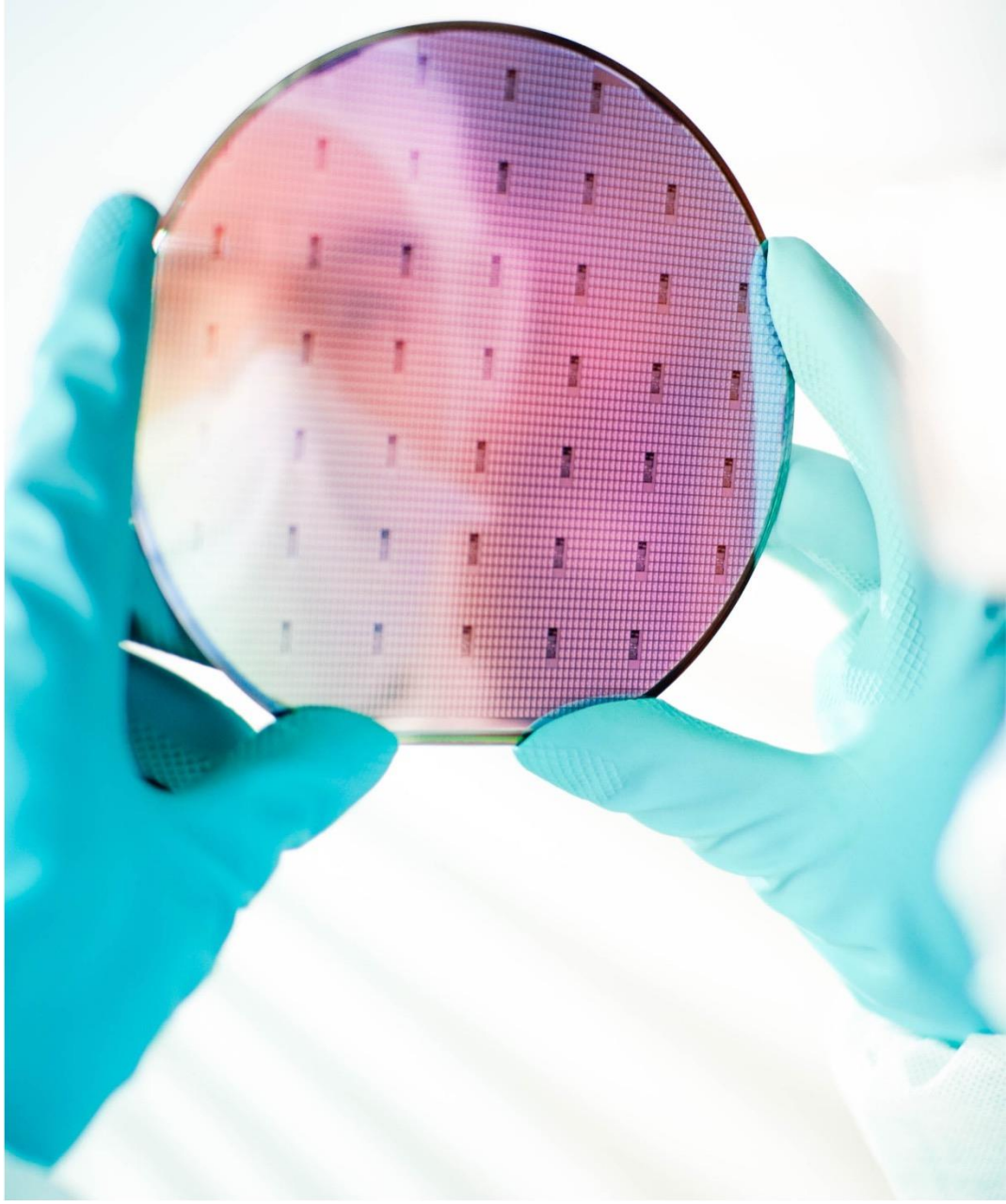
05

Foscarbidopa/ Foslevodopa

ABBV-951



Foscarbidopa/ Foslevodopa

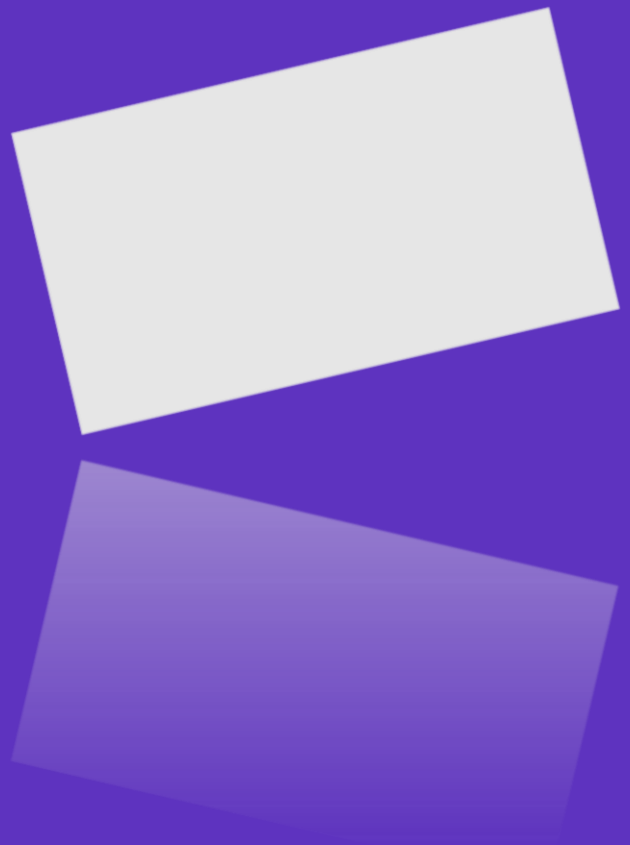
ABBV-951

Innovator: AbbVie

Type/MoA (Mechanism of Action): Carbidopa and levodopa prodrugs

Indications	Continuous 24-hour subcutaneous infusion to treat motor fluctuations in patients with advanced Parkinson's disease
Why is it a drug to watch	• First subcutaneous carbidopa/levodopa infusion to market, addressing noted shortcomings with DUOPA/DUODOPA (e.g., surgical requirements, complications).
Impact on market	• ~ 2.8 Mn diagnosed prevalent cases of Parkinson's disease in the G7 markets in 2021 •Delivering levodopa-carbidopa via subcutaneous infusion.
Treatment gaps addressed	• The ability to offer multiple dose strengths at one insertion site might prove a strong advantage. • 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). • could be an alternative for patients ineligible for DBS or who do not want to undergo surgery • With its continuous delivery, foscarbidopa/foslevodopa optimizes the pharmacokinetic/pharmacodynamic (PK/PD) profile of the standard of care- profound relief for patients with Parkinson's disease, especially those in the later stages of the disease.

DTSR prediction



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.
- expected high pricing is likely to constrain access and uptake
- Concern is the high rates of discontinuation of foscarbidopa/foslevodopa reported in completed phase 3 trials.

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

Market overview and Patent expiry

- Patents estimated to expire beginning in 2039
- $0.88B expected sales in 2027

06, 07

Lecanemab

LEQEMBI™

Donanemab

LY-3002813

Lecanemab Product pack launched in US

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Lecanemab

LEQEMBI™

Donanemab

LY-3002813

Lecanemab

Innovator: Eisai Co Lt and Biogen Inc.

Type/MoA (Mechanism of Action): Anti-Aβ protofibril Mab

Donanemab

Innovator: Eli Lilly and Company

Type/MoA (Mechanism of Action): Anti-Aβ N3pG MAb

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Indications

Lecanemab: Treatment of mild cognitive impairment (MCI) due to Alzheimer's disease and mild Alzheimer's disease.
Donanemab: Treatment of MCI due to Alzheimer's disease and mild Alzheimer's disease.

Why is it a drug 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.
- 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.

Impact on market

- ~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
- Until the approval of ADUHELM, symptomatic therapy - only treatment option for patients with Alzheimer's disease.
- Acetylcholinesterase inhibitors and memantine, now generic, - 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).
- 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.
- Further trial results supporting the amyloid-beta hypothesis for Alzheimer's disease causality, as well as improved safety and delivery profiles.

Lecanemab DTSR prediction

Treatment gaps addressed

- 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

Hurdles might it need to overcome to reach blockbuster status

- Positive phase 3 outcomes, blockbuster sales for Lecanemab and Donanemab
- Entry of ADUHELM accomplished little to prime health system preparedness.
- 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.
- The regulatory and payer decisions on lecanemab - precedent for others in the class and uptake is expected to be slow until reimbursement terms are set.

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': PMDA
- July 2022 Biologics License Application (BLA) accepted and priority review granted: U.S. FDA ; January 6, 2023 Granted accelerated approval: U.S. FDA
- **Launched : 2023** United States **Expected launch 2024:** Japan and Europe

Lecanemab DTSR prediction

Donanemab DTSR prediction

Review and Approval status (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

Market overview and Patent expiry

- Lecanemab:Patents estimated to expire beginning in 2025
- Donanemab: Patents estimated to expire beginning in 2031
- Lecanemab:$1.02B expected sales in 2027
- Donanemab: $1.34B expected sales in 2027

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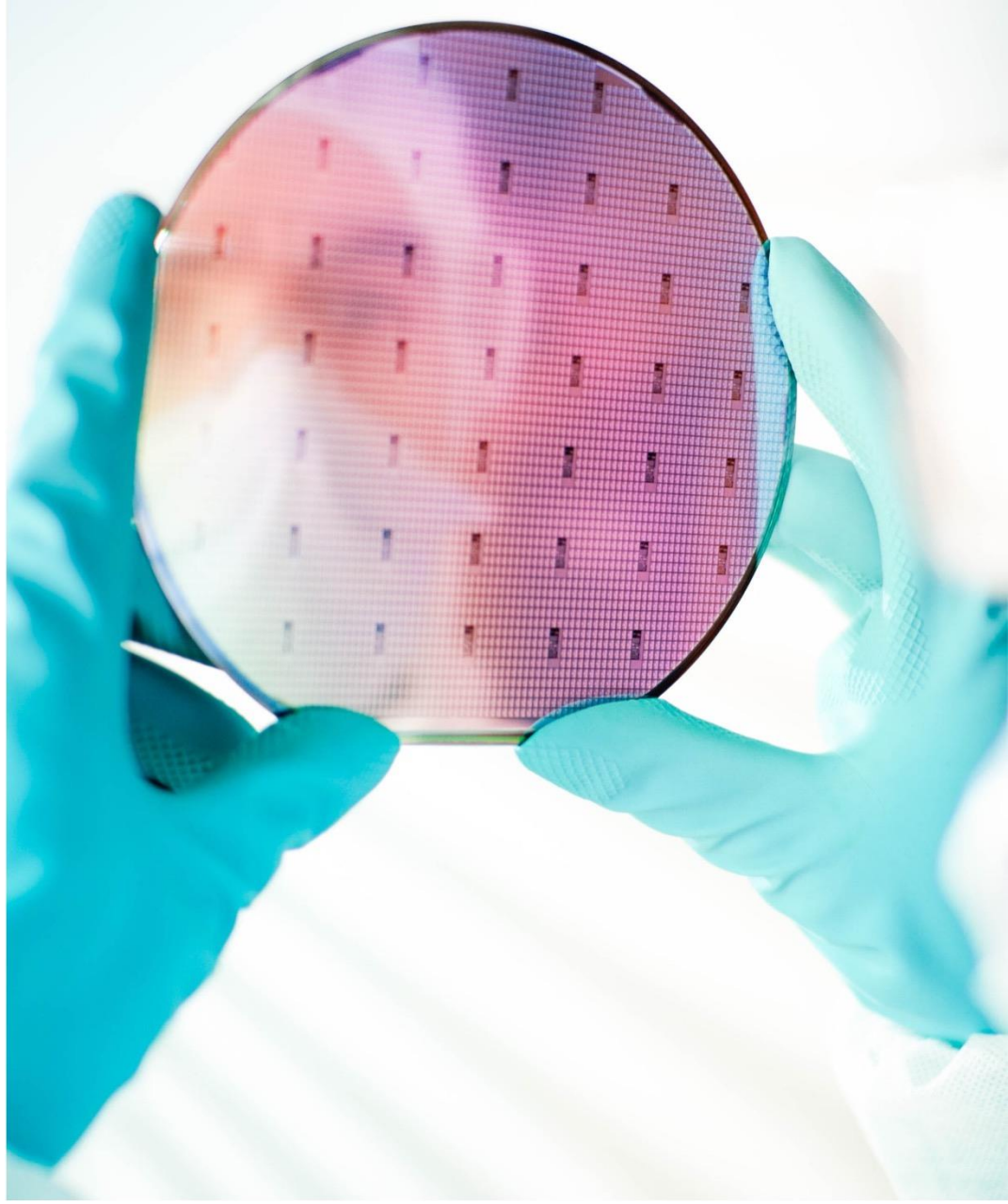
08

Lenacapavir

Sunlenca®/GS-6207

Product pack launched in US



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Lenacapavir

Sunlenca®/GS-6207

Innovator: Gilead Sciences Inc.

Type/MoA (Mechanism of Action): Long-acting HIV-1 capsid inhibitor

Indications

Treatment of multi-drug resistant (MDR) HIV

Why is it a drug to watch

- Lenacapavir inhibits HIV-1 at multiple stages during its lifecycle (capsid assembly, transport, and disassembly)
- Differentiates it from most other antivirals that target only one stage of viral replication.
- Opening a new avenue for developing long-acting therapies for people living with or at risk of HIV.
- No known cross resistance to other current drug classes.

Impact on market

- ~38.4m people had HIV globally in 2021. <10% i.e. Only 6 countries globally have achieved <10% HIV drug resistance rates in in long-term treated adults.
- competitive advantage given its convenient, twice-yearly, administration that will help address treatment burden and social stigma
- Rapid uptake is therefore anticipated - predicted - will account for more than one-half of yearly sales of long-acting regimens by 2031.

Treatment gaps addressed

- significant unmet medical need in particular for heavily treatment experienced people with MDR HIV
- 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.
- Lower gastrointestinal toxicity, reduction in related side effects and fewer drug-drug interactions will also make Lenacapavir more tolerable.

DTSR prediction

Hurdles might it need to overcome to reach blockbuster status

- 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
- 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.
- Will need to demonstrate better safety and efficacy than currently available long-action options.
- Pricing will also play a role in uptake-patent expiry of DESCOVY in 2025.

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

Market overview and Patent expiry

- Patents estimated to expire beginning in 2028
- $1.08B expected sales in 2027

The growing market in Mainland China

Optional author's name | Date

- ✓ China’s pharmaceutical market
- ✓ Government’s focus and strategic initiatives-pharma and biopharma
- ✓ Health 2030 vision of China
- ✓ 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.
- ✓ 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.
- ✓ Of the nine selected, eight are oncology drugs- a focus on addressing the increasing cancer burden in Mainland China
- ✓ Estimated that 4,820,000 new cancer cases and 3,210,000 cancer related deaths could occur in Mainland China in 2022.

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

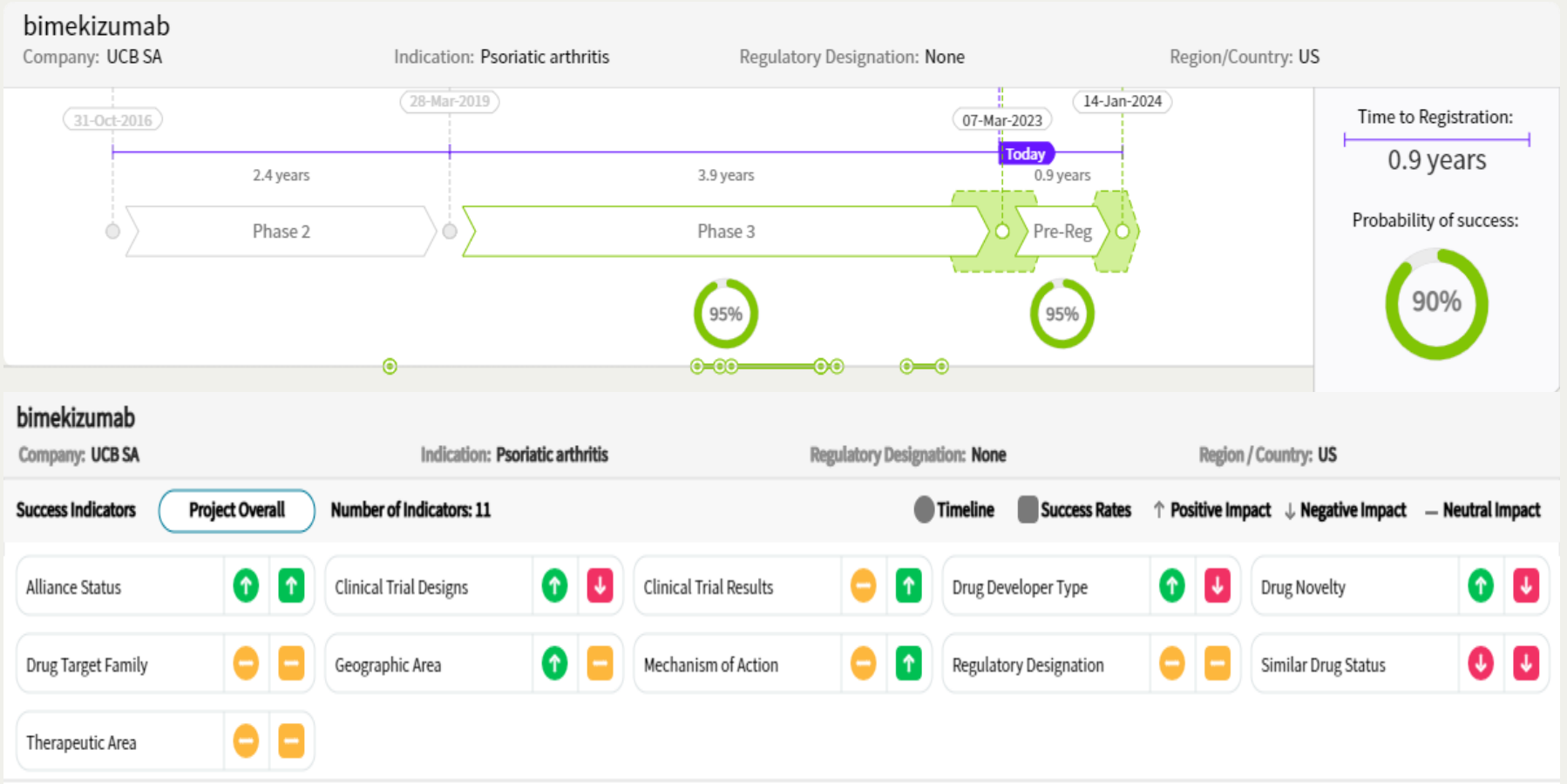
Nivolumab (OPDIVO®)	Bristol Myers Squibb	2014	2015	2018	7,523	2026	First-ever ICI to receive approval in Mainland China; approved to treat epidermal growth factor receptor (EGFR)-negative and anaplastic lymphoma kinase (ALK)-negative NSCLC, squamous cell carcinoma of head and neck (SCCHN) with PD-L1 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

Drug Timeline and Success Rates

01 — Bimekizumab
02 — Capivasertib
03 — Daprodustat
04 — Deucravacitinib
05 — Foscarbidopa/foslevodopa
06,07 — Lecanemab and Donanemab
08 — Lenacapavir

Bimekizumab DTSR SNAPSHOT (US/EU/Japan-Psoriatic Arthritis)- March 2023



Country	Years to registration	DTSR
Japan	0.9	90%
Europe	0.5	95%

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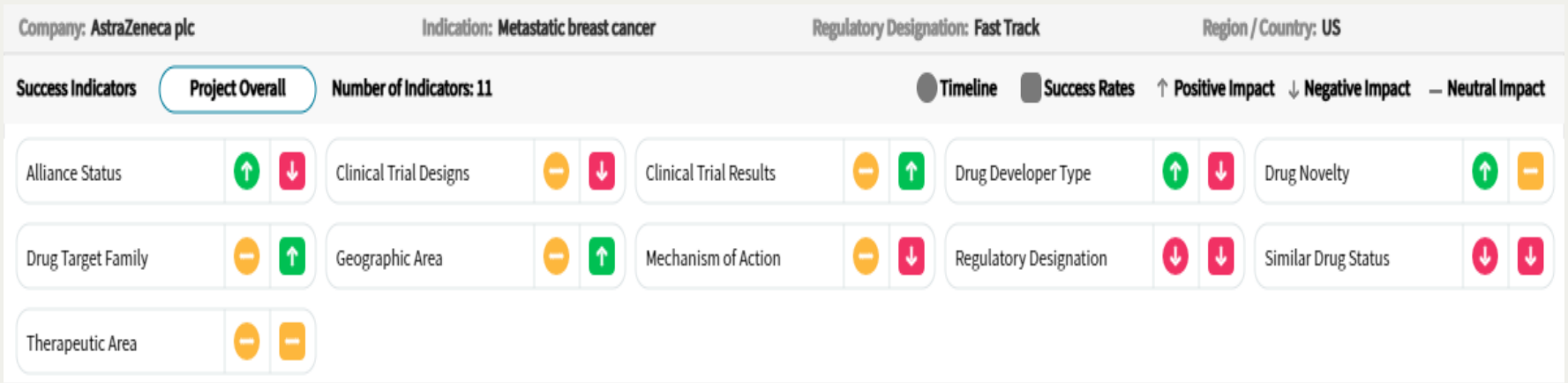
Capivasertib DTSR SNAPSHOT (US/China/Japan-Metastatic breast cancer)- March 2023



Country	Years to registration	DTSR
Europe	1.6	90%
Japan	1.4	90%
China	1.7	90%

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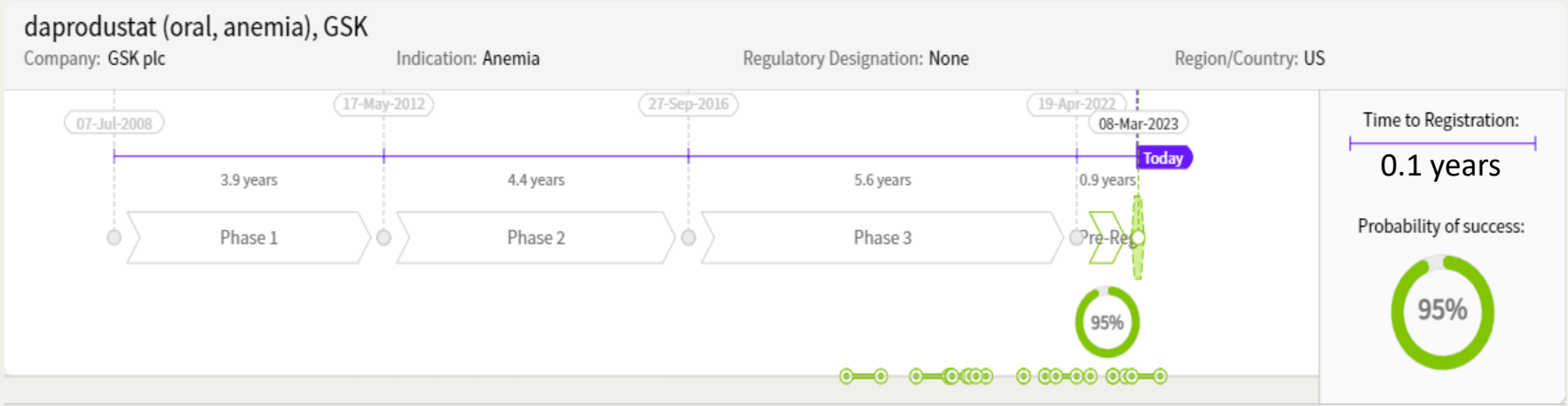
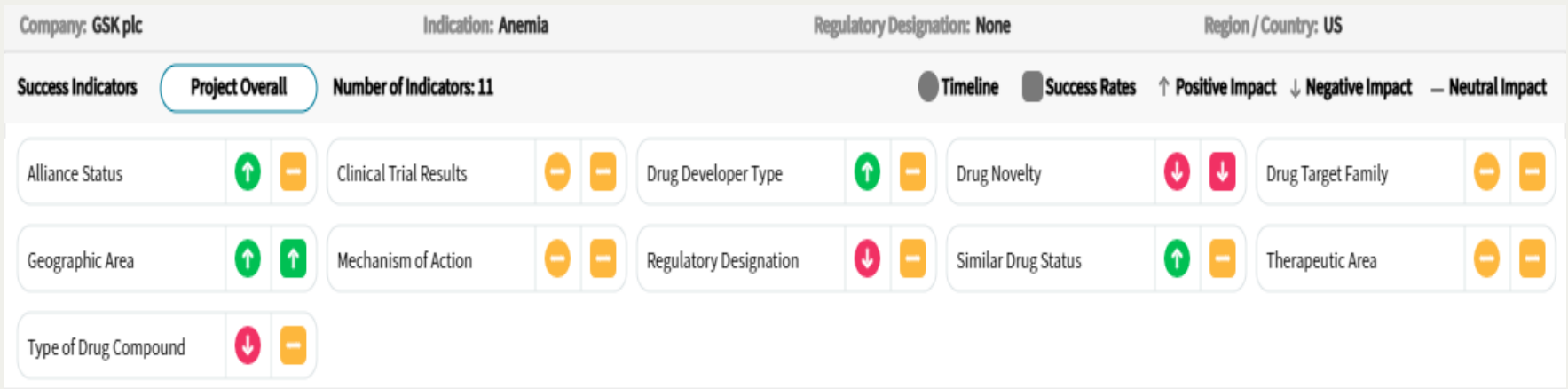
Daprodustat DTSR SNAPSHOT (US/EU/S.Korea- Anemia)- March 2023





Country	Years to registration	DTSR
South Korea	0.9	90%
Europe	0.2	95%

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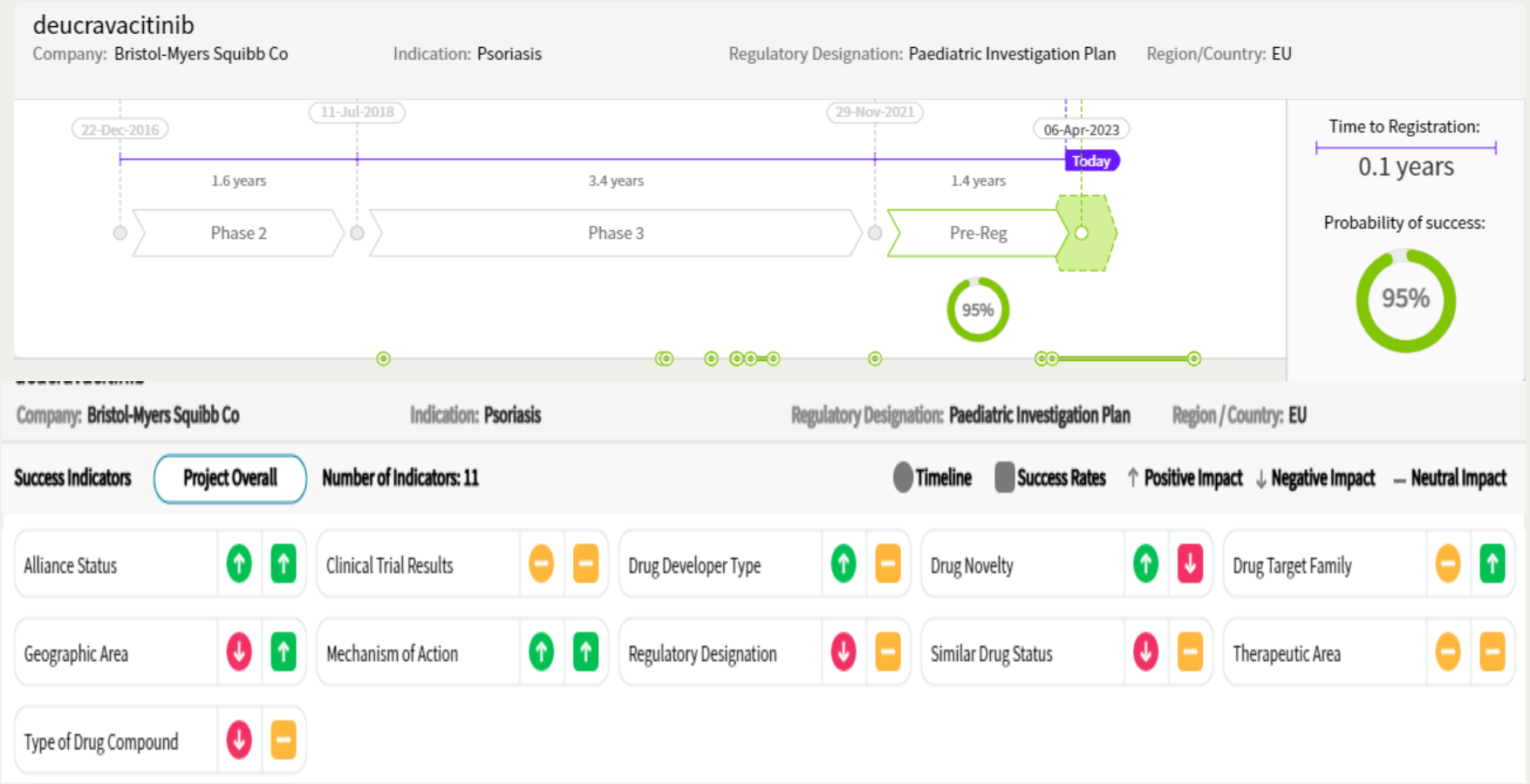
Deucravacitinib DTSR SNAPSHOT (EU/S.Korea/China- Psoriasis)- March 2023



Country	Years to registration	DTSR
China	0.6	95%
South Korea	0.8	90%

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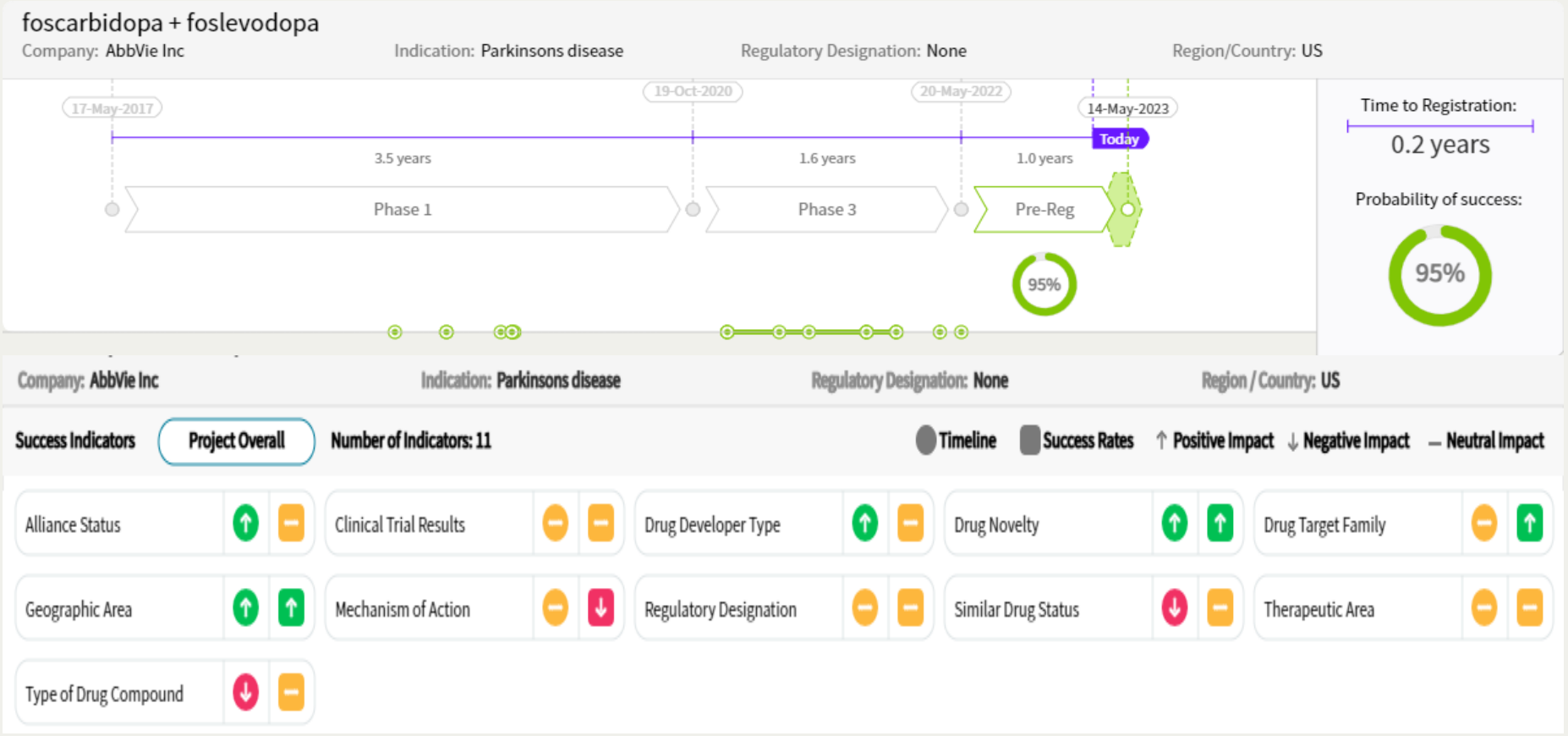
Foscarbidopa/ foslevodopa DTSR SNAPSHOT (US/EU/Japan)- Parkinson's)- March 2023



Country	Years to registration	DTSR
Europe	1.1	90%
Japan	0.1	95%

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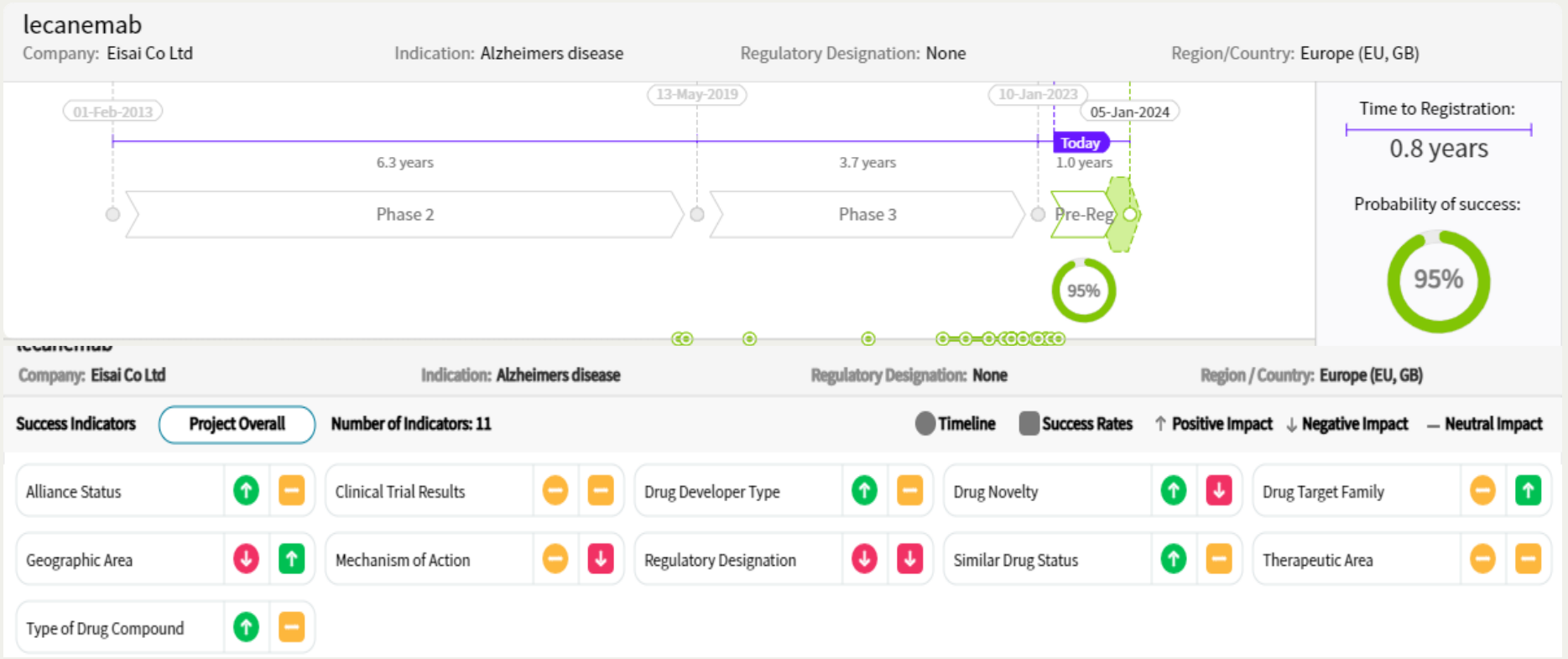
Lecanemab DTSR SNAPSHOT (SG/EU/S.Korea/China)- Alzheimer's disease- March 2023



Country	Years to registration	DTSR
South Korea	1.5	89%
China	1.2	95%
Japan	0.6	95%
Singapore	1.8	90 %

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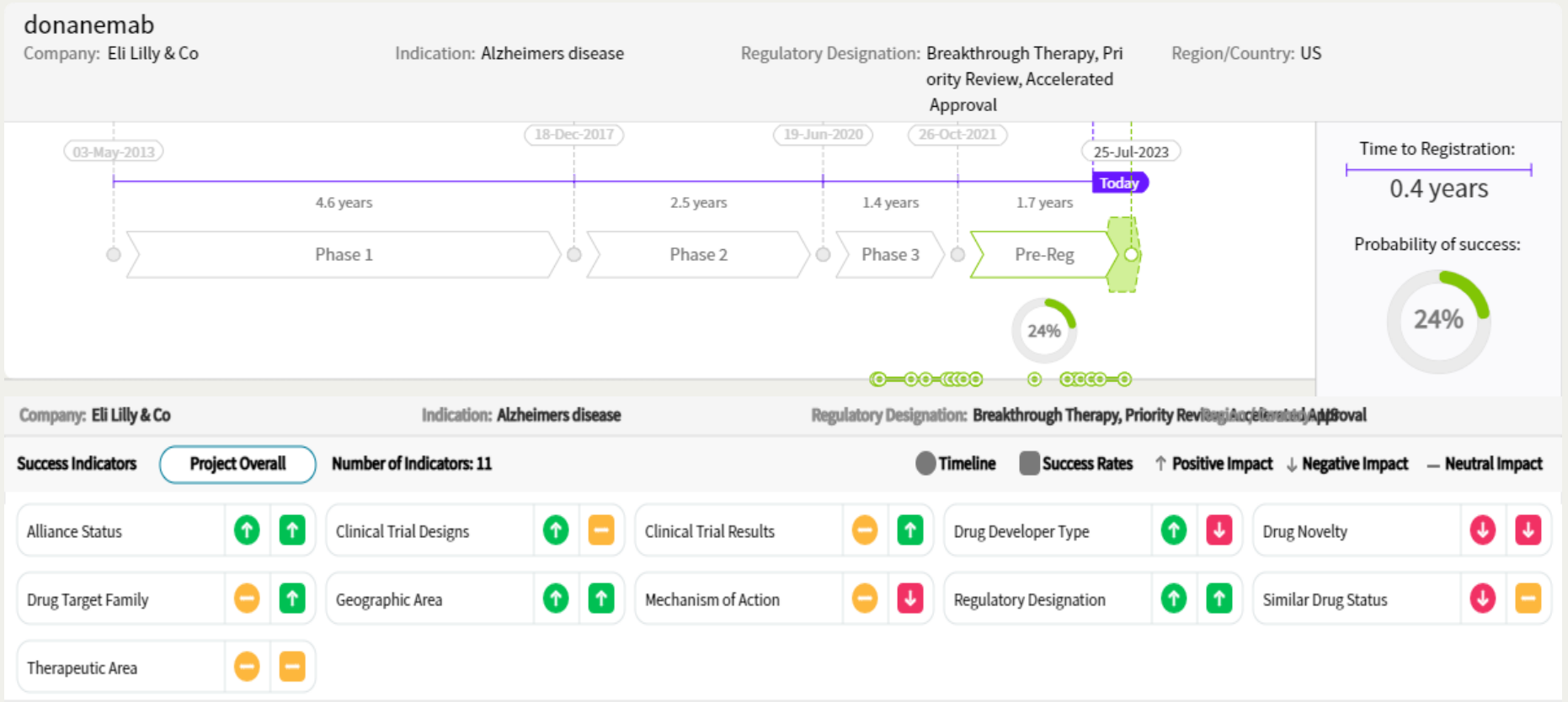
Donanemab DTSR SNAPSHOT - Alzheimer's disease- March 2023



Country	Years to registration	DTSR
Europe	5.5	49%
South Korea	5.2	50%
China	5.7	54%
Japan	5.6	59%

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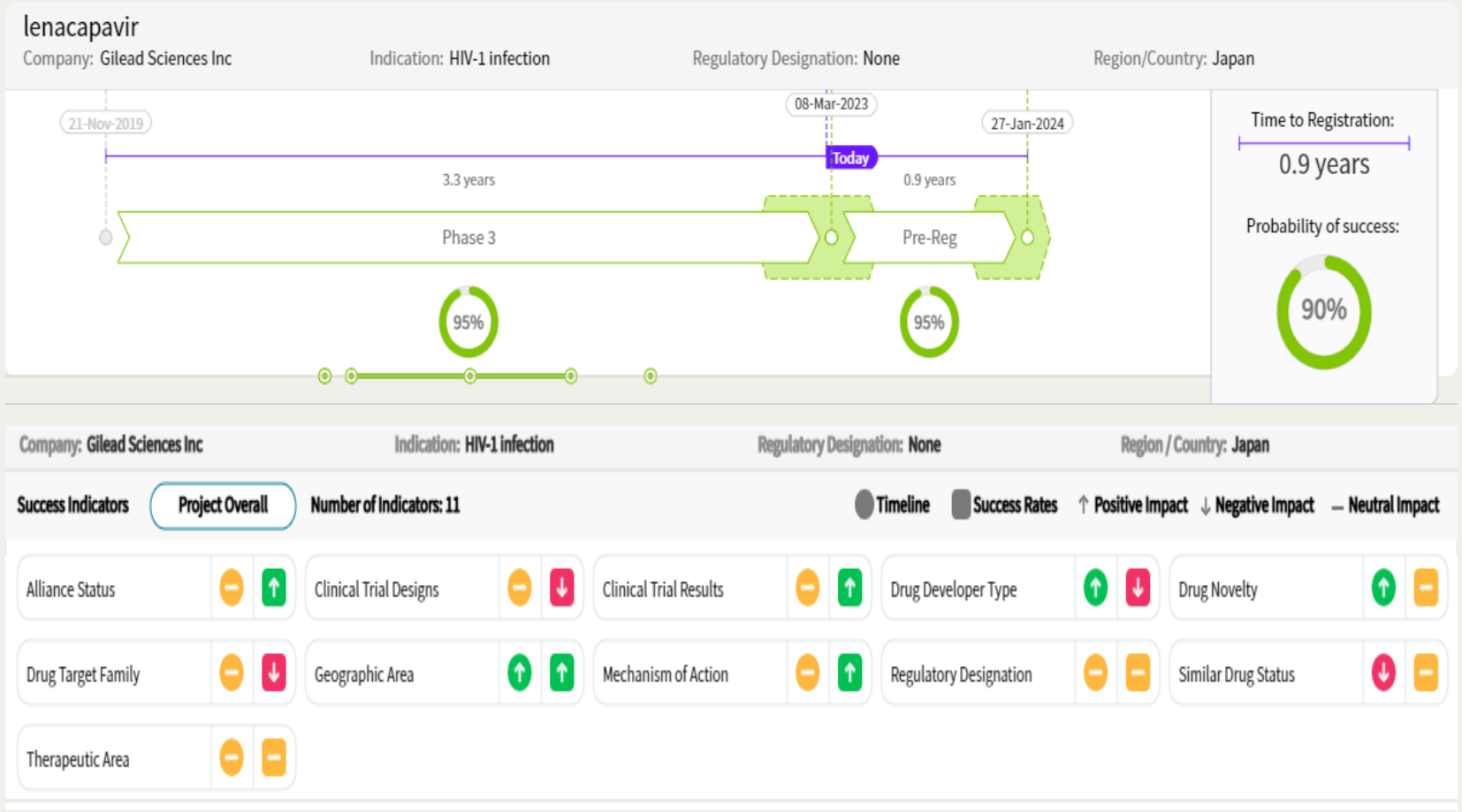
Lenacapavir DTSR SNAPSHOT (Japan-HIV-1 infection)- March 2023



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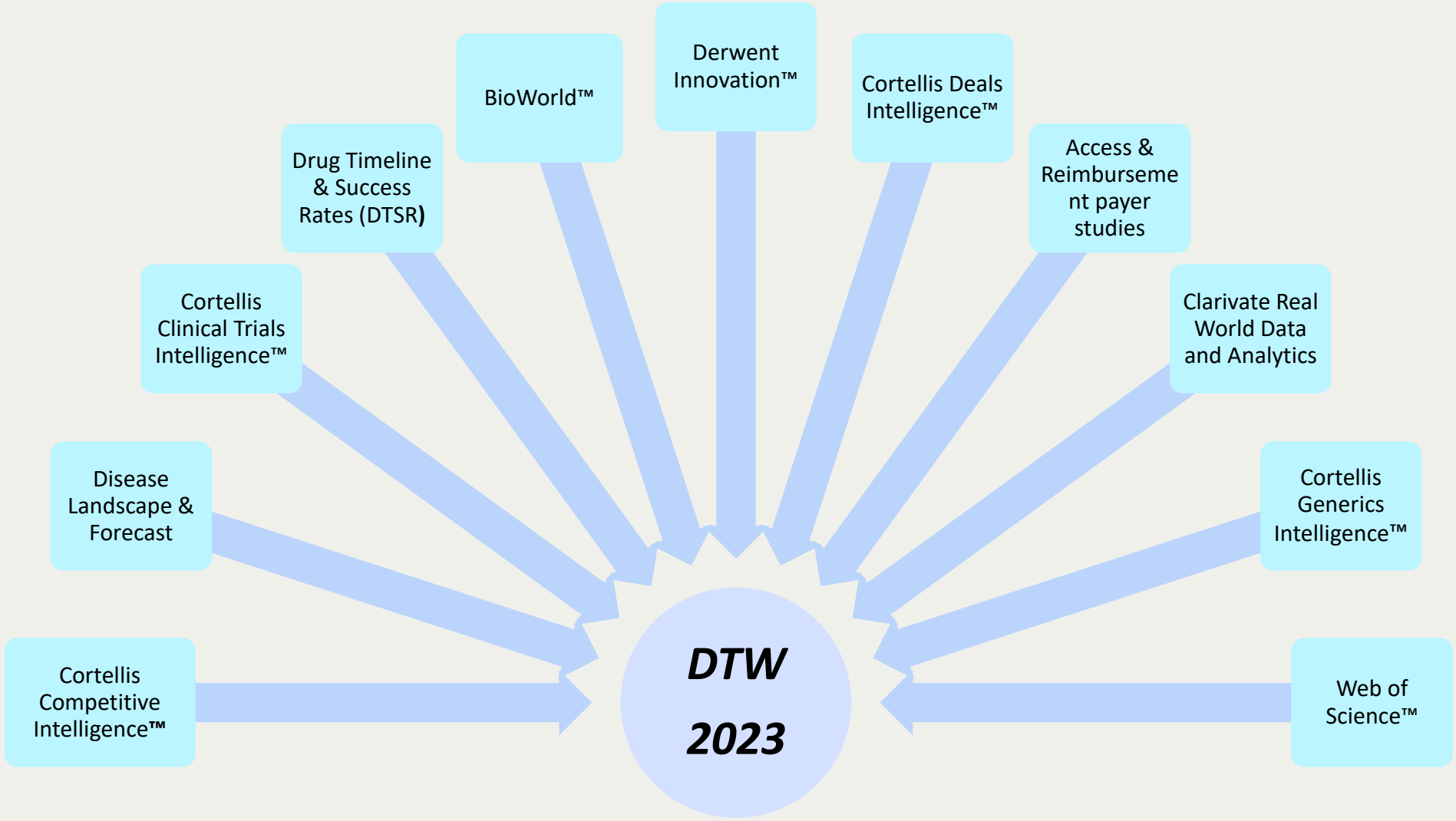

Eleven of Clarivate's many proprietary technologies, tools and techniques

Subscription solutions trusted by our global life sciences customers

Clarivate™

Thank you!

Over to Section -2 of the webinar

DR. HOZANA CASTILLO

Senior Business Solution Consultant
Clarivate

Dr. Hozana Castillo is a Senior Business Solution Consultant at Clarivate. She provides training and insights in platforms related to intelligent information applied to the entire pipeline of drug development, from early discovery to commercialization.

Dr. Hozana received her PhD in Science (Cellular and Tissue Biology) from University of Sao Paulo, Brazil and she was post doctoral fellow at the Australian Regenerative Medicine Institute (ARMI) focusing her research on the understanding of the cellular and molecular mechanisms of spinal cord regeneration in zebrafish. She was a researcher at the Brazilian Biosciences National Laboratory (LNBio) / Brazilian Center for research and Materials (CNPEM) from 2010 to 2019 working in the fields of regenerative medicine, genetics and developmental / cell biology.

Why is it a Drug to Watch?

- Likely will be first-in-class for ulcerative colitis and the third in the class for Crohn's disease.
- Potentially more efficacious and long-lasting treatment option for patients.
- Showed positive phase 2 results for patients with Crohn's disease (significant reductions in disease severity and increased rates of remission) and phase 3 results are promising.

Mirikizumab
LY-3074828

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

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Impact on the market

CD: 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.
UC: Mirikizumab has the potential for approval in the pediatric population, which means expanded patient population, differentiation from other in-class competitors, filling the gap in limited targeted therapies for this population.

Hurdles it might need to overcome

- The later market entry, after STELARA and other IL-23 inhibitors will likely restrain its uptake.
- In addition, the launch of biosimilar ustekinumab, which is expected in 2023, could encroach on the use of all IL-23 inhibitors.
- There will be many therapeutic options in a crowded space, mirikizumab will need to show significantly greater safety and efficacy to reach the blockbuster status

Treatment gaps addressed

Treatment gaps that mirikizumab could help fill include sustainable long-term remission and therapies with alternative mechanisms of action for patients intolerant or resistant to TNF-α inhibitors.

Mirikizumab
LY-3074828

Review and approval status:

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

Crohn's disease expected launch 2024: United States, Japan and Europe

Patents estimated to expire beginning in 2034

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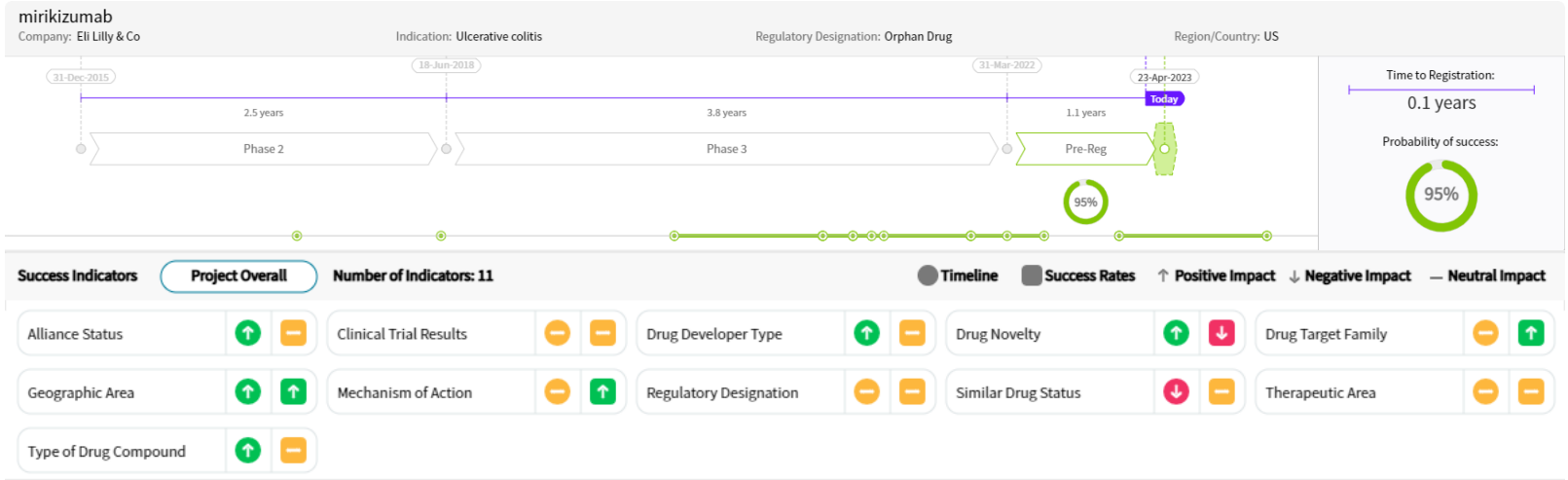
Drug forecast



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Predictive methodology is protected by U.S. Patent No.: 11,093,883 B2

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Indication	Country	Expected launch	Probability of Success
Ulcerative Colitis	South Korea	Jan 2024	90%
Ulcerative Colitis	China	Feb 2025	90%
Crohns disease	South Korea	Sep 2024	90%
Crohns disease	China	Feb 2025	90%

$0.595B

expected sales in 2027

10 Pegcetacoplan
EMPAVELI®/
ASPAVELI®/APL-2

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

Producer: Apellis Pharmaceuticals Inc.

Type: Complement C3 inhibitor

Why is it a Drug to Watch?

- Pegcetacoplan has launched already in the US and Europe for PNH, a rare hematological disease. It has generated $15.1 million in sales in 2021 in US to treat PNH. Additional global approvals for PNH will likely contribute to greater sales over the coming years.
- It is one of the few drugs to have completed phase 3 trials for GA, and it is anticipated to be the first drug to launch for GA, which has no approved pharmacotherapy.
- If launched when expected, pegcetacoplan will be the first GA therapy to market and the sales for GA will likely overcome the sales for PNH.

Pegcetacoplan
EMPAVELI®/ ASPAVELI®/APL-2

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

Impact on the market

- With the aging population across the major markets, the prevalence of GA is expected to continue increasing
- Pegcetacoplan is forecasted to have 76% of overall complement system inhibitor market share in the United States and Europe in 2027.

Hurdles it might need to overcome

- The need for monthly or bimonthly intravitreal administration for GA treatment might be a barrier to its uptake.
- 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.
- The complement inhibitor pipeline is crowded and pegcetacoplan could face great competition.

Treatment gaps addressed

- 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.
- For PNH longer-lasting treatments could improve both adherence and outcomes

Pegcetacoplan
EMPAVELI®/
ASPAVELI®/APL-2

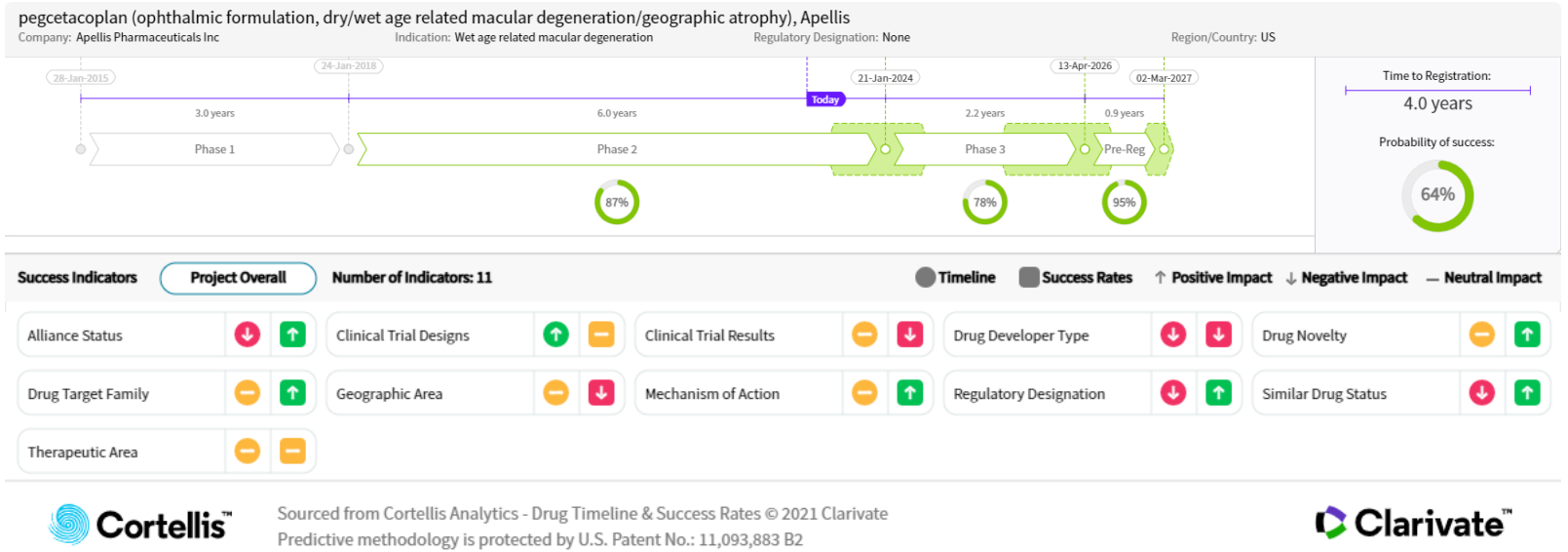
Review and approval status:

PNH Actual Launch
2021: United States
2022: Europe

GA Actual and expected launch
2027: United States,
2024: Europe

Patents estimated to expire beginning in 2033

Drug forecast



Indication	Country	Expected launch	Probability of Success
dry/wet age related macular degeneration/geographic atrophy	Europe	Feb 2024	95%

$1.312B

expected sales in 2027 for GA

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Why is it a Drug to Watch?

- Ritlecitinib is the first in a new class of oral, highly selective dual kinase inhibitors.
- It will likely benefit from its first-in-class status, rapid onset of action and expected label for both adults and adolescents.
- It is currently the only JAK inhibitor being evaluated for adolescent patients.

Ritlecitinib
PF-06651600

Impact:

~4.7m

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

Impact on the market

- This market is expected to grow to as much as $2.5 billion by 2030 in the US and EU5 markets, largely driven by JAK inhibitors.
- Numerous studies showing the efficacy of JAK inhibitors for hair regrowth has garnered interest in their use.
- 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 US and EU5, respectively.

Hurdles it might need to overcome

- Given the existing concerns about safety issues associated with JAK inhibitors, adoption will likely depend on the safety data from the phase 3 trial.
- Competition from other JAK inhibitors in the market or in late-stage development could also limit uptake.

Treatment gaps addressed

Alopecia areata often leads to a potentially negative impact on patients' daily lives and a significant emotional burden.

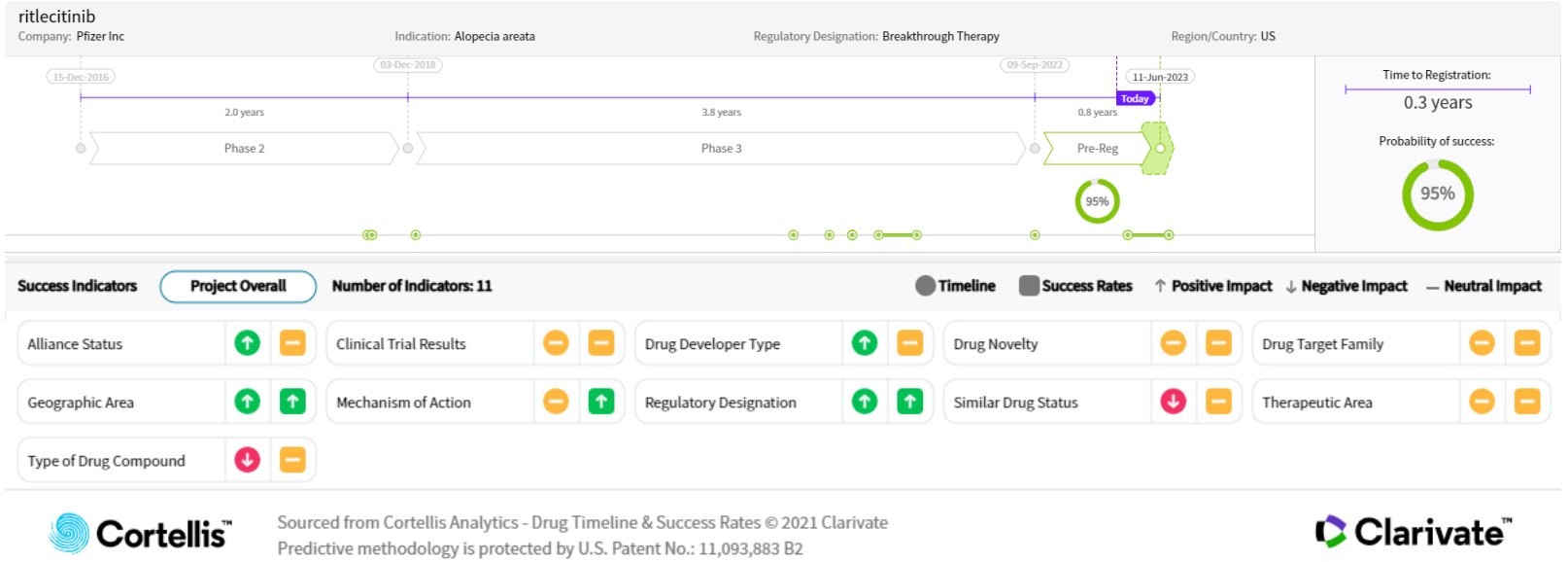
Ritlecitinib
PF-06651600

Review and approval status:

Expected launch 2023: United States, Europe and Japan

Patents estimated to expire beginning in 2039

Drug forecast



Indication	Country	Expected launch	Probability of Success
Alopecia Areata	China	Oct 2023	95%

$0.20B

expected sales in 2027

12 Sparsentan

Indications: Rare kidney disorders

Producer: Travere Therapeutics Inc

Type: Dual endothelin angiotensin receptor antagonist (DEARA)

Why is it a Drug to Watch?

- It 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 the progression of kidney disease for many patients.
- It could be the first treatment on the market to address both populations.

Sparsentan

Impact:

~200
–350k

People with IgA nephropathy globally

FSGS:

~1/7m

Affects approximately seven in one million individuals

Impact on the market

- The first commercially available treatment specifically for IgA nephropathy is TARPEYO™, which was launched in US 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.

Hurdles it might need to overcome

- Other potential competitors in what could become a competitive market are currently in late-stage development.

Treatment gaps addressed

- Current treatments 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.

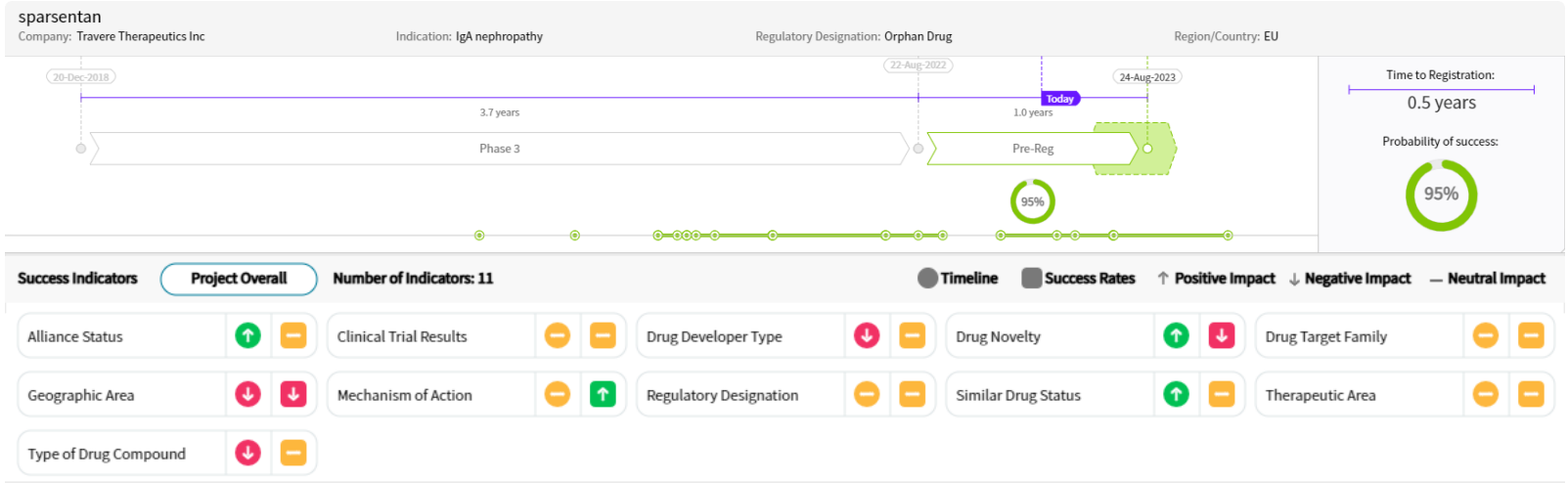
Sparsentan

Review and approval status:

Expected approval for IgAN
2023: Europe
2024: South Korea

Patents estimated to expire beginning in 2030

Drug forecast



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Indication	Country	Expected launch	Probability of Success
FSGS	US	Dec 2023	90%
FSGS	Europe	May 2024	90%
FSGS	South Korea	Mar 2024	90%

$0.81B

expected sales in 2027

Clarivate™

Why is it a Drug to Watch?

- Teclistamab is an off-the-shelf, first-in-class, T-cell redirecting, bispecific antibody targeted to B-cell maturation antigen (BCMA) and CD3.
- Ongoing phase 3 trials are expected to provide confirmation of clinical benefit in teclistamab and lead to label expansions in other multiple myeloma patient populations, including in combination with other approved agents.

Teclistamab
TECVAYLI®/ JNJ-64007957

Impact:

~72k

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

Impact on the market

- Teclistamab is forecast to achieve sales of $1.8 billion in 2031, across the major G7 markets.
- Expected to hold approximately 4% of the first-line ASCT market and 5% of the R/R multiple myeloma market in 2031.
- Can be combined with currently approved drugs and regimens to improve their efficacy.

Hurdles it might need to overcome

- Likely face stiff competition from other BCMA-targeted therapies and bispecific therapies (including bispecifics targeted to BCMA).
- Uncertainty over the optimal treatment sequences for some patients could prove to be a barrier to teclistamab's uptake.

Treatment gaps addressed

- Teclistamab has the potential to extend remissions and delay disease progression and partially fulfills the need for more effective therapies.
- Many patients may be eligible to receive teclistamab versus CAR T-cell therapies.

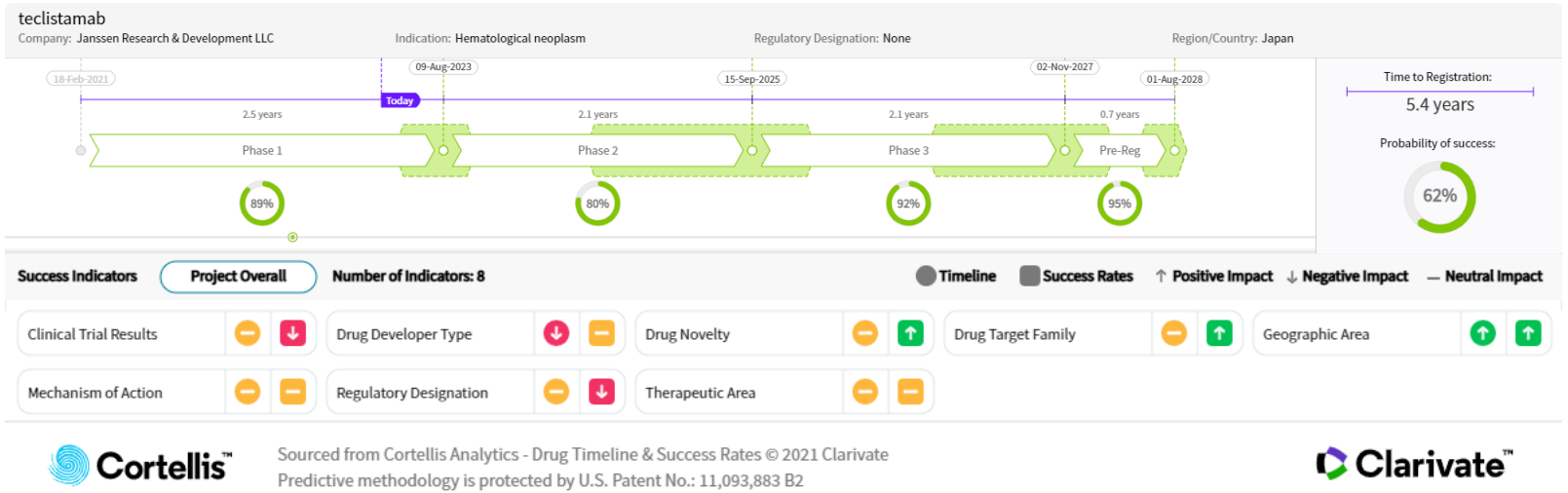
Teclistamab
TECVAYLI®/
JNJ-64007957

Review and approval status:

Expected and actual launch
2022: United States and Europe
2028: Japan

Patents estimated to expire beginning in 2036

Drug forecast



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Indication	Country	Expected launch	Probability of Success
Multiple myeloma	China	Jul 2032	90%

$1.8B

expected sales in 2031

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14 Teplizumab
PRV-031

Indications: Type 1 diabetes mellitus

Producer: Provention Bio Inc

Type: Anti-CD3 monoclonal antibody

Why is it a Drug to Watch?

- It 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.

Teplizumab
PRV-031

Impact:

~1.8m

cases of T1DM in the G7 markets in 2021

Impact on the market

- Advantage of being the first immunotherapy to market.

Hurdles it might need to overcome

- Identification of the eligible population, given the need for large-scale screening for high-risk individuals especially when testing for early T1DM antibodies is not routinely conducted.
- Not all individuals with the relevant antibodies progress to T1DM, which might indicate the need for an additional screening stage to determine eligibility.
- The daily intravenous administration for 12-14 days might be a barrier to uptake.

Treatment gaps addressed

- Disease-modifying drugs such as teplizumab have the potential to prolong disease progression and improve quality of life.

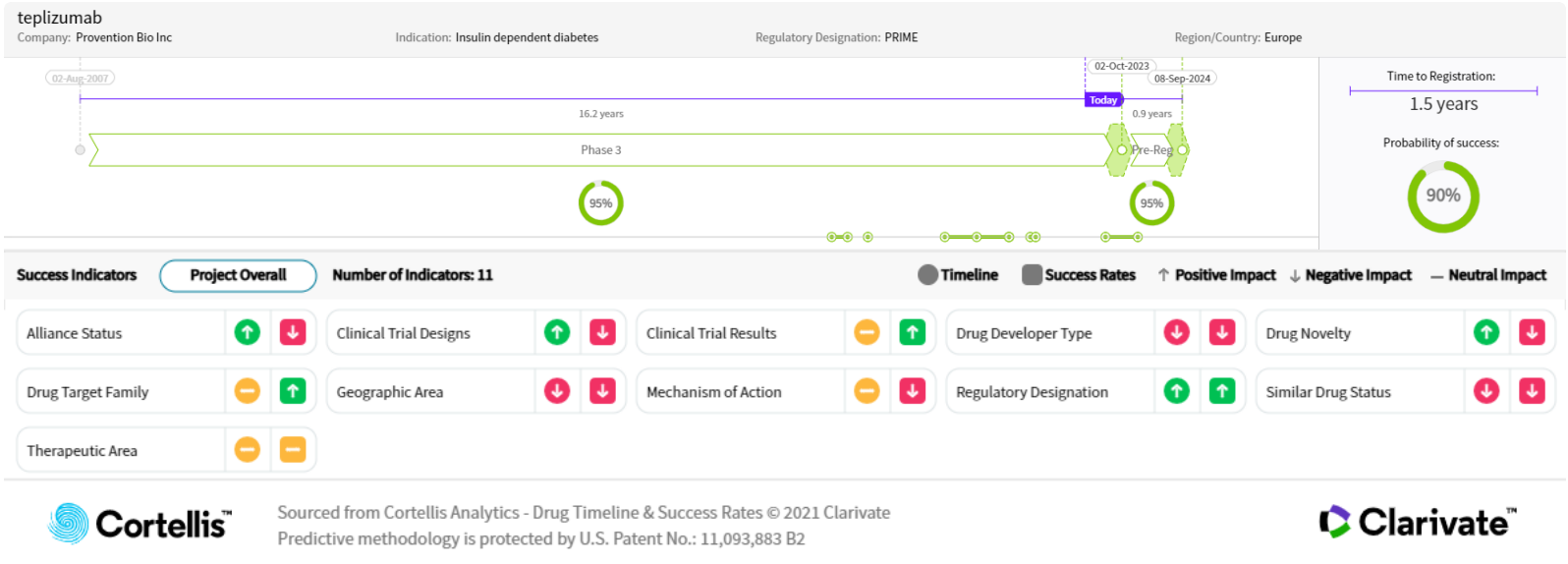
Teplizumab
PRV-031

Review and approval status:

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

Patents estimated to expire beginning in 2026

Drug forecast

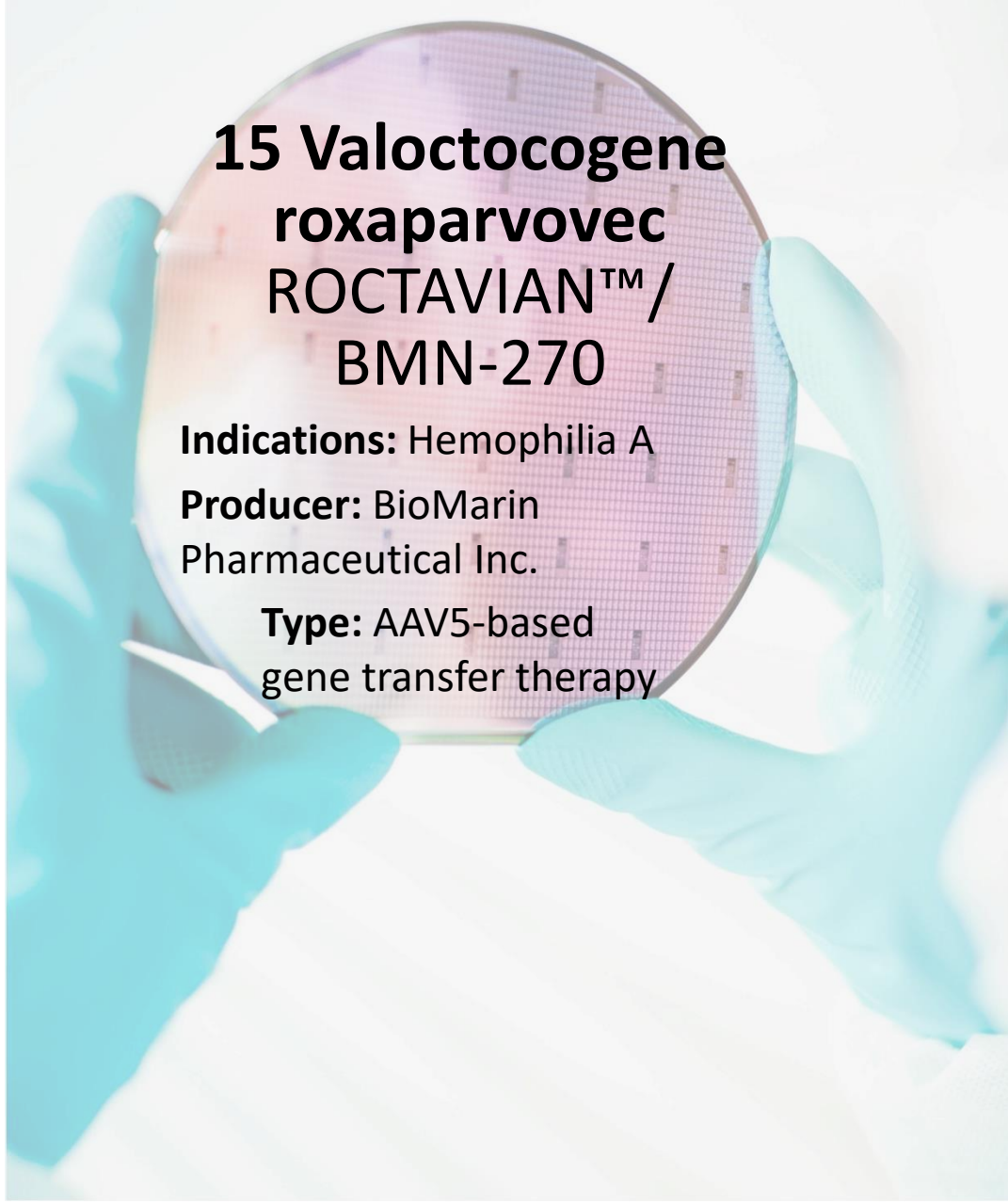


$0.39B

expected sales in 2027

Why is it a Drug to Watch?

- By restoring the expression of endogenous factor VIII (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.
- Treatment benefit is expected to last for years, minimize the need for replacement factor VIII (FVIII) and negate the use of other prophylaxis treatment.



Valoctocogene roxaparvovec ROCTAVIAN™/ BMN-270

Impact:

~16,500

cases of severe hemophilia A in the G7 markets in 2021

Impact on the market

- 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.
- Payer decisions could set the tone for future gene therapies.

Hurdles it might need to overcome

- Loss of FVIII expression over time, was observed in clinical trials. 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.

Treatment gaps addressed

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.

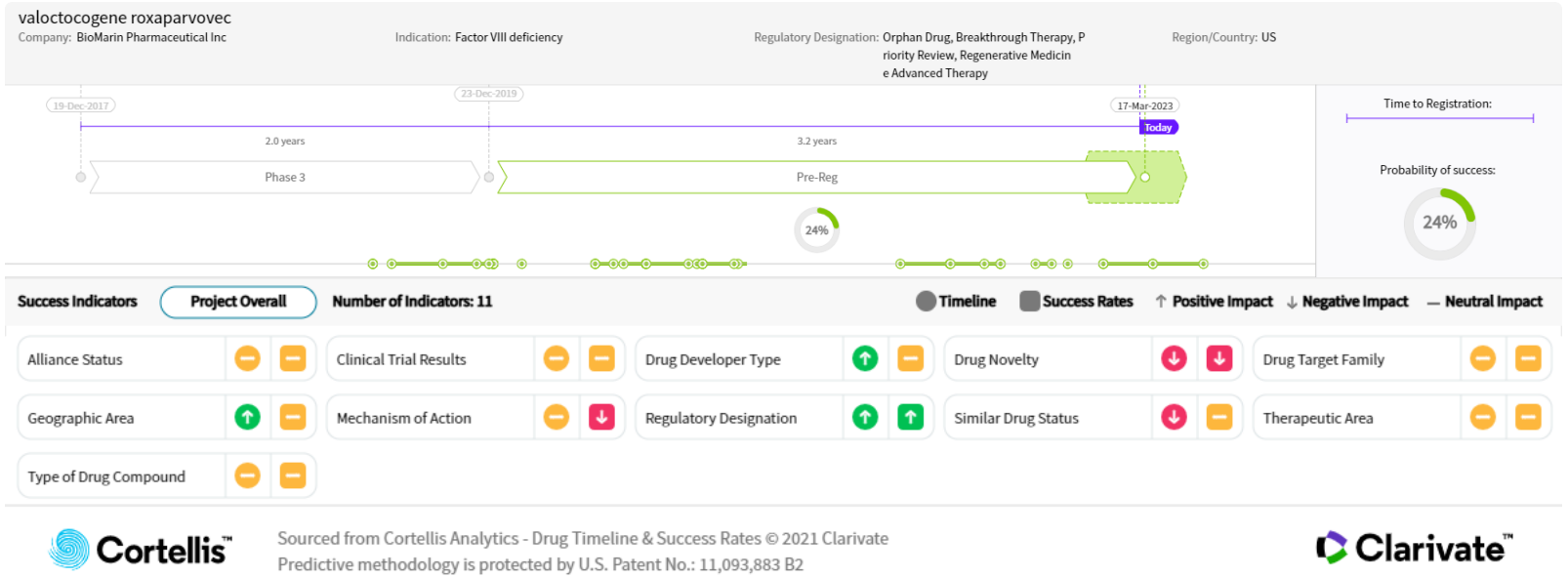
Valoctocogene roxaparvovec ROCTAVIAN™/ BMN-270

Review and approval status:

Actual and expected launch
2022: Europe
2023: United States

Patents estimated to expire beginning in 2033

Drug forecast



Indication	Country	Expected launch	Probability of Success
Factor VIII deficiency	South Korea	Feb 2024	90%

$1.09B

expected sales in 2027

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Progress towards personalized medicines

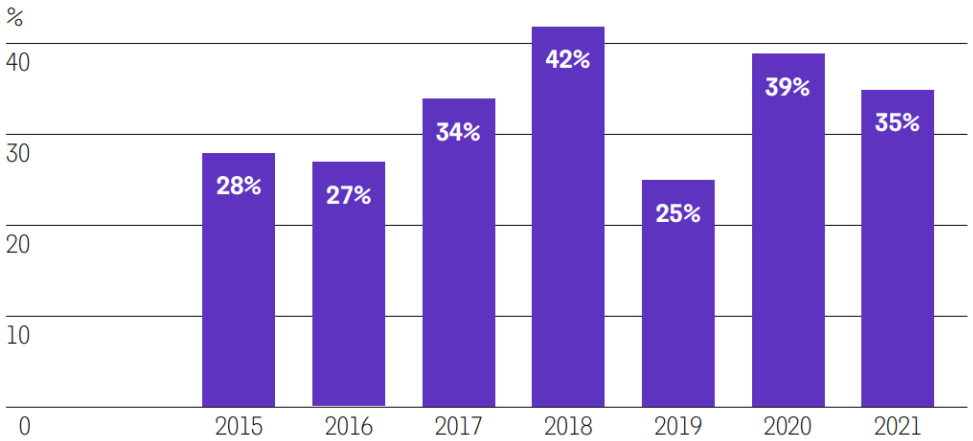
- The rise of personalized medicine has facilitated treatments for rare diseases and previously untreatable conditions.

- 2023 marks the 25-year anniversary of the approval of Herceptin®. A revolutionary treatment indicated for the roughly one in five breast cancer cases that are HER2-positive. Before Herceptin, these patients had very poor prognoses.

- Herceptin paved the path for future targeted drug development and approval. In the last decade personalized medicine has evolved from promise to reality, accounting for more than 25% of FDA approvals for the last seven years.

- 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.

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



Source: Personalized Medicines Coalition

Key takeaways

- Pharma companies continue to churn out innovative targeted treatments.
- Payers and providers seeking to manage the cost of the innovative medicines will need a clear view of pipelines and accurate forecasts.
- IP law firms with life science and healthcare practices will want to keep an eye on the patent disputes around emerging platforms.

Questions

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Thank you!