Drugs and Key Therapeutic Areas to Watch - 2022

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Dr. Reena V. Gupta
Dr. Hozana Castillo

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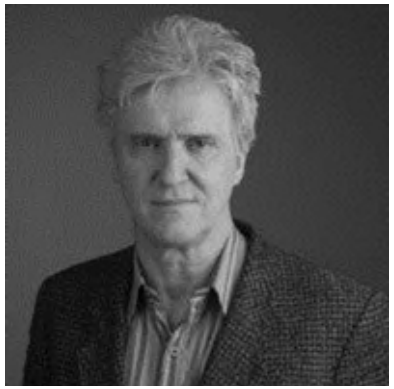
Agenda

Topic	Speaker
• Introduction	Ashish Chaudhry
• About Clarivate • Drugs to Watch Definition and Methodology	Mike Ward
• Drugs to Watch 2022 • Generics Landscape • Covid-19 vaccines and therapies	Dr. Reena V. Gupta
• Key therapeutic development areas to watch	Dr. Hozana Castillo
• Q&A	Madhurima Datta
• Thank you	Ashish Chaudhry

Profile

Mike Ward
Global Head of Life Sciences and Healthcare Thought Leadership
Clarivate

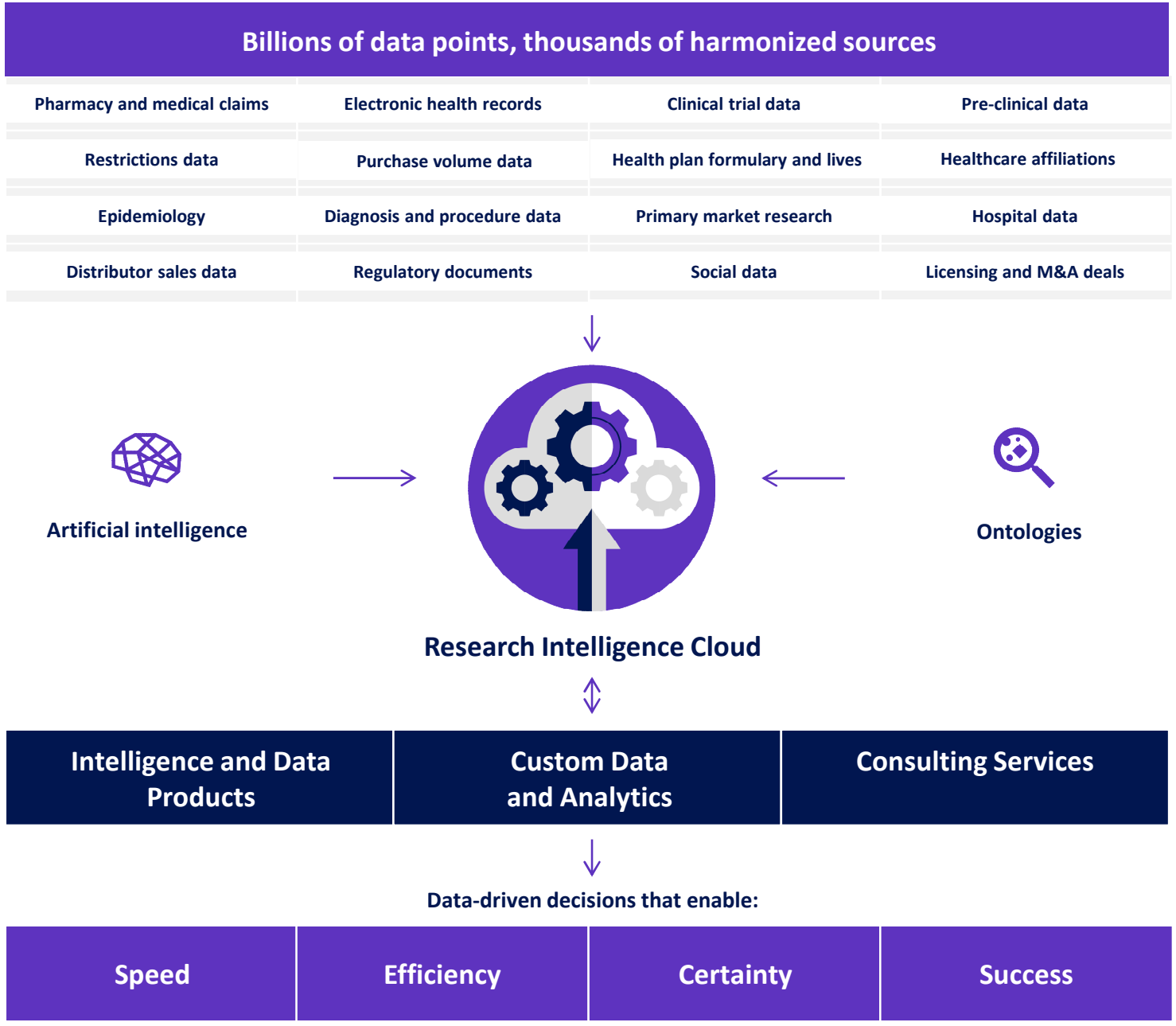


Mike Ward joined Clarivate in 2020, as global head of thought leadership. Mike has been analyzing and commenting on the global healthcare for more than 37 years.

He was formerly an award-winning business journalist and has managed editorial teams covering all aspects of the global healthcare industry.

Clarity to drive outcomes in a complex global healthcare ecosystem

Connected data and solutions to make critical decisions with speed and certainty



Clarivate™

We offer comprehensive, end-to-end solutions for life sciences and healthcare

Biopharma Intelligence

- Discovery, clinical and regulatory
- Portfolio strategy and business development
- Commercial and launch strategy
- Market access
- Customer engagement

Medtech Intelligence

- Product development
- Strategic portfolio planning
- Launch strategy
- Commercial effectiveness
- Market access

IP Intelligence

- Patent and sequencing
- Search patented chemical structure search
- Patent intelligence software and services
- Trademark research and protection

Healthcare Business Insights

- Revenue cycle
- Supply chain cost and quality
- Operational excellence

Clarivate partners with life sciences & healthcare organizations to advance the future of personalized medicine and care

Align R&D strategies to patient need

- Evaluate early-stage assets for clinical and commercial potential
- Align IP strategy with business strategy
- Optimize clinical trials
- Increase speed of regulatory approvals

Uncover market opportunity and investment needs

- Identify the right partners and deals
- Improve forecasting accuracy
- Plan a sound supply chain
- Protect market entry and patent navigation
- Maximize investment returns

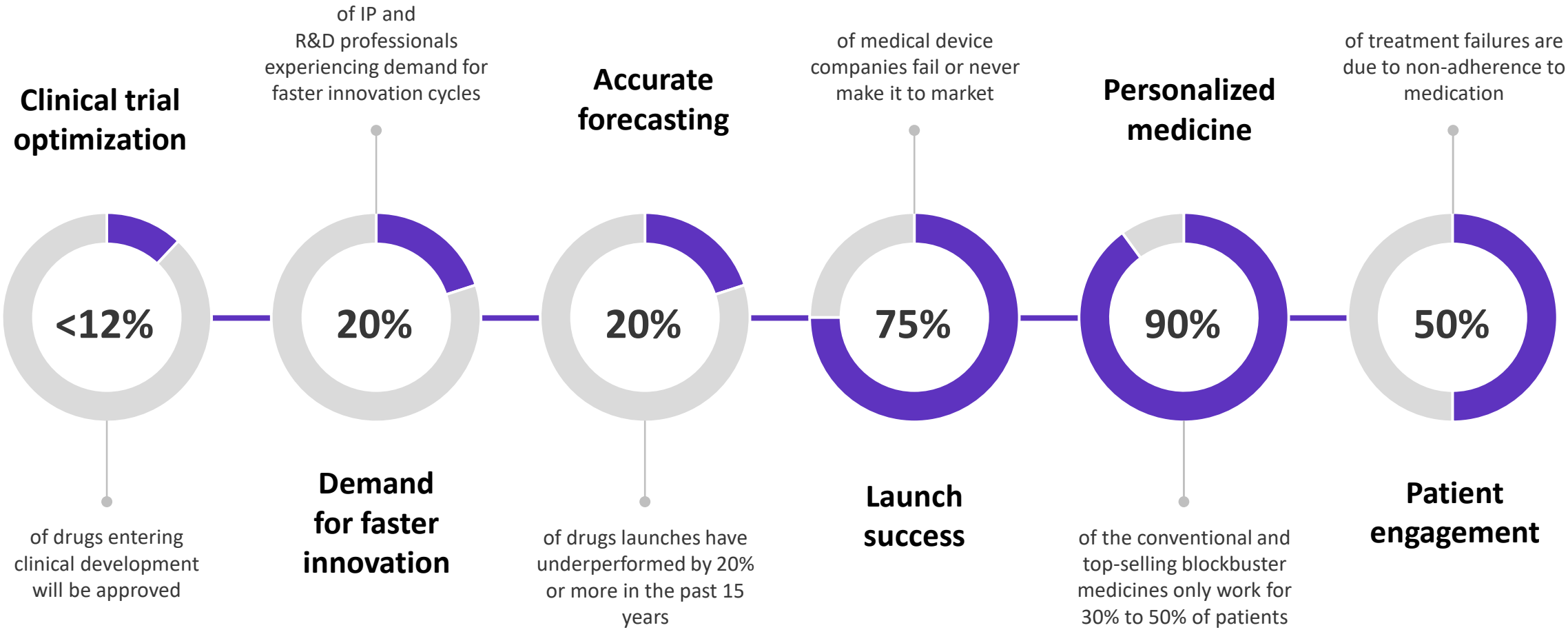
Optimize patient access

- Maximize commercial effectiveness throughout the product lifecycle
- Generate evidence and outcomes
- Secure favorable reimbursement
- Enhance hospital operational excellence

Identify customers and develop impactful engagement strategies

- Target stakeholders that matter most
- Align engagement strategy with the patient journey
- Develop messaging to support health decision making
- Maximize marketing spend

Opportunities to drive healthcare forward



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.

Selecting potential best-in-class/ first-in-class molecules that have key regulatory milestones in 2022 and are forecast to achieve sales of $1 billion plus five years after launch.

Drawing from expertise from over 160 analysts covering hundreds of diseases, drugs and markets and 11 integrated data sets that span the R&D and commercialization lifecycle.

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.

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.

Drug Timeline & Success Rates is a patented analytic tool that applies statistical modeling and machine learning to reliably and accurately forecast drug development milestones, timelines and probability of success.

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 & 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. behavior so clients can optimize their market access strategy and determine how to best position their brand to specific stakeholders.

Clarivate Real World Data 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.

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.

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.

Profile

DR. REENA V. GUPTA
Regional Solutions Consultant
Clarivate

Reena V. Gupta is a Regional Solutions Consultant at Clarivate for Life Sciences and Healthcare Intelligence Solutions.

She has a doctorate in Organic Chemistry and around 15 years of unique comprehensive experience in pharmaceutical industry holding multiple senior roles. She has a 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 of life saving affordable medicines across the globe.

AGENDA

1. Drugs to Watch- 2022
2. Generics in US
3. Covid Vaccines and Therapies-An Overview
4. Summary and Wrap up.

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Seven Drugs to Watch -2022

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ADAGRASIB

Innovator:

Mirati Therapeutics Inc and Zai Lab Ltd

Type/MoA (Mechanism of Action):

KRAS GTPase inhibitor

Review and Approval status

June 2021: US FDA :For patients with KRASG12C-positiveNSCLC following prior systemic therapy :Breakthrough Therapy Designation and Orphan Drug designation

November 2021: An NDA –USFDA submission has begun-Accelerated approval

Expected launch-United States:2022/Europe: 2023/Japan:2023

CRC: Expected launch United States: 2024/Europe: 2024/Japan: 2024

Indication

- Targeted treatment of cancers with $KRAS^{G12C}$ mutation
- Likely first such treatment option in patients with colorectal cancer (CRC) with this mutation; metastatic non-small-cell lung cancer (NSCLC)

Posology

- Twice-daily, second-line, oral treatment of advanced $KRAS^{G12C}$-positive solid tumours; metastatic NSCLC and CRC

Unmet need catered

- Effective therapy for this biomarker-defined population

Impact

- $KRAS^{G12C}$-mutant disease:
- 1. 11-13% of metastatic NSCLC
- 2. 3-4% of metastatic CRC

Market Overview

- **$1.23Bn** expected sales in 2026

Patent expiry

- Estimated in 2038

ADAGRASIB

DTSR prediction:

US: 95% probability of success
Approval before June 2022

Top competitors and market landscape

- LUMAKRAS™ (sotorasib)-first line.
- Experts view even greater potential with combination therapy -potential as the first-in class KRAS inhibitor approved for use in combination with ERBITUX in previously treated $KRAS^{G12C}$ mutation-positive metastatic CRC.
- Adagrasib is not in direct competition with other treatments, but it will be introduced as second- or third line therapy following standard of care chemotherapy with or without bevacizumab upon initial approval

Ongoing clinical studies/data available

- Phase 2-Data show promising safety and efficacy for CRC and NSCLC.
- Phase 2- Adagrasib and KEYTRUDA®(pembrolizumab)-first line combination therapy-ppreviously treated $KRAS^{G12C}$mutation-positive metastatic CRC
- Phase 3-Second-line monotherapy of NSCLC
- Phase 3-adagrasib plus ERBITUX® (cetuximab) secondary or third-line treatment for CRC

Potential Hurdles

- For NSCLC- Amgen's LUMAKRAS - advantage of being earlier to market for a relatively small patient population
- LUMAKRAS once daily administration compared with twice-daily for Adagrasib.
- Additional study results -hinted-at superior efficacy and safety- influence its uptake.
- For CRC, even smaller patient population- limit its overall sales potential.

FARICIMAB

Innovator:

Roche and Chugai Pharmaceutical

Type/MoA (Mechanism of Action):
Bispecific VEGF/Ang-2 mAb

Review and Approval status

Approved by the U.S. FDA in Jan 2022 for nAMD and DME
July 2021: EMA validated the MAA for nAMD and DME
June 2021: Submitted to MHLW in Japan for nAMD and DME

Expected launch:
United States/ Europe/Japan: 2022

Indication

- For patients with diabetic macular edema (DME) or wet age-related macular degeneration (AMD)

Posology

- Intravitreal (IVT)-administration for treatment of DME and wet AMD
- Also being studied to treat retinal vein occlusion (RVO)

Unmet need catered

- Offers a potentially more convenient option as it will be administered less frequently, on average, than the standard of care-treatment choices include invasive, burdensome administration that limits treatment uptake.
- First bispecific antibody to launch in ophthalmology, it also has the potential to be more efficacious than current standard of care.

Impact

- ~15% of adults with T2DM have DME
- ~3.6M people have wet AMD in the G7 markets

Market Overview

- **$1.31B** expected sales in 2026

Patent expiry

- **Estimated in 2034**

FARICIMAB

DTSR prediction Dec 2021:

US: 95% probability of success
Approval before May 2022

APPROVED in Jan 2022

Top competitors and market landscape

- Mainly VEGF inhibitors including the standard of care EYLEA® (aflibercept; Regeneron Pharmaceuticals Inc)
- Less-frequent dosing schedule will be attractive to both clinicians and patients. Faricimab has a more convenient dosing schedule of 16 weeks (demonstrated to be effective for 52% of DME patients and 80% of wet AMD patients in clinical trials), compared with the 8-week (or occasionally, 12-week) schedule for EYLEA and LUCENTIS® (Genentech).
- Prevalence of both DME and wet AMD are expected to continue increasing, with aging population and rising rates of diabetes
- Novel MOA of faricimab might ultimately provide greater efficacy than VEGF inhibitors, although existing results show similar efficacy and safety- reduce the overall market share of VEGF inhibitors by 67% in 2030
- Potential candidate for patients with nonresponse to other treatments

Ongoing clinical studies/data available

- Development is also ongoing in other ophthalmic settings, including retinal vein occlusion (RVO)
- A Study to Investigate Faricimab Treatment Response in Treatment-Naive, Underrepresented Patients With Diabetic Macular Edema
- Phase III trial of (i) faricimab versus aflibercept in macular edema secondary to central retinal or hemiretinal vein occlusion (ii) macular edema due to branch retinal vein occlusion

Potential Hurdles

- The key consideration is entry into a market where the standard of care is providing the therapeutic response needed, with minimal side effects.
- Clear demonstration of superior efficacy in clinical trials, adoption of faricimab might be challenged by an unwillingness to switch therapies.
- Safety profile is currently consistent with existing therapies, side effects such as inflammation or vein occlusion occurring post marketing could affect uptake

LECANEMAB
DONANEMAB

Innovator:

Lecanemab : Eisai Co Ltd and Biogen Inc

Donanemab: Eli Lilly and Company

Type/MoA (Mechanism of Action):

Lecanemab : Anti-Aβ protofibril Mab

Donanemab : Anti-Aβ N3pG Mab

Indication

- Alzheimer's Disease

Posology

- **Lecanemab :** IV infusion every 2 weeks for the treatment of mild cognitive impairment (MCI) due to AD and mild AD
- **Donanemab :** IV infusion every 4 weeks for the treatment of MCI due to AD and mild AD

Unmet need catered

- Regulatory success of anti-Aβ Mabs could infuse more investment into dementia and influence companies' decisions about which drugs to develop, potentially bypassing other MOAs to develop next-gen anti-amyloid drugs.
- Critical need for patients has long been safe, effective DMTs that slow cognitive and functional decline-Slow update of ADUHELM-limit patient benefit
- Lecanemab and donanemab could offer improved risk/ benefit profiles over ADUHELM
- Additional therapies could eventually provide greater patient choice and potentially greater affordability

Impact

- ~38M people with AD globally
- >30% expected increase in total prevalent cases of early AD in the G7 markets by 2029 due to aging population

Market Overview

- **Lecanemab : $1.68B** expected sales in 2026
- **Donanemab : $4.52B** expected sales in 2026

Patent expiry

- **Lecanemab :** eestimated to expire beginning in 2025
- **Donanemab :** estimated to expire beginning in 2031

3,4/7

LECANEMAB DONANEMAB

Review and Approval status

Lecanemab :

June 2021: Breakthrough Therapy Designation
Dec 2021 Fast track designation : U.S. FDA
September 2021:Rolling BLA submitted to the U.S. FDA based on phase 2 data. Expected to be complete in 1H22
Expected Launch: United States: 2022/ Europe: 2024/Japan: 2024

Donanemab:

June 2021: Breakthrough Therapy Designation: U.S. FDA
October 2021 : Rolling BLA submitted to the U.S. FDA based on phase 2 data. Expected to be complete in 1Q22

Expected launch: United States: 2022 /Europe: 2025/Japan: 2025

Top competitors and Market landscape

- Anti-Aβ MAbs lecanemab and donanemab are poised to follow on the heels of the U.S. FDA's landmark accelerated approval of ADUHELM
- Data across clinical trials suggest that sufficient exposure to optimal doses of anti-Aβ MAb therapy could be clinically effective in early AD
- Until the approval of ADUHELM, symptomatic therapy was the only treatment option for patients with AD. Acetylcholinesterase inhibitors and memantine, now generic, have been and will continue to be the standard of care across mild, moderate and severe disease
- Many more drugs from a range of mechanisms of action (MOAs like Other anti-Aβ DMTs, 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.

Ongoing clinical studies/data available

- Lecanemab Phase 3 studies –ongoing in patients with early AD and preclinical AD-. Data from early AD are expected in the second half of 2022
- Lecanemab Phase 2 efficacy results showed a reduction in decline from baseline on the AD Composite Score (ADCOMS) and other metrics over 78 weeks and rapid, deep amyloid plaque clearance. Risk of amyloid-related imaging abnormalities (ARIA; 10%) was lower than with ADUHELM (40%) and donanemab (20%)
- Donanemab Phase 3 are ongoing in patients with early AD and preclinical AD, Data from early AD are expected in the first half of 2023.
- Donanemab 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 (20%) than with ADUHELM (40%).
- A small phase 3 trial will compare donanemab with ADUHELM head-to-head to assess superiority of amyloid plaque reduction in early AD patients - data expected in the second half of 2022.

3,4/7

LECANEMAB DONANEMAB

Lecanemab : US-DTSR prediction:
95% probability of success-Approval before July 2022

Donanemab: US- DTSR prediction:
95% probability of success –Approval before Aug 2022

Potential Hurdles

- Market demand and pricing questions remain about these drugs.
- Ongoing controversy regarding ADUHELM's approval, pending payer decisions and data readouts.
- Regulatory decisions on ADUHELM from the European Medicines Agency (EMA) and Japan's MHLW are pending, which will set expectations for the approvability of others in the class in these geographies and impact global sales potential
- Challenges in access, reimbursement and affordability; patient/physician awareness to drive early 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.

TEZEPELUMAB

Innovator:
Amgen and AstraZeneca

Type/MoA (Mechanism of Action):
MAb inhibiting thymic stromal lymphopoietin (TSLP)

Review and Approval status
September 2018: For patients with severe asthma without an eosinophilic phenotype-Breakthrough Therapy; Orphan drug Designation: U.S. FDA
April 2021: BLA submitted to the FDA
July 2021: FDA granted priority review.

Jan 2022: In January 2022, the product has been launched in the US for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma

August 2021: Filing submitted in the EU
May 2021: Filing submitted in Japan

Expected Launch: United States: 2022/Europe & Japan: 2023

Indication
- First-in-class biologic-Game changer for patients with non-TH2 or TH2-low asthma whose asthma is not well-controlled with inhaled corticosteroids, the current standard of care

Posology
- Monthly subcutaneous (SC) injection for treatment of severe asthma

Unmet need catered
- Approved, it is the first-in-class biologic for this patient population.
- Is a first-line biologic for severe TH2-low asthma and a treatment option for patients with TH2-high asthma for whom existing therapies have failed.
- Dependence on oral corticosteroids for disease control is often not wholly effective and is associated with long-term side effects.

Impact
- 30% of patients with severe asthma have a TH2-low phenotype

Market Overview
- **$1.17B** expected sales in 2026

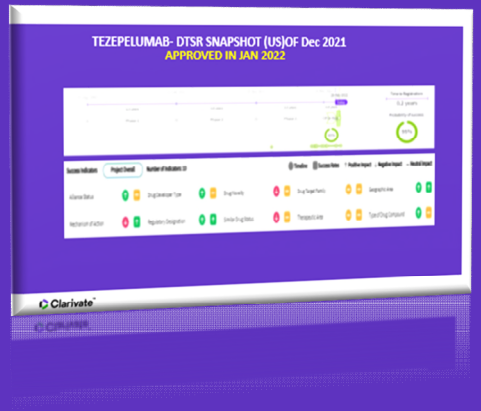
Patent expiry
- Expected to expire beginning in 2028

TEZEPELUMAB

US-DTSR prediction of Dec 2021:

95% probability of success with approval before Feb 2022

APPROVED IN DEC 2021



Top competitors and market landscape

- Novel MOA of Tezepelumab is a step forward in addressing the high level of variability within the asthma patient population.
- Because of its MOA, high eosinophil levels do not need to be confirmed prior to administration, eliminating the need for a blood test, which could also make it attractive as a first-line option for TH2-high asthma
- Mainstays of symptomatic treatment are oral corticosteroids, but Tezepelumab is a first-in-class humanized MAb and the only member of the anti-TSLP approved by FDA.

Ongoing clinical studies/data available

- In the phase 3 trial, Tezepelumab was well-tolerated, by patients with severe asthma, and resulted in reductions in the asthma exacerbation rate (AER),compared with placebo, of: 70% for TH2-high asthma patients, 41% for TH2-low asthma patients and 39% for non-TH2 asthma patients.
- Studies ongoing: Evaluate Tezepelumab in Adults With Chronic Spontaneous Urticaria; Severe Uncontrolled Asthma; Children With Asthma, Efficacy and Safety of Tezepelumab in Participants With Severe Chronic Rhinosinusitis With Nasal Polyposis; Tezepelumab Home Use Study.

Potential Hurdles

- Tezepelumab will face significant competition in patients with TH2-high asthma-expected to be used as a later-line therapy given physician familiarity with existing biologics.
- Later-to market entry compared with other biologics for this patient population, payer restrictions could constrain uptake, similar to other high-priced biologics.
- For patients with TH2-low asthma, there is no competition.
- For both phenotypes, the niche population of patients with uncontrolled severe asthma could limit its overall patient share.

TIRZEPATIDE

Innovator:

Eli Lilly and Company

Type/MoA (Mechanism of Action):

GLP-1/gastric inhibitory polypeptide (GIP) receptor agonist

Review and Approval status

October 2021: NDA submitted to the FDA ,Oct 2021 MAA submitted to the EMA ; Dec 2021: Submission in Japan

Expected launch:

United States: 2023 /Europe: 2023/Japan: 2023

Indication

- Diabetes related obesity

Posology

- Weekly SC administration to treat T2DM
- Also being studied to treat obesity and non-alcoholic steatohepatitis (NASH)

Unmet need catered

- New treatment that can more effectively address both weight loss and glycemic control than existing treatments is of great interest to the industry

Impact

- ~ 462 million people globally have T2DM .
- 1.4% annual increase in drug-treated populations in G7 due to increasing rates of obesity and the aging population

Market Overview

- **$4.55B** expected sales in 2026

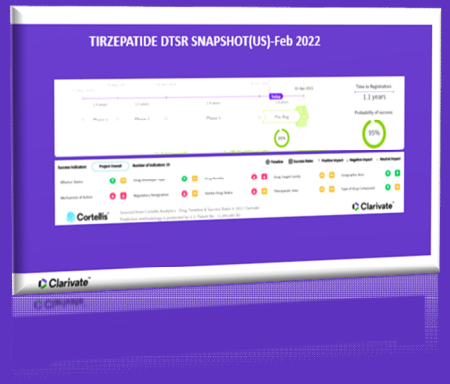
Patent expiry

- Estimated to expire beginning in 2031

TIRZEPATIDE

US-DTSR prediction:

95% probability of success - Approval expected before April 2023



Top competitors and market landscape

- Eli Lilly has a long history of bringing T2DM therapies to market.
- Tirzepatide has demonstrated superiority over Semaglutide (GLP-1 receptor agonist), which is the most efficacious noninsulin T2DM therapy currently available, which could result in a significant market advantage over other therapies.
- With the promising results for both weight loss (clinically significant 15% weight loss) and glycemic control demonstrated to date, Tirzepatide could help delay disease progression and therefore delay the transition to insulin-based treatment.

Ongoing clinical studies/data available

- Large-scale (>20,000 patients) have shown greater efficacy for weight reduction and glycemic control (HbA1c) than any other approved non-insulin T2DM therapy.
- Phase 3 trials are ongoing, including a large cardiovascular outcomes trial (CVOT; n=12,500) comparing the efficacy of Tirzepatide with -placebo background therapy, insulin, TRULICITY® (dulaglutide),-OZEMPIC® (Semaglutide).
- Sufficient data, including regarding CV risk, are now available for regulatory submissions.

Potential Hurdles

- One concern-Phase 2 trials was the large number of patients discontinuing Tirzepatide because of gastrointestinal side effects-however, these subsided after time.
- Barriers to uptake, -patients who require less weight loss or glycemic control, could include the need to titrate Tirzepatide.
- The availability of sodium-glucose co-transporter-2 (SGLT-2) inhibitors in generic formulations, competition from nearly as efficacious GLP-1 receptor inhibitors such as OZEMPIC® and RYBELSUS®
- The high cost of Tirzepatide.

VUTRISIRAN

Innovator:
Alnylam® Pharmaceuticals

Type/MoA (Mechanism of Action):
siRNA transthyretin (TTR) gene inhibitor delivered using a GalNAc-conjugate delivery platform

Review and Approval status
May 2018: Orphan Drug designation by FDA and EMA for the treatment of ATTR
May 2020: Fast Track designation by the FDA for the treatment of the hATTR - related polyneuropathy in adults
In June 2021, an NDA was accepted by the FDA ;April 14, 2022: PDUFA date

September 2021: Submitted to the EMA
Dec 2021: Filed in Japan

Expected launch:
United States: 2022 / Europe: 2022

Indication
- Wildtype ATTR polyneuropathy

Posology
- Every-three-month SC administration for treatment of ATTR polyneuropathy

Unmet need catered
- Few treatment options
- More convenient dosing than other ATTR-specific drugs on the market
- Relatively convenient administration method (SC vs IV infusion).

Impact
- Two subtypes of ATTR:
  - Hereditary ATTR (hATTR): 1,233 people in the United States in 2021
  - Wild-type ATTR: 1,300 people in the United States in 2021

Market Overview
- **$1.42B** expected sales in 2026

Patent expiry
- Estimated to expire beginning in 2037

VUTRISIRAN

US- DTSR prediction:

95% probability of success-Approval expected before April 2022

Top competitors and market landscape

- The market is currently composed of therapies approved for other indications (e.g., multiple myeloma) that are used off-label to treat the effects of amyloid buildup in nerves and major organs (e.g., the heart and liver)
- For hereditary ATTR polyneuropathy, there are two approved drugs: ONPATTRO, administered intravenously every three weeks, and TEGSEDI® (Inotersen), administered via SC injection once a week.
- Treatment also includes chemotherapy and, as a last resort, organ transplant
- With its MOA, vutrisiran should help slow, if not stop, the accumulation of amyloid throughout the body. It has generally mild side effects, compared with TEGSEDI and standard chemotherapy.

Ongoing clinical studies/data available

- Phase 3 trials are underway-Results to date have shown improvements in polyneuropathy, quality of life and cardiac biomarkers.
- Vutrisiran demonstrated statistically significant efficacy on the same key endpoints for hATTR polyneuropathy as ONPATTRO® (patisiran) but with a more convenient administration method (SC vs onehour IV infusion) and less frequent dosing (every three months vs weekly or every three weeks).
- It has demonstrated good tolerability and an encouraging safety profile

Potential Hurdles

- Vutrisiran might face some competition from ONPATTRO and TEGSEDI for patients with hATTR polyneuropathy, especially with the limited patient population
- (If) Enters into the market at a high price

- Generics in US

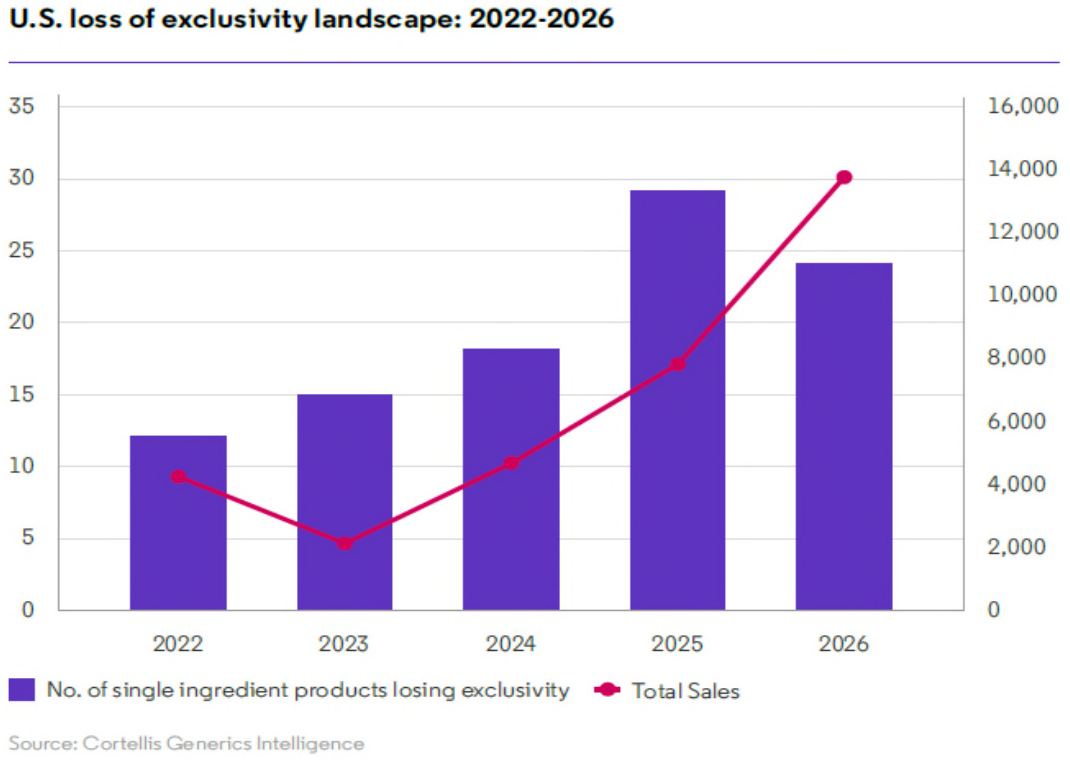
OVER THE NEXT 5 YEARS

95+
Molecules

$32.6B
Total Sales

Predicted to lose Exclusivity in the U.S. market.

- Generics broaden access to medicines, offer potentially substantial cost savings to patients and payers alike and sustain innovation. Also, some patients potentially being able to access therapy for the first time.
- Generics comprise most prescriptions in the world's top markets, with biosimilars also beginning to make a serious impact.
- Biosimilars -difficult, risky and expensive to develop, and it is nearly impossible to precisely duplicate them. The approvals process is far more rigorous.
- Key branded drugs losing exclusivity in 2021 and beyond include BROVANA® (arformoterol tartrate), CALQUENCE® (acalabrutinib), HUMIRA® (adalimumab), JANUVIA®(sitagliptin), VEMLIDY® (tenofovir alafenamide), VIMPAT® (lacosamide) and XARELTO® (rivaroxaban). As the **drugs** with the **potentially greatest competition in 2022,** this report highlights **JANUVIA**, **VIMPAT and HUMIRA**



COVID-19 VACCINES AND THERAPIES

An Overview

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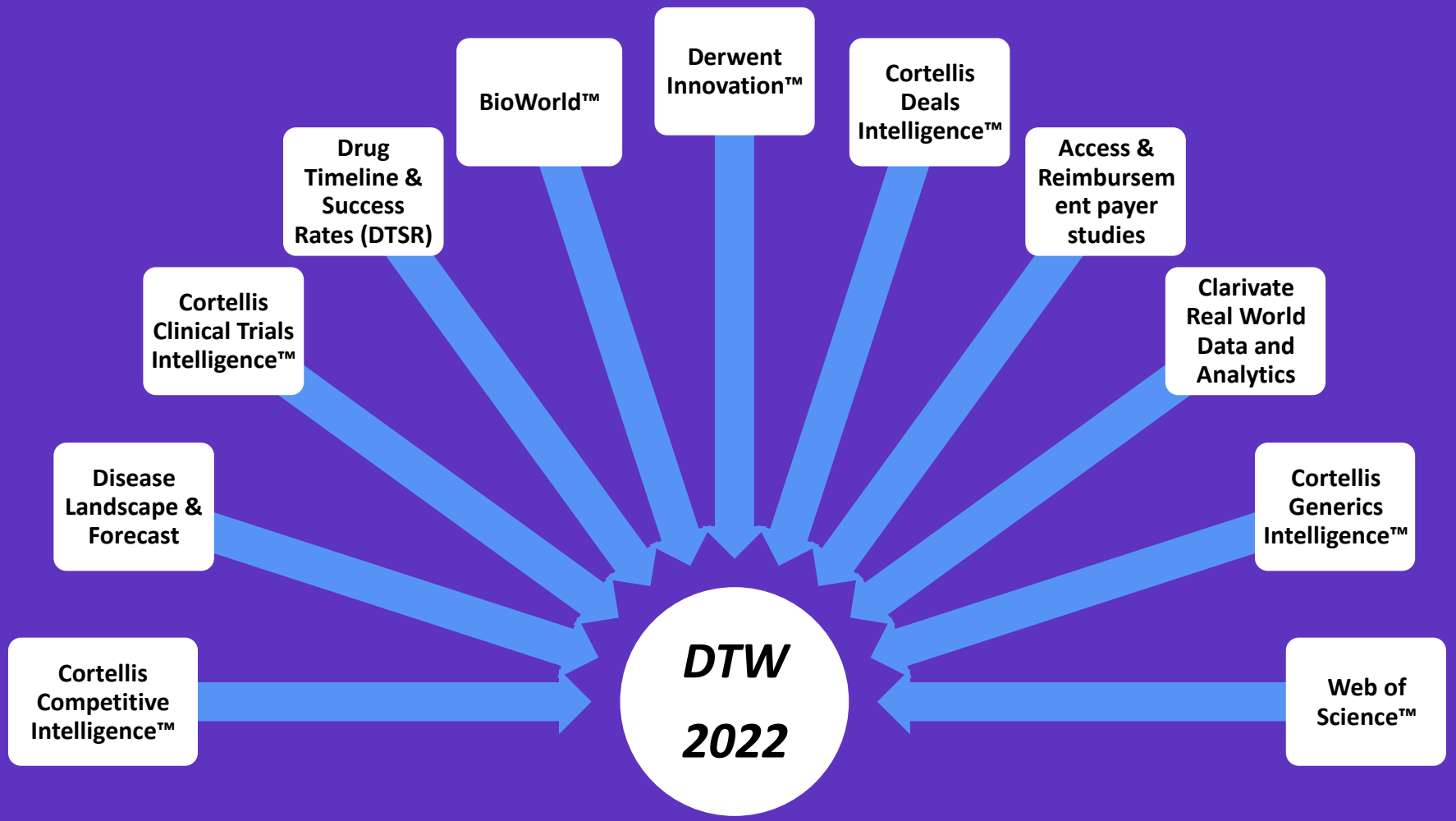
- Development activity over the past 18 to 24 months has been dominated by vaccines and therapies targeted at ending the COVID-19 pandemic, resulting in **more than 240 vaccines in development** and **more than 750 therapies in development.**
- Not all have succeeded to market, but the learnings accumulated over this time have been folded into other programs, both for COVID-19 and other therapeutic areas such as oncology and other infectious diseases such as the flu and HIV

Refer DTW 2022 Report for :

- Name of the respective Company(s)
- Approved countries/regions

Type of Vaccine/Therapy	Vaccine name
Single-dose recombinant viral vector vaccine	Ad5-nCoV(Convidecia™); JNJ-78436735(Ad26.COV2-S)
Two-dose recombinant viral vector vaccine	AZD-1222 (Vaxzevria;COVISHIELD™; ChAdOx1 nCoV-19);Gam-COVID-Vac (Sputnik V)
Two-dose inactivated vaccine	BBIBP-CorV;CoronaVac;COVAXIN®;CoviVac
Two-dose, lipid nanoparticle RNA vaccine	mRNA-1273 (TAK-919; elasomeran;SPIKEVAC™);Tozinameran (BNT-162b2, COMIRNATY®)
Two-dose synthetic peptide	EpiVacCorona
Three-dose DNA	ZyCov-D
Three-dose protein subunit	ZF2001(RBD-dimer, Zifivax)
COVID-19 therapies with full or emergency use approval	
Corticosteroid	Dexamethasone phosphate (DEXAVAN)
Broad-spectrum antiviral; Viral RNA-dependent, RNA polymerase inhibitor	Favipiravir (Reeqonus™, Avigan®)
	Remdesivir (VEKLURY®);
Janus kinase inhibitor	Baricitinib (OLUMIANT®)
Mab	Bamlanivimab (LY-3819253, LY-CoV555)
	Casirivimab and imdevimab (REGEN-COV™; Ronapreve™;REGN-10933 plus REGN-10987; REGN-COV2);Etesevimab (LY-CoV016);Regdanvimab (Regkirona; CT-P59);Sotrovimab (GSK4182136,VIR-7831, VIR-7832);Tocilizumab (Actemra; Roactemra);Tixagevimab and cilgavimab (AZD-7442;combination of AZD-8895; AZD-1061; Evusheld
Main protease (Mpro) inhibitor	Nirmatrelvir and ritonavir (PF-07321332; PAXLOVID™)

SUMMARY



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

Subscription solutions trusted by our global life sciences customers

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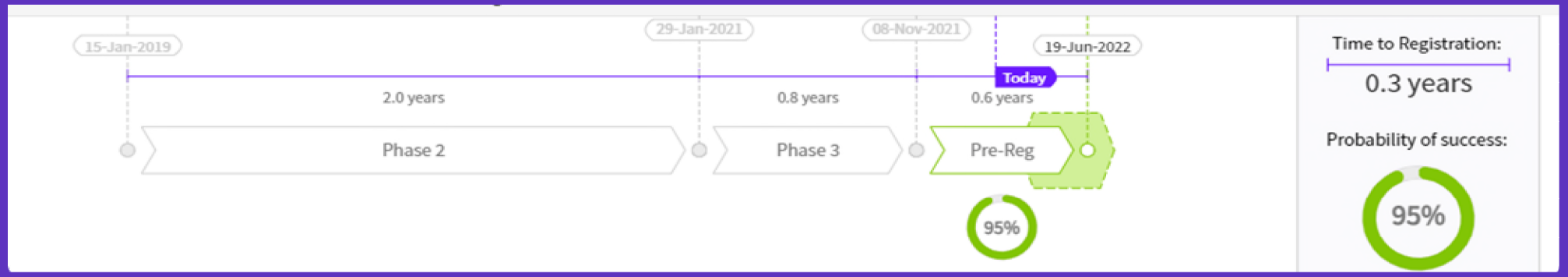
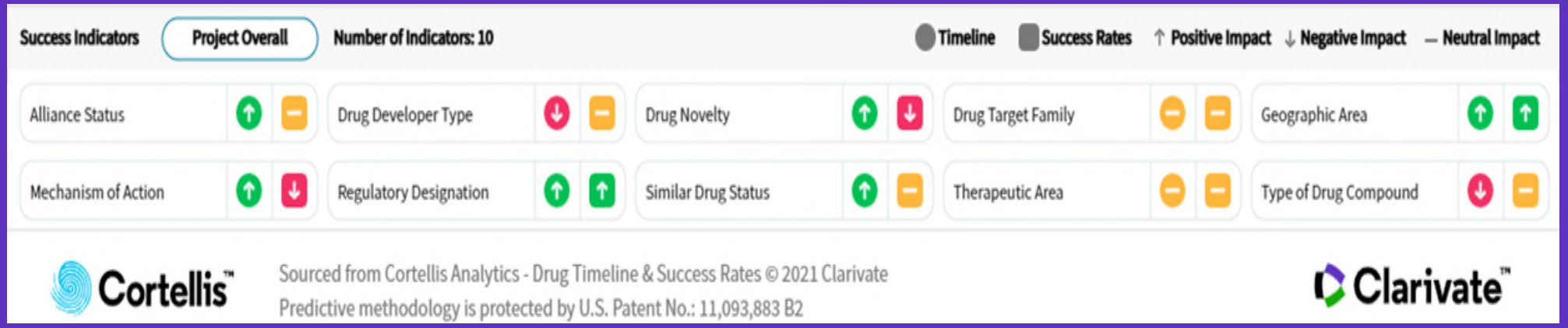
KEY TAKE AWAYS

1. Drug approvals are unpredictable, but these seven candidates show great promise to realize improved patient outcomes, as well as financing the next generation of innovative medicines.
2. Drug makers are making great strides towards unlocking new technologies that will facilitate truly personalized medicines.
3. Treatments often come with an enormous price tag, so proving their value will be an ever more critical task for pharma companies seeking to win market approval and make them accessible to patient
4. Regulators are showing an openness to new technologies and methodologies and an appetite for bold action against diseases for which there are few or no treatments.
5. Pharma’s battle against COVID-19 continues.

ADAGRASIB DTSR SNAPSHOT (US)-Feb 2022

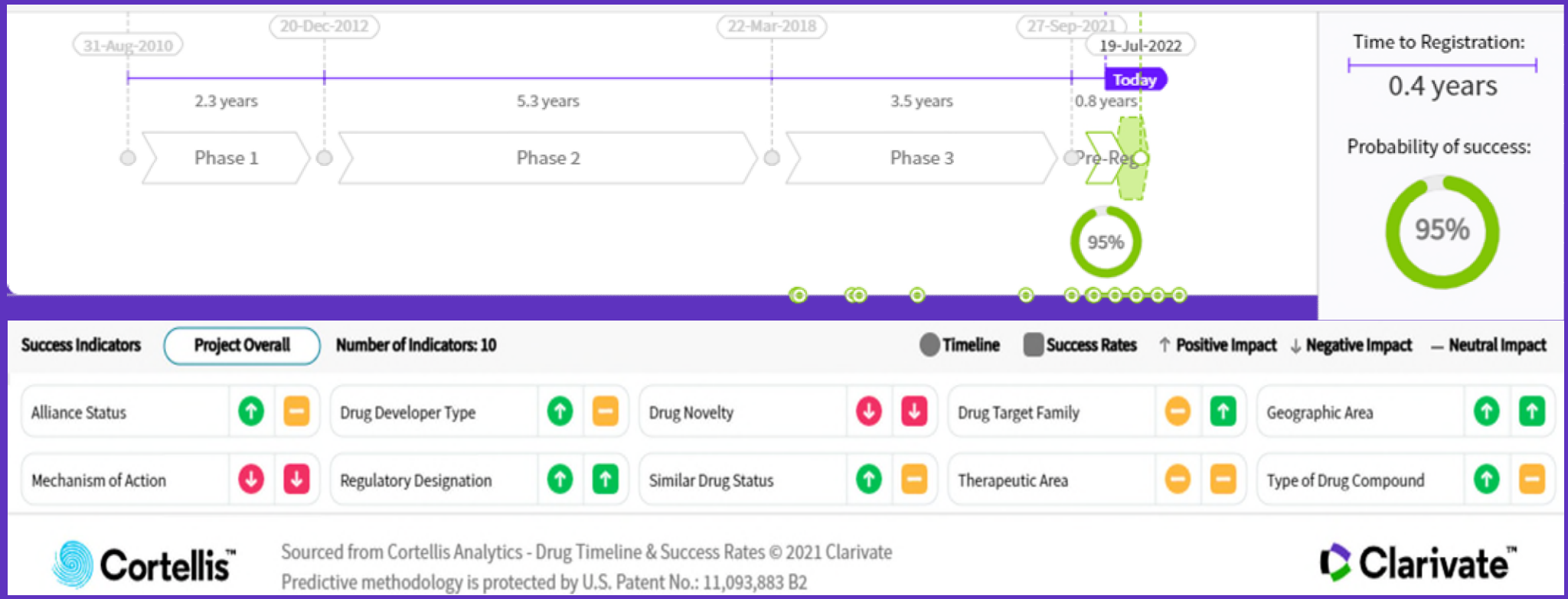




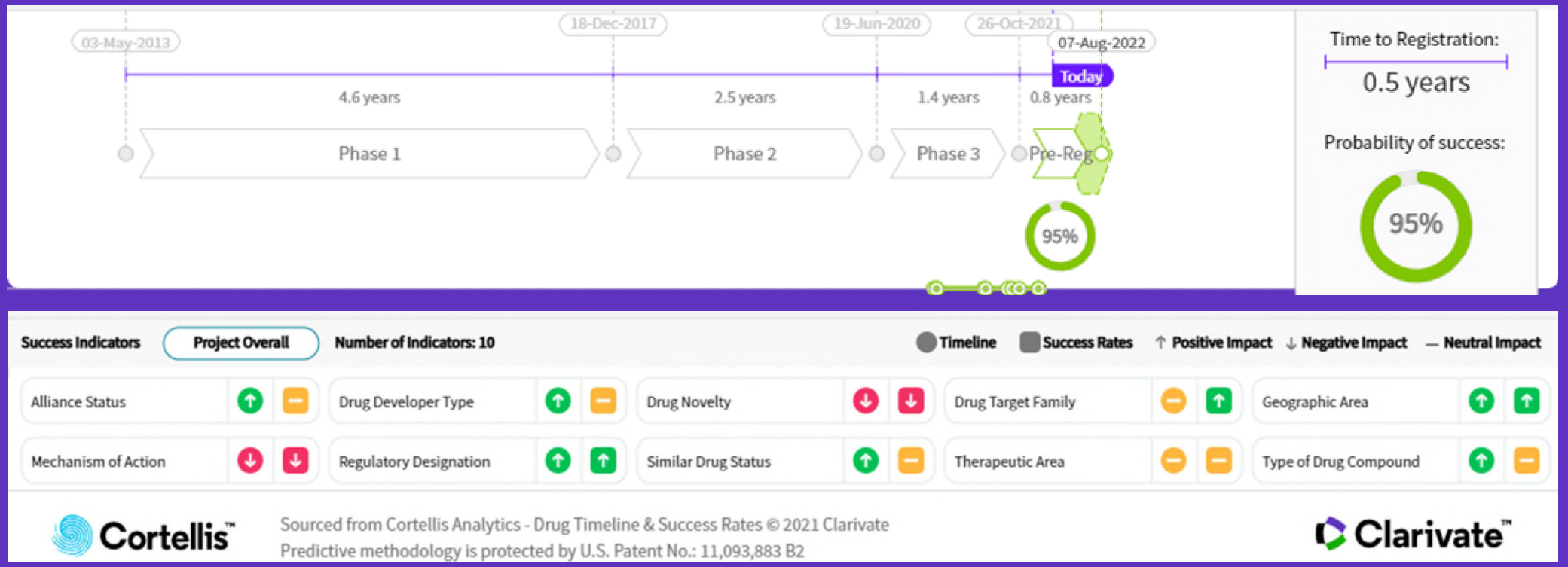
FARICIMAB DTSR SNAPSHOT OF Dec 2021 (US)

APPROVED IN JAN 2022

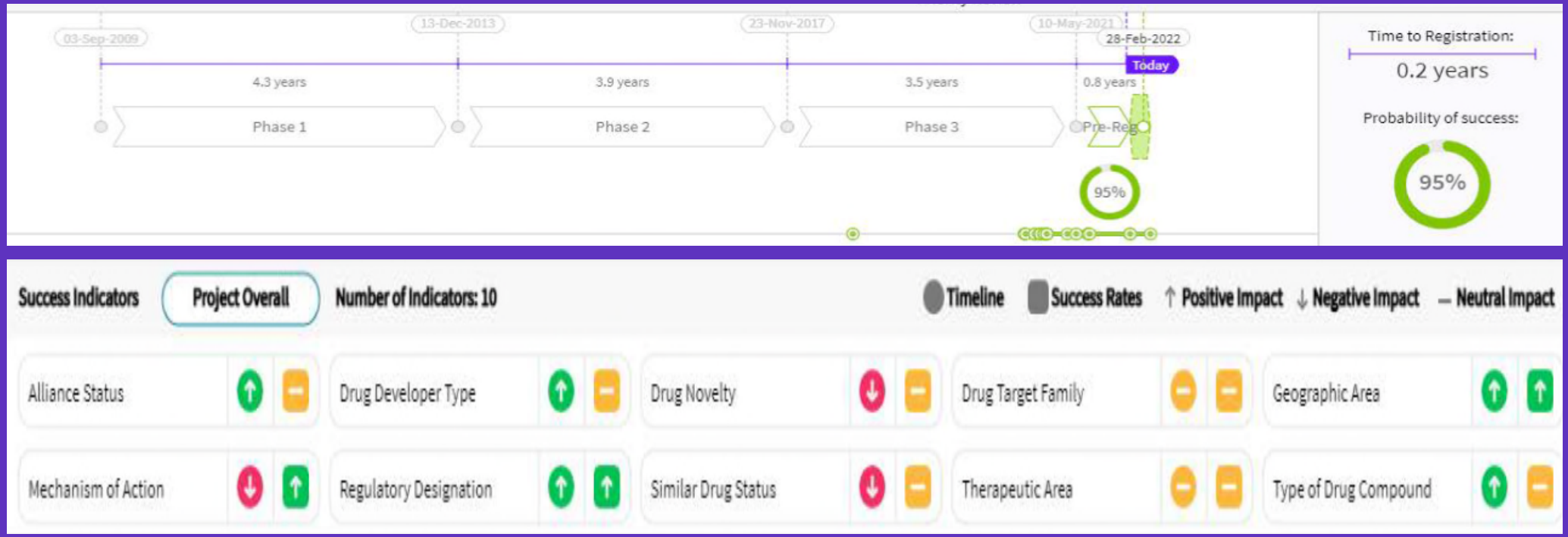
LECANEMAB DTSR SNAPSHOT(US)-Feb 2022



DONANEMAB DTSR SNAPSHOT(US)-Feb 2022



TEZEPELUMAB- DTSR SNAPSHOT (US)OF Dec 2021
APPROVED IN JAN 2022



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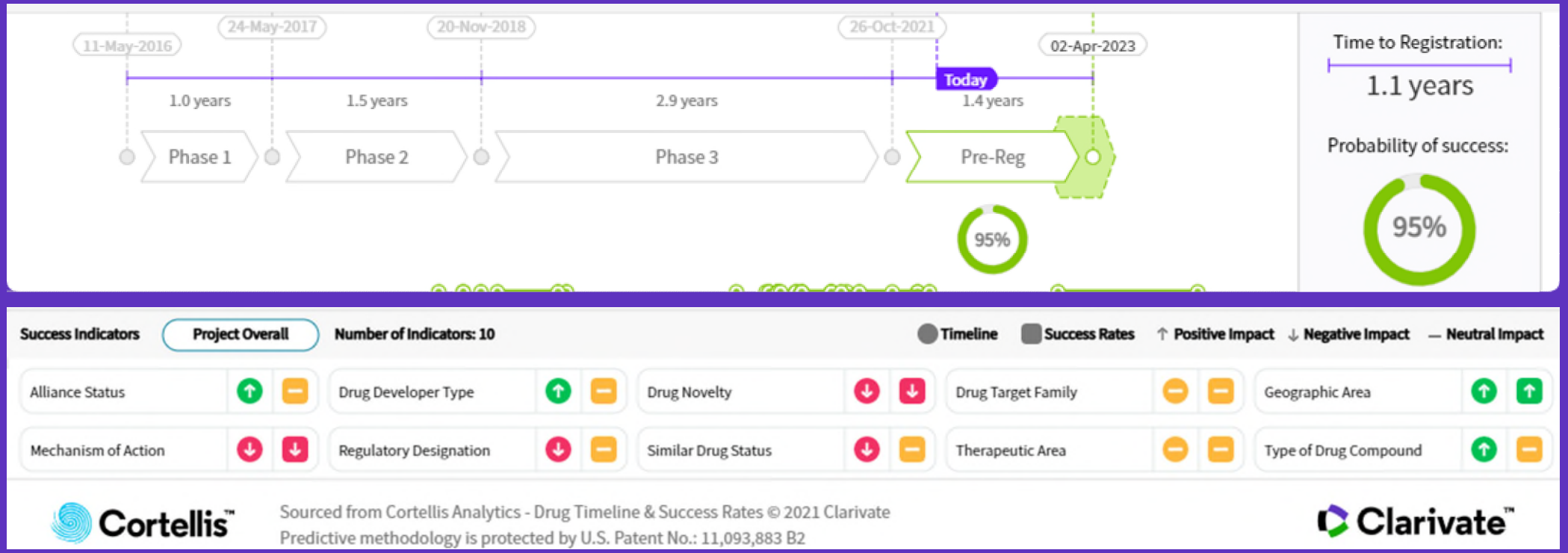
TIRZEPATIDE DTSR SNAPSHOT(US)-Feb 2022



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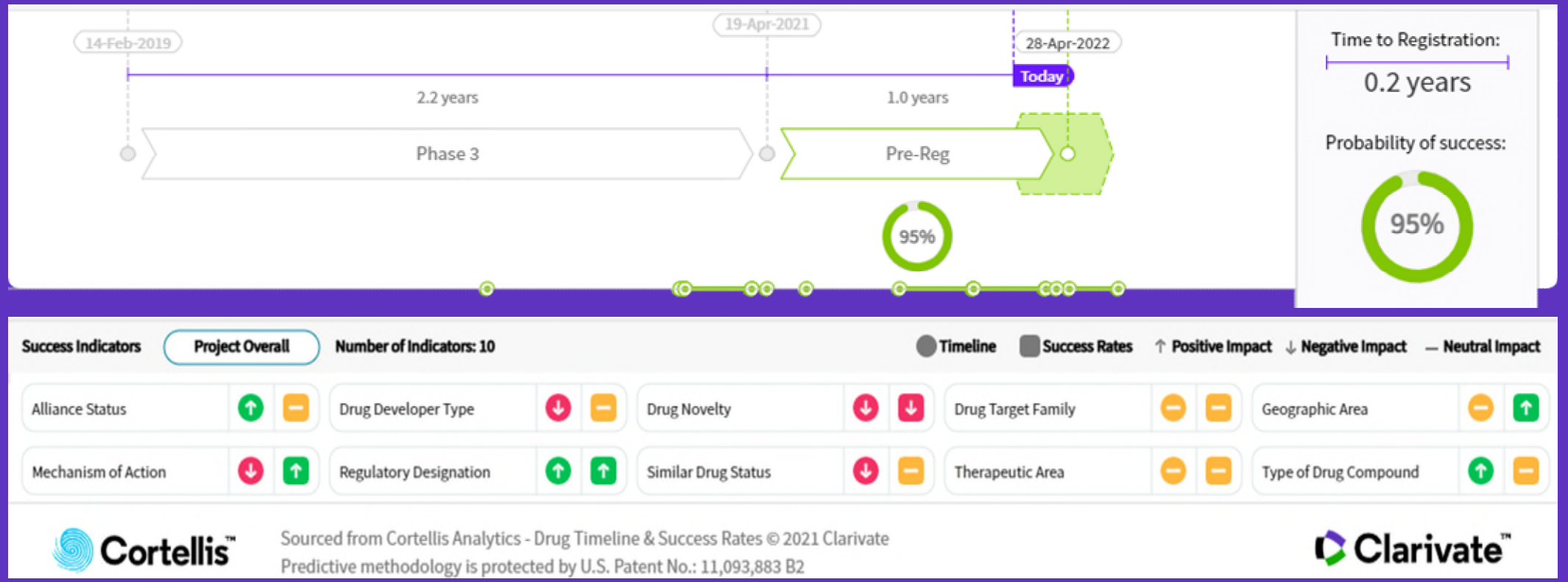

Profile

DR. HOZANA CASTILLO
Regional Solutions Consultant
Clarivate

Dr. Hozana Castillo is a Solutions 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. She also holds an adjunct researcher position at the Australian Regenerative Medicine Institute (ARMI).

Hozana Castillo received her PhD in Sciences (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.

Key Therapeutic Development Areas to Watch - 2022

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Cell and gene therapy

62%

Increase in academic articles from 2011 to 2020

4.5K

Active clinical trials* with 399,965 anticipated patients

32

Active companies

Clarivate™

Cell and gene therapies are transforming treatment for rare diseases and certain oncology indications

Cell therapies

Approved: Five CAR-T cell therapies by the U.S. FDA since the first in 2017 (four of which are approved in the EMA, two in Japan and one in China).
Indications: B-cell precursor acute lymphoblastic leukemia (ALL), diffuse large B-cell lymphoma, follicular lymphoma, mantle cell lymphoma and multiple myeloma.
Results: substantially higher remission rates than chemotherapy and other targeted therapies.
Clinical development: include T cell receptor (TCR-T), CAR-NK (natural killer) and tumor-infiltrating lymphocyte (TIL).

Other advancements

- The development of allogeneic cell therapies for hematologic cancers.
- Label expansions of CAR-T cell therapies to earlier lines of treatment in hematological malignancy.
- Dual-targeting CAR-T cell therapies.

Gene therapies

Approved / indications: include those to treat rare genetic disorders such as spinal muscular atrophy and inherited retinal dystrophies such as retinitis pigmentosa and Leber's congenital amaurosis.
Clinical development: diseases such as Duchenne muscular dystrophy.

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Clarivate™

Market access & impact

- Address typically under-served patient populations.
- Potential to have a long-term clinical benefit after a single administration, reduce the treatment burden and long-term treatment costs.
- Allogeneic options that use donor cells instead of a patient's own CAR T-cells could significantly increase patient access through a more standardized manufacturing process.
- Payer's concerned: substantial financial burden on the healthcare system due to the high expense of gene and CAR-T cell therapies.
- Insurance companies are paying providers to administer CAR-T cell therapies on a case-by-case basis.
- Discussions on new payment models with pharma companies to ensure patients have access to treatments.

Challenges

Cell therapies

- Reduce the manufacturing time, currently takes a median 2-3 weeks after the patient's cells are extracted and can be treatment prohibitive in patients with aggressive cancers.
- Market threat from other drug therapies, bispecific antibodies for hematologic diseases have demonstrated very promising clinical results, particularly in aggressive non-Hodgkin's lymphoma.

Gene therapies

- Small patient populations and narrow window in which treatment would be of most benefit.
- Expensive to develop and are typically priced high to recoup some of the development costs.
- Need to collect long-term data to assess safety and durability.

CRISPR

6946%

Increase in academic articles from 2011 to 2020

62

Active clinical trials* with 3,675 anticipated patients

5

Active companies

Clarivate™

CRISPR techniques have the potential to transform therapeutic approaches for diseases with very few treatment options

Therapies

- Orphan diseases have been a focus for several companies.
- Promising results for ATTR in the Ph 1, Intellia Therapeutics Inc's and for sickle cell and beta thalassemia in the Ph 1, CRISPR Therapeutics and Vertex Pharmaceuticals.
- Development is underway for immune-oncology: techniques to edit autologous T cells for hard-to-treat cancers such as multiple myeloma and melanoma.
- COVID-19 has also propelled CRISPR development, including a CRISPR-Cas13-based strategy, PAC-MAN, that can effectively degrade RNA from SARS-CoV-2 sequences in human lung epithelial cells.

Market access & impact

- Data from current clinical trials expected to be available within the next 5 years: inform how quickly CRISPR will be translated into clinical therapeutics.
- Patients with life-debilitating diseases, such as Duchenne muscular dystrophy, ATTR and beta-thalassemia, are likely to be the first to benefit.

Challenges

- Technical: off-target effects and immunotoxicities.
- It remains unknown how long it will take for CRISPR to have a commercial and clinical impact.
- Regulatory review of a novel technique, ethical concerns from the public, and the need for widespread education.

Drug Discovery driven by AI and ML

500%

Increase in academic articles from 2011 to 2020

4.5K

Active clinical trials* with ~400,000 anticipated patients

13

Active companies

Clarivate™

AI and ML have the potential to significantly reduce time for drug discovery and development

Application

- Can reduce the friction and loss from drug development steps, frontload experimental designs and create iterative feedback loops by using new models to leverage all the data.
- Numerous organizations are using AI methods to inform toxicology, to understand metabolics, for lead generation, and to predict efficacy.
- Some collaborations are establishing a full end-to-end development program, such as the agreement between Scientia and GlaxoSmithKline plc to develop clinical drug candidates for chronic obstructive pulmonary disease (COPD).

Market access & impact

- Applications of AI to access and analyze large datasets will contribute to streamlining drug development, from preclinical discovery through synthetic control arms, which can be particularly useful for rare disease populations.
- Potential to speed time to and to address unmet needs for many different patient populations.

Challenges

- Overcoming the perception of AI as a mysterious component (“black box”) and instilling confidence in algorithmic outcomes.
- Ensuring the quality of the data, it is important that the dataset has not had bias introduced.

RNA therapies

36%

Increase in academic articles from 2011 to 2020

46

Active clinical trials* with 2,575 anticipated patients

21

Active companies

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RNA therapies offer another avenue of targeted treatments for diseases that have been lacking therapeutic options

Therapies

- RNAi drugs such as vutrisiran from Alnylam Pharmaceuticals Inc could help fill the treatment gap for patients with hard-to-treat diseases.
- Use of messenger RNA (mRNA) by Moderna and BioNTech SE for COVID-19 vaccines.

Future directions

- Investments to determine where the advantages of mRNA will have the greatest benefit (therapeutic vaccines and therapies for active disease): • Safety • Degradation by normal cellular processes • Ability to regulate the half-life in vivo • Ability to modify it for greater stability and translatability.
- saRNA has the potential to allow delivery of lower concentrations.

Market access & impact

- Development of vaccines using RNA technology have the potential to address long-standing public health challenges and reduce the infectious disease burden in many countries worldwide.
- Competition in certain therapeutic areas, due to other targeted therapies entering the market at the same time. However, some RNA therapies might be less expensive and therefore have an advantage.

Challenges

- Innate challenges of instability and high innate immunogenicity.

Target Cancer Therapies

193%

Increase in academic articles from 2011 to 2020

276

Active clinical trials* with 37,533 anticipated patients

17

Active companies

Clarivate™

Targeted cancer therapies are advancing personalized medicine for patients with oncological indications that have a specific genetic component or mutation

Therapies

- Drugs such as adagrasib are offering hope of an efficacious treatment for diseases that have long been considered undruggable, including cancers with $KRAS^{G12C}$ mutation.

Opportunities

- Companies are finding ways to differentiate themselves against competitors by identifying niche patient populations who have unmet treatment needs.
- Companies find ways to navigate the crowded oncology market and achieve a solid commercial return.

Market access & impact

- For patients who have drug resistant mutations that have failed prior therapies — both non-targeted and targeted — the entry of new therapies is beneficial for disease outcomes and quality of life.
- Market pricing and reimbursement decisions will have an impact on how soon and how many patients are able to take advantage of exciting, targeted drugs in the pipeline.
- Planning for both the drug and companion diagnostic will be beneficial to successfully launch the drug.

Challenges

- Lack of diagnostic infrastructure and high treatment costs could be barriers to patient access.

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Thank you

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