IPD ANALYTICS

INDUSTRY-LEADING DRUG LIFE-CYCLE INSIGHTS

Drug Pipeline Report: 2H 2022

What's Inside…

In this report, IPD Analytics provides detailed summaries of key drugs nearing potential FDA approval in the coming months.

Our team of pharmacists, PhD scientists, and intellectual property attorneys continuously monitor and update our comprehensive pipeline intelligence database.

Use this report as a companion to our online Payer & Provider Insights and Clinical Development Tracker areas, which provide up-to-date clinical pipeline information on thousands of products across various disease classes and therapeutic areas. In tandem, these reports deliver insight into trending classes that will affect the competitive landscape and your drug spend.

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Executive Edge

In this issue of our Drug Pipeline Report, we provide streamlined insight into 44 high-impact drugs in the clinical pipeline that are nearing potential approval by the U.S. Food and Drug Administration (FDA), including:

- AXS-05 (Axsome Therapeutics) for major depressive disorder
- AMX0035 (Amylyx Pharmaceuticals) for amyotrophic lateral sclerosis
- Lecanemab (Biogen; Eisai) for Alzheimer's disease (AD)
- Deucravacitinib (Bristol Myers Squibb) for Plaque psoriasis (PsO)
- Teplizumab (Provention Bio) for delay of clinical type 1 diabetes
- Roctavian (valoctocogene roxaparvovec; BioMarin) for hemophilia A
- Etranacogene dezaparvovec (uniQure) for hemophilia B
- Sparsentan (Travere Therapeutics) for immunoglobulin A nephropathy

For each product in the report, our experts include commentary using the following framework:

- **Clinical Summary**
- **Place in Therapy**
- **Approval Outlook**
- **Estimated Price**

As these data evolve quickly, please refer to our therapeutic class summaries on the Payer and Provider Insights portal, or customize reports by filtering our online Clinical Development Tracker, a comprehensive database that includes current pipeline agents across more than 120 disease classes.

Behavioral Health

AXS-05 (bupropion/dextromethorphan)/Axsome

Route of Administration	Mechanism of Action	Indication(s)	Status
Oral	Norepinephrine-dopamine reuptake inhibitor (NDRI) N-methyl-D-aspartate (NMDA) receptor antagonist Sigma-1 receptor agonist	Major depressive disorder (MDD)	Pending Approval (2H 2022)

Clinical Summary

- If approved, AXS-05 will be the first oral treatment for MDD that targets the NMDA receptor.
- The Phase 3 GEMINI trial (NCT04019704) and the Phase 2 ASCEND trial (NCT03595579) were both included in the NDA filing for AXS-05. The trials found a statistically significant improvement in the Montgomery-Åsberg Depression Rating Scale and found AXS-05 to be well tolerated.
- In the GEMINI trial, AXS-05 was found to have statistically significant improvements in depression symptoms beginning at Week 1.
- AXS-05 is also being investigated in other indications, including Alzheimer's disease agitation and smoking cessation.

Place in Therapy

- If approved, AXS-05 will represent an alternative treatment option for patients with MDD, with a unique mechanism of action compared to all other oral agents available today.

Approval Outlook

- The original PDUFA date of August 22, 2021 was missed.
- In April 2022, Axsome stated that it had agreed to certain unspecified postmarketing requirements/ commitments proposed by the FDA.
- Approval is expected in 2H 2022.

Estimated Price

- Based upon the cost of other brand products approved for MDD or postpartum depression (PPD) and the novel mechanism of action, the estimated annual price of AXS-05 is $10,000–$25,000; the wholesale acquisition cost of brand competitors ranges from $5,500 to $16,000 annually.

CNS

AMX0035 (taurursodiol; sodium phenylbutyrate)/Amylyx

Route of Administration	Mechanism of Action	Indication(s)	Status
Oral	Nitrogen-binding agent; bile acid	Amyotrophic lateral sclerosis (ALS)	Pending Approval (09/29/2022)

Clinical Summary

- AMX0035 is an oral fixed-dose combination of two drugs, sodium phenylbutyrate and taurursodiol.
- AMX0035 resulted in slower functional decline than placebo as measured by the Amyotrophic Lateral Sclerosis Functional Rating Scale Revised (ALSFRS-R) score in the Phase 2 CENTAUR clinical trial (NCT03127514) in patients with ALS who had an onset of symptoms within the previous 18 months.
- In the CENTAUR open-label extension (OLE) (NCT03488524), using the March 1, 2021 cutoff date, the difference in median survival was 4.8 months (23.5 months for AMX0035 versus 18.7 months in the group originally assigned to placebo; $P = 0.0475$).
- A Phase 3 trial (PHOENIX) (NCT05021536) is currently ongoing, with a primary completion date expected in November 2023.

Place in Therapy

- If approved, AMX0035 will expand the existing treatment options, which currently consist of generic riluzole and Mitsubishi Tanabe's Radicava (edaravone) and Radicava ORS (oral suspension).
- In the CENTAUR trial, 77% of patients were currently using riluzole or Radicava; therefore, AMX0035 could be added to existing therapy.

Approval Outlook

- On March 30, 2022, the FDA's Peripheral and Central Nervous System Drugs Advisory Committee (PCNSDAC) met to discuss AMX0035. The committee voted 6 to 4 that the data from the CENTAUR trial and OLE do not establish the conclusion that AMX0035 is effective in the treatment of ALS.
- The FDA originally assigned AMX0035 a PDUFA date of June 29, 2022. However, on June 3, 2022, Amylyx announced that the FDA had extended the PDUFA date to September 29, 2022, to allow more time to review additional analyses of data from Amylyx's clinical studies.
- On July 5, 2022, Amylyx announced that the FDA plans to reconvene the PCNSDAC on September 7, 2022, to discuss the additional data from the clinical studies.

Estimated Price

- $100,000–$300,000 per year.
- Likely in the $175,000-per-year range based on the current price of Radicava. We expect AMX0035 may be priced at a premium to intravenous Radicava.

CNS (cont.)

Lecanemab/Biogen; Eisai

Route of Administration	Mechanism of Action	Indication(s)	Status
Intravenous	Amyloid beta protein inhibitor	Alzheimer's disease (AD)	Pending Approval (01/06/2023)

Clinical Summary

- A humanized IgG1 monoclonal antibody that binds to soluble amyloid beta aggregates (oligomers and protofibrils) with high selectivity over monomer and insoluble fibrils.
- Administered as a 60-minute intravenous infusion every 2 weeks using weight-based dosing and without the need for titration.
- The Phase 2 Study 201 failed to meet the criteria for success at 12 months, but 18-month analyses demonstrated a reduction in brain amyloid along with a reduction of clinical decline across various clinical and biomarker endpoints.
- The Phase 3 CLARITY AD trial is a confirmatory study evaluating the effect on cognition using the Clinical Dementia Rating–Sum of Boxes (CDR-SB).

Place in Therapy

- Could become the second FDA-approved anti-amyloid monoclonal antibody.
- May have potentially greater plaque reduction effects and a potentially better side-effect profile than Biogen's Aduhelm (aducanumab-avwa).

Approval Outlook

- The FDA accepted Eisai's rolling BLA submission under the accelerated approval pathway and granted Priority Review. The PDUFA date is January 6, 2023.
- The indication being sought is for the treatment of mild cognitive impairment (MCI) due to AD and mild AD (collectively known as early AD [EAD]) with confirmed presence of amyloid pathology in the brain.
- Topline results from CLARITY AD are expected in fall 2022. Depending upon the results, submission for full FDA approval may occur by 1Q 2023.
- Approval under the accelerated pathway will affect how the product will be handled under the Centers for Medicare and Medicaid Services (CMS) National Coverage Determination for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease.

Estimated Price

- $25,000–$100,000 per year, based on Aduhelm price.

Dermatology

Deucravacitinib/Bristol Myers Squibb (BMS)

Route of Administration	Mechanism of Action	Indication(s)	Status
Oral	Tyrosine kinase 2 (TYK2) inhibitor	Plaque psoriasis (PsO)	Pending Approval (09/10/2022)

Clinical Summary

- In the head-to-head Phase 3 POETYK-PSO-1 (NCT03624127) and POETYK-PSO-2 (NCT03611751) studies, deucravacitinib 6 mg once daily outperformed placebo and Amgen's Otezla (apremilast) at 16, 24, and 52 weeks in adults with moderate to severe PsO.
- The co-primary endpoints were measured at Week 16 and included the proportion of subjects with a static Physician Global Assessment (sPGA) score of 0 (clear) or 1 (almost clear) and the proportion of subjects achieving a 75% reduction from baseline in the Psoriasis Area and Severity Index score (PASI 75).
- Deucravacitinib is also being studied in psoriatic arthritis, lupus, Crohn's disease, and ulcerative colitis.

Place in Therapy

- Deucravacitinib may impact sales of Otezla with its demonstrated superior efficacy in PsO compared to Otezla. Based on cross-trial comparisons, deucravacitinib appears to be less efficacious than biologics overall. The anticipated entry of biosimilar Humira and Stelara in 2023 may impact the uptake of deucravacitinib.
- The FDA's interpretation of deucravacitinib safety data may impact utilization based on similarities in the mechanism of action to Janus kinase (JAK) inhibitors. A Boxed Warning for deucravacitinib would give Otezla a strong competitive edge along with Otezla's first-to-market status.

Approval Outlook

- The PDUFA date is September 10, 2022.

Estimated Price

- $25,000–$100,000 per year based on pricing at parity with the annual WAC of AbbVie's oral JAK inhibitor, Rinvoq (upadacitinib), which is $69,000.

Diabetes

Teplizumab/Provention Bio

Route of Administration	Mechanism of Action	Indication(s)	Status
Intravenous	Anti-CD3 antibody	Delay of clinical type 1 diabetes (T1D) in at-risk individuals	Pending Approval (11/17/2022)

Clinical Summary

- Teplizumab is under review for the delay of clinical T1D in at-risk individuals.
- Extended follow-up data from the Phase 2 TN-10 trial (NCT01030861) found that patients at high risk of developing T1D who were treated with a 14-day course of teplizumab had a median time to diagnosis of 59.6 months versus 27.1 months in placebo-treated patients.
- This agent received Breakthrough Therapy designation.
- An FDA advisory committee voted in favor (10 to 7) that the benefits of teplizumab outweigh the risks.

Place in Therapy

- There have been no disease-modifying drugs for the treatment of T1D since the development of insulin a century ago.
- If approved, there would be much interest in a treatment that could delay the onset of T1D by 2 years, particularly in a population of school-aged children, given the lack of therapeutic options for patients who are at high risk of developing diabetes.

Approval Outlook

- In July 2021, Provention Bio announced that the FDA issued a CRL and stated that a single, low-dose pharmacokinetics/pharmacodynamics (PK/PD) bridging study in healthy volunteers to compare the planned commercial product with the original product failed to show comparability.
- In addition, the FDA cited several additional considerations related to product quality and did not cite any clinical deficiencies related to the efficacy and safety data packages submitted.
- On February 22, 2022, Provention Bio resubmitted the BLA (accepted on March 21, 2022 with a PDUFA date of August 17, 2022).
- On June 30, 2022, the FDA extended the PDUFA date by 3 months to November 17, 2022, because it considered Provention Bio's response to an information request to be a major amendment to the BLA resubmission, which requires additional time for review.

Estimated Price

- $100,000–$300,000 for one course of therapy.
- Price estimation is difficult, as there are no other similar therapies. It is unclear if additional therapy courses may be required in the future.

Hematology

Etranacogene dezaparvovec (AMT-061)/uniQure

Route of Administration	Mechanism of Action	Indication(s)	Status
Intravenous	Gene therapy	Hemophilia B	Pending Approval (11/2022)

Clinical Summary

- Etranacogene dezaparvovec uses an AAV5 vector to carry a gene variant of factor IX (FIX) that generates more-active-than-normal FIX proteins.
- This agent has received Breakthrough Therapy designation.
- Key data from the Phase 3 HOPE-B trial (NCT03569891) found that treatment with etranacogene dezaparvovec in patients with severe or moderately severe disease produced mean FIX activity of 39.0 IU/dL at 6 months and 36.9 IU/dL at 18 months post infusion. Additionally, 98% of patients treated with a full dose discontinued use of prophylaxis. The treatment was effective in patients with pre-existing antibodies and well tolerated.
- The FDA had previously placed a clinical hold on the trial due to a case of liver cancer that was later found to be unrelated to treatment with etranacogene dezaparvovec.

Place in Therapy

- Current treatment of hemophilia B involves lifelong prophylactic infusions of FIX to replace or supplement low levels of clotting factor.
- If approved, etranacogene dezaparvovec would be the first gene therapy available for the treatment of hemophilia B that is intended to be a one-time treatment. The durability of this treatment is unknown.

Approval Outlook

- On May 24, 2022, uniQure announced that the FDA accepted the BLA for etranacogene dezaparvovec under Priority Review. A decision is anticipated in November 2022.

Estimated Price

- $2,000,000–$3,000,000 for a one-time treatment.
- Likely $2,500,000 for a one-time treatment, based on the anticipated cost of hemophilia gene therapy treatments.

Hematology (cont.)

Roctavian (valoctocogene roxaparvovec)/BioMarin

Route of Administration	Mechanism of Action	Indication(s)	Status
Intravenous	Gene therapy	Hemophilia A	Received CRL on 08/18/2020; potential FDA filing in 3Q 2022

Clinical Summary

- Roctavian (valoctocogene roxaparvovec) uses an adeno-associated virus serotype 5 (AAV5) vector to carry a functional copy of the *F8* gene that contains instructions for making factor VIII.
- This agent has received Regenerative Medicine Advanced Therapy (RMAT), Breakthrough Therapy, and Orphan Drug designations.
- The Phase 3 GENEr8-1 (NCT03370913) study (N = 134) found that treatment with Roctavian resulted in an 85% reduction in ABR and factor VIII use decreased 98% from baseline. Participants had at least one adverse event (16.4% reported serious adverse events). Elevations in alanine aminotransferase levels occurred in 85.8% of participants and were managed with immunosuppressants. No development of factor VIII inhibitors or thrombosis occurred in any of the participants.
- In May 2022, BioMarin announced updated results from its ongoing open-label Phase 1/2 study (6-year and 5-year post-treatment follow-up), which demonstrated sustained hemostatic efficacy of the investigational therapy. All but one participant remained off factor VIII treatment at the time of data cutoff and safety remained consistent with previously reported data.

Place in Therapy

- If approved, Roctavian would be the first gene therapy approved for the treatment of hemophilia A that is intended to provide a one-time treatment. The durability of this treatment thus far appears to be about 6 years.

Approval Outlook

- In August 2020, BioMarin received a CRL. The FDA requested completion of a Phase 3 trial and submission of 2-year follow-up data.
- On May 31, 2022, BioMarin announced that the FDA requested additional data and analysis and that the agency is not requiring additional preclinical or clinical testing. As a result, BioMarin is delaying the BLA resubmission to September 2022.

Estimated Price

- $2,000,000–$3,000,000 for a one-time treatment.
- The estimate above was suggested by BioMarin's leadership.

Nephrology (cont.)

Sparsentan/Travere Therapeutics

Route of Administration	Mechanism of Action	Indication(s)	Status
Oral	Endothelin receptor antagonist (ERA)/ angiotensin II receptor blocker (ARB)	Immunoglobulin A nephropathy (IgAN)	Pending Approval (11/17/2022)

Clinical Summary

- Sparsentan's Phase 3 pivotal trial in IgAN (PROTECT; NCT03762850) is ongoing in over 400 patients randomized 1:1 to sparsentan or irbesartan (active control). All patients enrolled in the study were 18 years of age and older with IgAN and persistent proteinuria despite use of an angiotensin-converting enzyme (ACE) inhibitor or ARB.
- The interim proteinuria endpoint was evaluated after 36 weeks and was found to be statistically significant. Patients receiving sparsentan achieved a mean reduction in proteinuria from baseline of 49.8% versus 15.1% in the irbesartan group after 36 weeks.
- Sparsentan's treatment effect on estimated glomerular filtration rate (eGFR) slope over 110 weeks is the study's confirmatory endpoint; topline results of this endpoint are expected by the end of 2023.

Place in Therapy

- Sparsentan was studied as a once-daily oral therapy and would be the second drug approved for IgAN. Calliditas' Tarpeyo (budesonide) was recently approved in December 2021.
- Sparsentan was not studied in combination with other therapies; however, due to its unique mechanism of action, it could be used in combination with other pipeline therapies in the future.

Approval Outlook

- On May 16, 2022, Travere Therapeutics announced that the FDA had accepted its NDA for accelerated approval; the PDUFA date is now set for November 17, 2022.
- The FDA has stated it will not be conducting an advisory committee meeting for sparsentan.

Estimated Price

- $100,000–$300,000.
- Based on analogs such as Calliditas Therapeutics' Tarpeyo (budesonide) for IgAN, ChemoCentryx's Tavneos (avacopan) for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, and Aurinia Pharmaceuticals' Lupkynis (voclosporin) for lupus nephritis, we estimate a WAC of between $100,000 and $200,000 per year.
- We can envision Travere Therapeutics will offer flat pricing across all strengths, effectively pricing the treatment of IgAN and focal segmental glomerulosclerosis (FSGS) at parity (FDA filing expected by the end of 2022).

Products Included in the Original Report

Product/Manufacturer	Therapeutic Area
Adagrasib (MRTX849)/Mirati Therapeutics	Oncology
AMX0035 (taurursodiol; sodium phenylbutyrate)/Amylyx	CNS
ATT-GAA: Cipaglucosidase Alfa (ATB200) and Miglustat (AT2221)/Amicus Therapeutics	Endocrine and Metabolic
AXS-05 (bupropion/dextromethorphan); Axsome	Behavioral Health
Beti-cel (betibeglogene autotemcel)/bluebird bio	Hematology
Bimekizumab/UCB	Dermatology
CUTX-101 (copper histidinate)/Cyprium Therapeutics	Endocrine and Metabolic
Daprodustat/GSK	Nephrology
Deucravacitinib/Bristol Myers Squibb	Dermatology
Donanemab/Eli Lilly	CNS
Efanesoctocog Alfa (BIVV001)/Sanofi	Hematology
Eli-cel (elivaldogene autotemcel; Lenti-D)/bluebird bio	CNS
Etranacogene dezaparvovec (AMT-061)/uniQure	Hematology
Fezolinetant (ESN364)/Astellas	Obstetrics/Gynecology
Futibatinib (TAS-120)/Taiho Oncology	Oncology
Givinostat (ITF2357)/Italfarmaco	CNS
Hepcludex (bulevirtide)/Gilead	Infectious Disease
Lecanemab/Biogen; Eisai	CNS

Product/Manufacturer	Therapeutic Area
Mirikizumab (LY3074828)/Eli Lilly	Gastrointestinal
Mirvetuximab soravtansine (IMGN853)/ImmunoGen	Oncology
Mosunetuzumab/Roche	Oncology
MYL-1601D/Viatris; Biocon	Diabetes
Nirsevimab/AstraZeneca; Sanofi	Infectious Disease
Nuplazid (pimavanserin)/Acadia	CNS
Olipudase Alfa/Sanofi	Endocrine and Metabolic
Omaveloxolone/Reata	CNS
Omecamtiv mecarbil/Cytokinetics	Cardiovascular
Pamrevlumab/FibroGen	CNS
Pegcetacoplan (APL-2)/Apellis	Ophthalmology
Peginterferon Lambda (Lambda)/Eiger Biopharmaceuticals	Infectious Disease
Poziotinib/Spectrum Pharmaceuticals	Oncology
Rinvoq (upadacitinib)/AbbVie	Gastrointestinal
Ritlecitinib/Pfizer	Dermatology
Roctavian (valoctocogene roxaparvovec)/BioMarin	Hematology
Sabizabulin (VERU-111)/Veru	Infectious Disease
SER-109/Seres Therapeutics	Infectious Disease
Sparsentan/Travere Therapeutics	Nephrology
Spesolimab (BI 655130)/Boehringer Ingelheim	Dermatology

Product/Manufacturer	Therapeutic Area
Teplizumab/Provention Bio	Diabetes
Ublituximab (TG-1101)/TG Therapeutics	CNS
Vamorolone/Santhera; ReveraGen	CNS
Vyjuvek (beremagene geperpavec; B-VEC)/Krystal Biotech	Dermatology
Zavegepant (BHV-3500)/Biohaven	Migraine
Zuranolone (SAGE-217/BIIB125)/Sage; Biogen	Behavioral Health

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About Payer & Provider Insights

IPD's Payer & Provider Insights combine advanced pharmaceutical landscape market visibility with a team of Executive Clinical Pharmacists to provide comprehensive pharmacy and therapeutic management strategy, supporting formulary, clinical, contracting, and market-access decisions.

Understand Key Clinical, Cost, Utilization, Reimbursement, and Market-Competition Factors

Review Formulary Management Considerations and Opportunities and Strategies and P&T Committee Planning Support

Anticipate Market Shifts, Pipeline Events, Manufacturer Life-Cycle Management Strategies, and Financial Implications

Access Published Guidelines, Health Outcomes, Pharmacoeconomics, and Clinical Trials