IPD ANALYTICS

INDUSTRY-LEADING DRUG LIFE-CYCLE INSIGHTS

Drug Pipeline Sample Report: 1H 2022

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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.

This report is used as a companion to our online Clinical Development Tracker, which provides 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.

DRUG PIPELINE REPORT

Sample Report Contents

Executive Edge

In this issue of our Drug Pipeline Report, we provide streamlined insight into 40 high-impact drugs in the clinical pipeline that are nearing potential approval by the U.S. Food and Drug Administration (FDA), including:

- Tirzepatide (Eli Lilly) for diabetes
- Donanemab (Eli Lilly), lecanemab (Biogen) and gantenerumab (Roche) for Alzheimer's disease
- Fezolinetant (Astellas) for vasomotor symptoms due to menopause
- Vutrisiran (Alnylam) for polyneuropathy of hereditary transthyretin-related amyloidosis (hATTR-PN)

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

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

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.

If you have any questions or feedback, contact us directly by emailing healthcare@ipdanalytics.com.

Regulatory Terms

Table 1 includes common terms used by the FDA to denote the regulatory status of pipeline agents.

Table 1. Common FDA/Regulatory Terms

Acronym	Term	Definition
ANDA	Abbreviated New Drug Application	Contains data that are submitted to FDA for review and potential approval of a generic drug product.
BLA	Biologics License Application	Comprehensive document submitted to FDA to formally request approval for a new drug; similar to NDA except BLAs relate to biological products.
Breakthrough Therapy	Breakthrough Therapy designation	Expedites the development and review of drugs that are intended to treat a serious condition when clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies.
CRL	Complete Response Letter	Reflects FDA's complete review of data submitted in an NDA or BLA and the FDA has decided not to approve it in its present form.
EUA	Emergency Use Authorization	Facilitates the availability and use of medical countermeasures during public health emergencies. EUA allows the use of unapproved medical products, or unapproved uses of approved products to diagnose, treat, or prevent serious or life-threatening diseases or conditions when certain criteria have been met, including that there are no adequate, approved, or available alternatives.
Fast Track	Fast Track designation	A process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need.
FDA	United States Food and Drug Administration	The agency responsible for ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices, and the safety of the U.S. food supply, cosmetics, and products that emit radiation.
NDA	New Drug Application	Comprehensive document submitted to FDA to formally request approval for a new drug (pertains to traditional small molecules).
Orphan Drug	Orphan Drug designation	Provides orphan status to drugs and biologics intended for the treatment, prevention, or diagnosis of a rare disease or condition.
PDUFA	Prescription Drug User Fee Act	Goal date for FDA to make a decision on whether or not to approve a new drug.
sBLA	Supplemental Biologics License Application	Similar to an sNDA except sBLAs relate to biological products.
sNDA	Supplemental New Drug Application	Application to allow a company to make changes in a product that already has an approved NDA; includes adding a new indication (use).

CNS

Donanemab/Lilly

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

Clinical Summary

- In March 2021, Lilly presented results from its Phase 2 TRAILBLAZER-ALZ trial of donanemab at the International Conference on Alzheimer's & Parkinson's Diseases.
- Results were mixed in the trial of 272 patients, with donanemab meeting its primary endpoint by showing a 32% reduced rate of cognitive decline relative to placebo as measured by the Integrated Alzheimer's Disease Rating Scale (iADRS), although it was not shown to halt further decline.

Clinical Summary (cont.)

- A key next step is the large, 1500-patient, Phase 3 TRAILBLAZER-ALZ2 study of the cognitive efficacy and safety of donanemab, which is ongoing and will read out in mid-2023.

Place in Therapy

- Donanemab is a monoclonal antibody similar to aducanumab, but designed to target a form of amyloid beta present only in amyloid plaques, called N3pG. Lilly has suggested donanemab may be a more effective anti-amyloid agent than ones previously studied due to its specific action.

Approval Outlook

- On October 26, 2021, Lilly announced that it had initiated the rolling submission of the BLA for donanemab for the treatment of Alzheimer's disease. Lilly is seeking approval for donanemab under the accelerated approval pathway, and the FDA previously granted Breakthrough Therapy designation to donanemab. Based on the FDA's approval of Aduhelm due to its ability to remove amyloid plaque, Lilly is seeking approval under this same surrogate endpoint pathway, and not approval based on improved cognitive function.
- Potential accelerated approval in 2022.

Diabetes

Tirzepatide/Lilly

Route of Administration	Mechanism of Action	Indication(s)	Status
Subcutaneous	Glucagon-like peptide-1 (GLP-1)/glucose-dependent insulinotropic polypeptide (GIP)	Type 2 diabetes	Pending Approval (2Q 2022)

Clinical Summary

- Topline results from five of seven Phase 3 tirzepatide studies, the SURPASS-1, -2, -3, -4, and -5 trials, have been released through 2021.
- The overall safety profile of tirzepatide was similar to that of the established GLP-1 receptor agonist class, with gastrointestinal side effects being the most commonly reported adverse events.
- Across SURPASS-2, -3, and -5, tirzepatide reduced A1c by an average of over 2 percentage points and led to a weight loss of 15–28 pounds.

Place in Therapy

- Results do not necessarily suggest that tirzepatide will replace existing GLP-1 agonists, but it will add a significant new competitor to established GLP-1 agonists, such as Novo Nordisk's Ozempic and Rybelsus and Lilly's own drug, Trulicity.
- The highest doses of Ozempic may be competitive to tirzepatide, although at the lower doses, with which most patients are treated, tirzepatide may have the advantage.
- Tirzepatide's new mechanism of action may have more A1c efficacy than GLP-1 agonists and lead to greater weight loss.

Approval Outlook

- Tirzepatide is now under review with the FDA for type 2 diabetes. Lilly submitted an NDA for tirzepatide in October 2021, with potential approval in 2Q 2022.

Endocrine and Metabolic (cont.)

Vutrisiran/Alnylam Pharmaceuticals

Route of Administration	Mechanism of Action	Indication(s)	Status
Subcutaneous (SC)	Small interfering RNA (siRNA)	Polyneuropathy of hereditary transthyretin-related amyloidosis (hATTR-PN)	Pending Approval (04/14/2022)

Clinical Summary

- Vutrisiran is an RNA-interference therapy that inhibits the production of transthyretin (TTR) protein, thereby reducing levels in the bloodstream.
- Its subcutaneous, quarterly administration is more convenient than the currently available RNAi-based hATTR-PN therapy Onpattro (patisiran), administered by intravenous infusion once every 3 weeks.
- Received Orphan Drug and Fast Track designations.
- Application supported by the Phase 3 HELIOS-A trial (NCT03759379), which evaluated vutrisiran versus external placebo. Vutrisiran met all primary and secondary endpoints, with statistically significant improvements in neuropathy, quality of life, and gait speed, relative to external placebo.

Place in Therapy

- If approved, vutrisiran will be an additional treatment option for hATTR-PN patients, which currently include Alnylam's Onpattro and Ionis/Akcea's Tegsedi.
- Vutrisiran combines the convenience of subcutaneous administration and a more desirable safety profile versus Tegsedi, likely positioning it to be a preferred product, if approved.

Approval Outlook

- On June 25, 2021, Alnylam announced the FDA accepted its NDA submission for vutrisiran for hATTR-PN, and a decision is expected on April 14, 2022.

Obstetrics/Gynecology

ESN364 (fezolinetant)/Astellas Pharma

Route of Administration	Mechanism of Action	Indication(s)	Status
Oral	Neurokinin-3 (NK3) receptor antagonist	Vasomotor symptoms due to menopause (hot flashes)	Filing expected in 2022 or early 2023

Clinical Summary

- The global BRIGHT SKY program includes three Phase 3 clinical trials (SKYLIGHT 1, SKYLIGHT 2, and SKYLIGHT 4) in women with moderate to severe vasomotor symptoms (VMS) associated with menopause.
- Both SKYLIGHT 1 and SKYLIGHT 2 met all co-primary endpoints, showing a statistically significant reduction from baseline in the frequency and severity of moderate to severe VMS at Week 4 and Week 12 for women who received fezolinetant 30 mg and 45 mg once daily versus placebo.
- SKYLIGHT 4 is a 52-week, double-blind, placebo-controlled trial to evaluate the long-term safety of fezolinetant, with results pending.

Place in Therapy

- If approved, fezolinetant would be a first-in-class, oral, nonhormonal treatment option for VMS associated with menopause in women who cannot or choose not to take hormone therapy.

Approval Outlook

- Approval is likely, provided the long-term safety results are positive.
- Astellas is expected to submit the NDA for fezolinetant in 2022 or early 2023.

Full Report Product Index:

Product/Manufacturer	Therapeutic Area
Bimekizumab/UCB	Dermatology
BIVV009 (sutimlimab)/Bioverativ/Sanofi	Hematology
Bulevirtide/Gilead	Infectious Disease
BXCL501 (dexmedetomidine HCl)/BioXcel	Behavioral Health
Cibinqo (abrocitinib)/Pfizer	Dermatology
Deucravacitinib/Bristol-Myers Squibb	Dermatology
Donanemab/Lilly	CNS
Eli-cel (elivaldogene autotemcel; Lenti-D)/ bluebird bio	CNS
ESN364 (fezolinetant)/Astellas	Obstetrics/Gynecology
Gantenerumab/Genentech, Roche	CNS
GSK3844766A/GSK	Infectious Disease
Jardiance (empagliflozin)/BI, Lilly	Cardiovascular
JNJ-4528/Janssen	Oncology
Kimmtrak (tebentafusp)/Immunocore	Oncology
Lecanemab/Biogen, Eisai	CNS
Lumevoq (GS010; lenadogene nolparvovec)/GenSight	Ophthalmology
Mavacamten/Bristol-Myers Squibb	Cardiovascular
Mino-Lok/Citius Pharmaceuticals	Infectious Disease
MK-7264 (gefapixant)/Merck	Respiratory
Pacritinib/CTI Biopharma	Oncology

Product/Manufacturer	Therapeutic Area
PF-06928316/Pfizer	Infectious Disease
RE-021 (sparsentan)/Ligand, Travere	Nephrology
Rinvoq (upadacitinib)/AbbVie	Dermatology
Skyrizi (risankizumab-rzaa)/AbbVie	Gastrointestinal and Nutritional Diseases
Somatrogon/Pfizer	Endocrine and Metabolic
TAB001 (toripalimab)/Junshi, Coherus	Oncology
Tebipenem/Spero	Infectious Disease
Tezspire (tezepelumab)/AstraZeneca, Amgen	Respiratory
Tirzepatide/Eli Lilly	Diabetes
Vadadustat/Akebia	Hematology
Vutrisiran/Alnylam	Endocrine and Metabolic
Vyjuvek (beremagene geperpavec)/Krystal Biotech	Dermatology