

Drug and Biologic Pipeline Update

Q1 2021



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IngenioRx's quarterly *Drug and Biologic Pipeline Update*

Our Q1 2021 edition provides in-depth analyses of important agents coming in the near term. We examine a potential gene therapy for a rare blood disorder, an oral drug for an autoimmune disorder that may offer an alternative to long-term steroid treatment, and a biologic for a rare complication of stem cell transplants. In addition, we provide important information on the biosimilar landscape, current treatment and pipeline for atopic dermatitis, and market trends that may affect the pipeline.

We continue to closely monitor the drug and biologic pipeline and provide this publication as part of our goals to improve health, reduce waste, lower total cost of care for pharmacy and medical, and estimate future cost impact.

-
- | | | | |
|---|----------------------------|---|-------------------------------------|
| 3 | Top emerging new therapies | 6 | Other significant product approvals |
|---|----------------------------|---|-------------------------------------|
-
- | | | | |
|---|--|----|-----------------------|
| 8 | Analysis: update on the biosimilar landscape | 10 | Therapy market trends |
|---|--|----|-----------------------|
-
- | | |
|----|-----------------------------|
| 11 | Update on atopic dermatitis |
|----|-----------------------------|

Unless otherwise noted, the information contained in this document was obtained from the Centers for Disease Control and Prevention ([cdc.gov](https://www.cdc.gov)), the Food and Drug Administration ([fda.gov](https://www.fda.gov)), clinicaltrials.gov, releases from pharmaceutical manufacturers, and [UpToDate.com](https://www.upToDate.com) (registration required). Information in this document is accurate as of January 12, 2021.



Top emerging new therapies

We expect these products to have significant impact on health plans and members.

AVACOPAN

Product:

Avacopan

Indication:

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis

Estimated FDA approval:

July 2021

Therapeutic class:

Complement 5a receptor inhibitor

Route of administration:

Oral

FDA designations:

Orphan

Manufacturer:

ChemoCentryx

Condition:

ANCA-associated vasculitis is an autoimmune condition characterized by the inflammation of blood vessels. While it often affects the respiratory tract and kidneys, there are several types of ANCA-associated vasculitis with varying symptoms depending on which areas of the body are involved. ANCA-associated vasculitis has an annual incidence rate of 20 per million in Europe and North America. Risk increases with age, and mortality is high due to infection, cardiovascular disease, and malignancy.^{1,2,3,4}

Role in treatment:

The current standard of care for ANCA-associated vasculitis is high-dose corticosteroid therapy used along with immunosuppressants. Certain individuals may be refractory to or intolerant of current therapy.^{1,5} Avacopan provides an alternative treatment option for use in combination with immunosuppressants. It also has the potential advantage of a more-favorable safety profile compared with high-dose corticosteroids.

Efficacy:

When used in combination with immunosuppressants, avacopan established noninferiority in the percent of patients who achieved disease remission, as well as superiority in sustaining remission at 52 weeks, compared to prednisone.⁶

Safety:

Patients treated with avacopan had fewer serious adverse events compared with patients treated with prednisone.⁷

Financial impact:

Analysts predict avacopan pricing at \$80,000 annually, with projected peak U.S. sales of \$1.2B.⁸ For those unable to tolerate the side effects associated with long-term corticosteroid use, avacopan may be an attractive option. Drug spend could noticeably increase within the commercial and senior population, where avacopan use is expected to be highest.

IngenioRx view:

Avacopan may be an option for patients who are refractory to or intolerant of current high-dose corticosteroid treatment regimens for ANCA-associated vasculitis. More data may be needed to confirm the role of avacopan in maintenance of remission.⁹

1 Yates M, Watts R. ANCA-associated vasculitis. *Clin Med (Lond)*. 2017;17(1):60-64. doi:10.7861/clinmedicine.17-1-60.

2 ANCA Vasculitis News. *ANCA Vasculitis Symptoms* (Accessed January 2021): <https://ancavasculitisnews.com>.

3 ANCA Vasculitis News. *What is ANCA Vasculitis?* (Accessed January 2021): <https://ancavasculitisnews.com>.

4 Geetha D, Jefferson J.A. ANCA-Associated Vasculitis: Core Curriculum 2020. *American Journal of Kidney Disease*. 2019;75(1):124-137. <https://doi.org/10.1053/j.ajkd.2019.04.031>.

5 Smith, R.M., Jones, R.B. & Jayne, D.R. Progress in treatment of ANCA-associated vasculitis. *Arthritis Res Ther* 14, 210 (2012). <https://doi.org/10.1186/ar3797>

6 U.S. Pharmacist. *FDA Accepts NDA for Avacopan in ANCA-Associated Vasculitis* (October 14, 2020): uspharmacist.com.

7 ChemoCentryx, Inc. ChemoCentryx, Inc. Announces FDA Acceptance of the Avacopan New Drug Application (NDA) for the Treatment of ANCA-Associated Vasculitis (September 17, 2020): ir.chemocentryx.com.

8 MarketWatch. *Drug maker ChemoCentryx shares rocket on blockbuster potential in rare autoimmune disease* (November 27, 2019): marketwatch.com.

9 Tesar V, Hruskova Z. Avacopan in the treatment of ANCA-associated vasculitis. *Expert Opin Investig Drugs*. 2018 May;27(5):491-496. doi: 10.1080/13543784.2018.1472234. Epub 2018 May 8. PMID: 29718732.

LENTIGLOBIN/ZYNTEGLO

Product:

LentiGlobin™ (U.S.); Zynteglo® (EU) (betibeglogene autotemcel)

Indication:

Transfusion-dependent beta thalassemia (TDT)

Estimated FDA approval:

Late 2021 to early 2022

Therapeutic class:

Gene therapy

Route of administration:

Intravenous (IV) infusion

FDA designations:

Breakthrough; Fast Track; Orphan

Manufacturer:

bluebird bio

Condition:

Beta thalassemia is an inherited blood disorder caused by mutations in the hemoglobin beta gene. These mutations result in defective red blood cells (RBCs) that have little or no hemoglobin, the protein responsible for oxygen transport. Severe forms of beta thalassemia cause symptomatic anemia, a condition where the body does not receive enough oxygen. Patients who require regular RBC transfusions to manage anemia are classified as having transfusion-dependent anemia. Approximately 1,000 people in the United States have the most severe form of beta thalassemia, transfusion-dependent beta thalassemia (TDT).^{10,11}

Role in treatment:

LentiGlobin would be the first FDA-approved gene therapy for TDT. This personalized therapy is made from a patient's own hematopoietic stem cells (HSC), which are then genetically modified to produce unaffected RBCs. Prior to receiving a one-time IV dose of LentiGlobin, patients must undergo myeloablation, a process that drastically reduces bone marrow activity.¹² In Europe, where LentiGlobin is approved under the brand name Zynteglo for TDT, treatment is reserved for patients who qualify for but cannot find a matched HSC transplant donor.¹³ Hematopoietic cell transplantation (HCT) using a matched donor is a potentially curative therapy for TDT, but lack of a suitable donor represents a major barrier and eliminates this option for many individuals.

Efficacy:

Interim data from three trials are promising and found the majority of evaluable patients given a single dose of LentiGlobin achieved independence from blood transfusions, defined as no longer needing RBC transfusions for at least a year with stable RBC levels. With only 60 patients treated in trials thus far, we await additional data from phase 3 trials that will more clearly define its significance in TDT.

Safety:

Though there have been no deaths or cases of cancer, serious side effects like low platelets, the cells that help blood clot, and liver disease have occurred. Overall, the safety appears consistent with the myeloablation regimen required for LentiGlobin administration.^{14, 15, 16, 17}

Financial impact:

LentiGlobin U.S. pricing is estimated at \$2M per patient, a slight premium to the announced European Union price, where the therapy is already approved. Analysts predict domestic sales to peak at \$1.1B for its use in beta thalassemia,¹⁸ with the highest financial impact expected in the Medicaid population. Despite excitement over a potential curative therapy for those without a matched HSC transplant donor, analyst sales estimates may be overly optimistic given the low prevalence of TDT, high toxicity associated with the required myeloablative regimen, and unknown long-term efficacy and safety.

IngenioRx view:

LentiGlobin would be the first FDA-approved gene therapy for TDT. Due to the complex harvesting and administration processes, LentiGlobin would likely be limited initially to specialized transfusion centers.¹⁰ While TDT is a rare disease, the anticipated high cost of this one-time gene therapy may result in significant interest in the medical and health plan communities.

10 National Organization for Rare Disorders. *Beta Thalassemia* (Accessed January 2021): rarediseases.org.

11 Bluebird bio. *It's time to challenge our understanding of TDT* (Accessed January 2021): challengedt.com.

12 National Cancer Institute. *Definition of myeloablation* (Accessed January 2021): cancer.gov.

13 European Medicines Agency. *Zynteglo* (Accessed January 2021): ema.europa.eu/en.

14 Locatelli F, Kwiatkowski JL, Thompson AA, et al. Abstract O074: Clinical outcomes following autologous hematopoietic stem cell transplantation with LentiGlobin gene therapy in the phase 3 Northstar-2 and Northstar-3 studies for transfusion dependent β -thalassemia. EBMT 46th Annual Meeting 2020. (Accessed January 2021): professionalabstracts.com.

15 National Heart, Lung, and Blood Institute. *Thrombocytopenia* (Accessed January 2021): nhlbi.nih.gov/health-topics/thrombocytopenia.

16 Yannaki E, Locatelli F, Kulozik AE, et al. Poster EP1494: Betibeglogene autotemcel (LentiGlobin for β -thalassemia) in patients with transfusion-dependent β -thalassemia and β^0/β^+ , β^+ IVS1-110/ β^+ IVS1-110, or β^0/β^+ IVS1-110 genotypes: updated results from the HGB-212 study. EHA Library 6/12/20 (Accessed January 2021): <https://library.ehaweb.org>.

17 Porter JB, Thompson AA, Walters MC, et al. Oral Presentation S296: Improvement in erythropoiesis in patients with transfusion-dependent β -thalassemia following treatment with betibeglogene autotemcel (LentiGlobin for β -thalassemia) in the phase 3 HGB-207 study. EHA25 Meeting 2020. (Accessed January 2021): <https://eha25-eha.web.ingrd.com>.

18 Decision Resources Group (accessed September 2020; registration required): insights.decisionresourcesgroup.com.

NARSOPLIMAB

Product:

Narsoplimab

Indication:

Hematopoietic stem cell transplant-associated thrombotic microangiopathy (HSCT-TMA)

Estimated FDA approval:

July 2021

Therapeutic class:

Monoclonal antibody targeting mannose-binding lectin-associated serine proteases

Route of administration:

Intravenous (IV) infusion

FDA designations:

Orphan, Breakthrough

Manufacturer:

Omeros Corporation

Condition:

HSCT-TMA is a life-threatening complication of stem cell transplants. It is caused by endothelial cell damage triggered by regimens used to prepare a patient for the procedure, immunosuppressants, and infection. It is most common in allogeneic transplants in which the cells come from a donor. Approximately 25,000 to 30,000 allogeneic transplants are performed in the United States and Europe every year. An estimated 40% of these experience HSCT-TMA. Mortality can exceed 90% in severe cases.

Role in treatment:

Narsoplimab would be the first FDA-approved therapy for this condition. Current treatment options include supportive care or alteration of immunosuppressive regimens. Soliris® (eculizumab injection; Alexion) is used off-label.¹⁹

Efficacy:

Narsoplimab was evaluated in a clinical trial in patients with severe HSCT-TMA and at high risk of death. The goal was to determine if using narsoplimab would increase the proportion of patients who achieved a set of response criteria, including improvements in laboratory markers and clinical status. Positive results found 65% of patients treated for at least four weeks of therapy were complete responders. The 100-day survival rate was 68% for all individuals treated with narsoplimab and 93% for complete responders.

Safety:

Safety and adverse events were similar to what is commonly seen in individuals who received a stem cell transplant, including nausea, vomiting, diarrhea, low potassium levels, decreased white blood cells, and fever.

Financial impact:

Although the product is expected to have a high cost, it is unlikely to have a major impact on overall drug spend due to the rarity of the condition.

IngenioRx view:

Narsoplimab would be the first FDA-approved treatment for HSCT-TMA. There is data to suggest that narsoplimab may improve the survival rate for patients receiving stem cell transplants.

¹⁹ Rosenthal J. Hematopoietic cell transplantation-associated thrombotic microangiopathy: a review of pathophysiology, diagnosis, and treatment. *J Blood Med.* 2016;7:181-186. Published 2016 Sep 2. doi:10.2147/JBM.S102235.

In addition to the treatments listed previously, there are other important drugs and biologics scheduled to receive FDA approval within the next 18 months.

**** Key:**

IM: intramuscular

IV: intravenous

SC: subcutaneous

Rolling submission: when a drug company submits completed sections of its application for review instead of waiting until every section of the application is completed; decision date is assigned when the application is complete



Orphan drug/rare disease; expected to be high cost, but with minimal impact to overall drug/medical spend due to low utilization



Potential to significantly increase overall drug/medical spend



New entrant into high spend/trending category



No significant impact to incremental spend based on initial analysis

Other significant product approvals

We expect these products to reach the market in 2021.*

Drug or biologic manufacturer	Indication/route**	Place in therapy	Estimated approval date	Impact on overall drug spend
Tralokinumab AstraZeneca	Atopic dermatitis/SC	Addition to class: would compete with Dupixent®	April 2021	
Fosdenopterin BridgeBio	Molybdenum cofactor deficiency type A/IV	First in class: would be first FDA-approved treatment for this indication	04/11/2021	
Abrocitinib Pfizer	Atopic dermatitis/oral	Addition to class: would be first oral janus kinase inhibitor for treatment of atopic dermatitis; would compete with Dupixent®	04/30/2021	
Pegcetacoplan Apellis	Paroxysmal nocturnal hemoglobinuria/SC	Addition to class: would compete with Soliris®	05/14/2021	
Relugolix Myovant	Uterine fibroids/oral	Addition to class: second GnRH antagonist approved for uterine fibroids; will compete with Oriahnn™; filing as a combination tablet with estradiol and norethindrone acetate	06/01/2021	
Bimekizumab UCB	Plaque psoriasis/SC	Addition to class: IL-17 inhibitor will compete with other biologics	July 2021	

* As of January 12, 2021.



Other significant product approvals (continued)

Drug or biologic manufacturer	Indication/route**	Place in therapy	Estimated approval date	Impact on overall drug spend
Teplizumab Provention Bio	Type 1 diabetes mellitus prevention or delay/IV	First in class: would be first FDA-approved therapy for prevention or delay of diabetes; potential safety issues	07/02/2021	
Avacopan ChemoCentryx	Anti-neutrophil cytoplasmic antibody-associated vasculitis/oral	Addition to class: would be first antibody complement 5a receptor inhibitor for this indication; will compete with prednisone	07/07/2021	
Narsoplimab Omeros Corporation	Hematopoietic stem cell transplant-associated thrombotic microangiopathy/IV	Addition to class: would be first FDA-approved treatment for this indication	07/17/2021	
Vosoritide BioMarin	Achondroplasia/SC	First in class: would be first FDA-approved treatment for this indication	08/21/2021	
Maralixibat Mirum	Alagille syndrome/oral	First in class: would be first FDA-approved treatment for this indication	2021 (rolling submission)	
Zynteglo®/ LentiGlobin™ (betibeglogene autotemcel) bluebird bio	Beta thalassemia/IV	First in class: would be first gene therapy approved for treatment of beta thalassemia	2021 (rolling submission)	

Analysis: update on the biosimilar landscape

A biosimilar is a biologic that is highly related to a U.S. Food and Drug Administration (FDA)-approved reference product in terms of structure and function. It also lacks clinically meaningful differences in terms of safety and efficacy.²⁰

Reports suggest that biosimilar use over the next five years may save over \$100B in U.S. sales, an almost five-fold increase in savings over the past five years.²¹ Cost savings due to biosimilars have been slow to emerge due to litigation and lack of interchangeability, causing delays in products reaching the market.

There are currently FDA-approved biosimilars for nine biologics. While biosimilars for 7 of the 9 biologics have launched, none are considered interchangeable or automatically substitutable by a pharmacist. Only one manufacturer is pursuing interchangeable status of a biosimilar, Cytelzo® (adalimumab), with a launch expected in 2023.^{22, 23, 24}

Biosimilar approvals

Brand name	Brand manufacturer	Biosimilar name	Biosimilar manufacturer	FDA approval	Launched
Enbrel	Amgen	Erelzi	Sandoz	8/30/16	No
		Eticovo	Samsung	4/25/19	No
Humira	Abbvie	Amjevita	Amgen	9/23/16	No
		Hadlima	Samsung, Merck	7/23/19	No
		Cyltezo	Boehringer Ingelheim	8/25/17	No
		Hulio	Fujifilm, Mylan	7/6/20	No
		Hyrimoz	Sandoz	10/30/18	No
		Abrilada	Pfizer	11/15/19	No

Pharmacy



20 U.S. Food & Drug Administration. *Biosimilar and Interchangeable Products* (Accessed January 2021); [fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products#generic](https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products#generic).

21 IQVIA Institute. *Biosimilars in the United States 2020–2024* (Accessed January 2021); [iqvia.com](https://www.iqvia.com).

22 Boehringer Ingelheim. *Boehringer Ingelheim announces resolution of Cyltezo® patent litigation* (May 14, 2019); [boehringer-ingelheim.us/](https://www.boehringer-ingelheim.us/).

23 U.S. Food & Drug Administration. *Biosimilar Product Information* (December 17, 2020); [fda.gov/drugs/biosimilars/biosimilar-product-information](https://www.fda.gov/drugs/biosimilars/biosimilar-product-information).

24 Regulatory Affairs Professionals Society, *Regulatory Focus*. *US Biosimilar Launches About to Turn a Corner* (March 16, 2020); [raps.org](https://www.raps.org).

Biosimilar approvals (continued)

Brand name	Brand manufacturer	Biosimilar name	Biosimilar manufacturer	FDA approval	Launched
Neupogen	Amgen	Granix	Teva	08/29/12	Yes
		Zarxio	Sandoz	03/06/15	Yes
		Nivestym	Hospira, Pfizer	07/20/18	Yes
Remicade	Janssen	Inflectra	Celltrion, Pfizer	04/05/16	Yes
		Renflexis	Samsung, Merck	04/21/17	Yes
		Avsola	Amgen	12/06/19	Yes
		Ixifi PF	Pfizer	12/13/17	No
Neulasta	Amgen	Fulphila	Mylan, Biocon	06/04/18	Yes
		Udenyca	Coherus	11/02/18	Yes
		Ziextenzo	Sandoz	11/04/19	Yes
		Nyvepria	Hospira, Pfizer	6/10/20	Yes
Epogen/Procrit	Amgen	Retacrit	Hospira, Pfizer	05/15/18	Yes
Avastin	Genentech, Roche	Mvasi	Amgen, Allergan	09/14/17	Yes
		Zirabev	Pfizer	6/27/19	Yes
Herceptin	Roche, Genentech	Kanjinti	Amgen, Allergan	09/14/17	Yes
		Ogivri	Mylan, Biocon	12/1/17	Yes
		Trazimera	Pfizer	3/11/19	Yes
		Herzuma	Celltrion, Teva	12/14/18	Yes
		Ontruzant	Samsung, Merck	1/18/19	Yes
Rituxan	Roche, Biogen, Genentech	Truxima	Celltrion, Teva	11/18/18	Yes
		Ruxience	Pfizer	7/23/19	Yes
		Riabni	Amgen	12/17/20	Yes

Medical

Sources:

U.S. Food & Drug Administration. *Biosimilar Product Information* (December 17, 2020): [fda.gov/drugs/biosimilars/biosimilar-product-information](https://www.fda.gov/drugs/biosimilars/biosimilar-product-information).

Regulatory Affairs Professionals Society, Regulatory Focus. US Biosimilar Launches About to Turn a Corner (March 16, 2020): [raps.org](https://www.raps.org).

25 Biosimilars Review & Report. Biosimilar approval status (Updated January 18, 2021): [biosimilarsrr.com](https://www.biosimilarsrr.com).

26 AbbVie. *AbbVie Here. Now. 2019 Annual Report on Form 10-K* (Accessed January 2021): <https://investors.abbvie.com>.

What can we expect when it comes to biosimilars?



Biosimilar pipeline –

There are approximately 108 additional biosimilars in development across 22 molecules, with at least six expected to gain FDA approval through 2021.^{21, 25}



Biosimilar anticipated for top-selling biologic, Humira –

With \$14.8B in U.S. sales in 2019, a potential launch of an interchangeable Humira biosimilar, Cytelzo, in 2023 may generate sizeable savings. Current price discounts for biosimilars vary but appear to offer an average discount of approximately 30%.^{21, 26} The market presence of various biosimilars for a single molecule may lead to competition and lower costs.^{21, 26}



Future biosimilars for insulins –

The FDA recently announced that insulins would be redefined as biologics. This enables them to go through a regulatory pathway that will better facilitate the development and serve as reference products for biosimilars.

Therapy market trends

1. The Centers for Disease Control and Prevention (CDC) recommends pre-exposure prophylaxis (PrEP) as a prevention strategy for human immunodeficiency virus (HIV) infection. Reports from clinical trials demonstrate that a consistent daily PrEP regimen may reduce the risk of contracting HIV from sex by approximately 2% to 3%.^{27,28} While an estimated 200,000 individuals in the U.S. use a PrEP regimen,²⁹ the eligible population that could benefit may be much higher. Descovy® and Truvada® are the only two FDA-approved medications for PrEP in individuals not infected with HIV. Current guidelines do not prefer one of these treatments over the other. Descovy costs approximately \$22K per year and is not available as a generic.³⁰ Truvada recently became available generically and offers a therapeutically comparable and cost-effective option with substantial savings to individuals and to the healthcare system. An injectable antiretroviral option for this indication that would be dosed every two months may be approved in the next couple of years. This could be an alternative for individuals who are not compliant with daily oral therapy.

2. In the United States, 12% of the population suffers from migraines. Recent FDA approvals have provided novel alternatives to current therapies. Global sales for the migraine market are expected to grow 14% annually through 2028.³¹ Approved therapies continue to grow as they seek expanded indications for pediatric patients, as well as broader labels to include treatment and prevention of migraines. Development of new molecular entities and reformulations on the horizon will also contribute to growth in this category.³²

27 Baeten JM, Donnell D, Ndase P, et al. Partners PrEP Study Team. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012 Aug 2; 367(5):399-410.

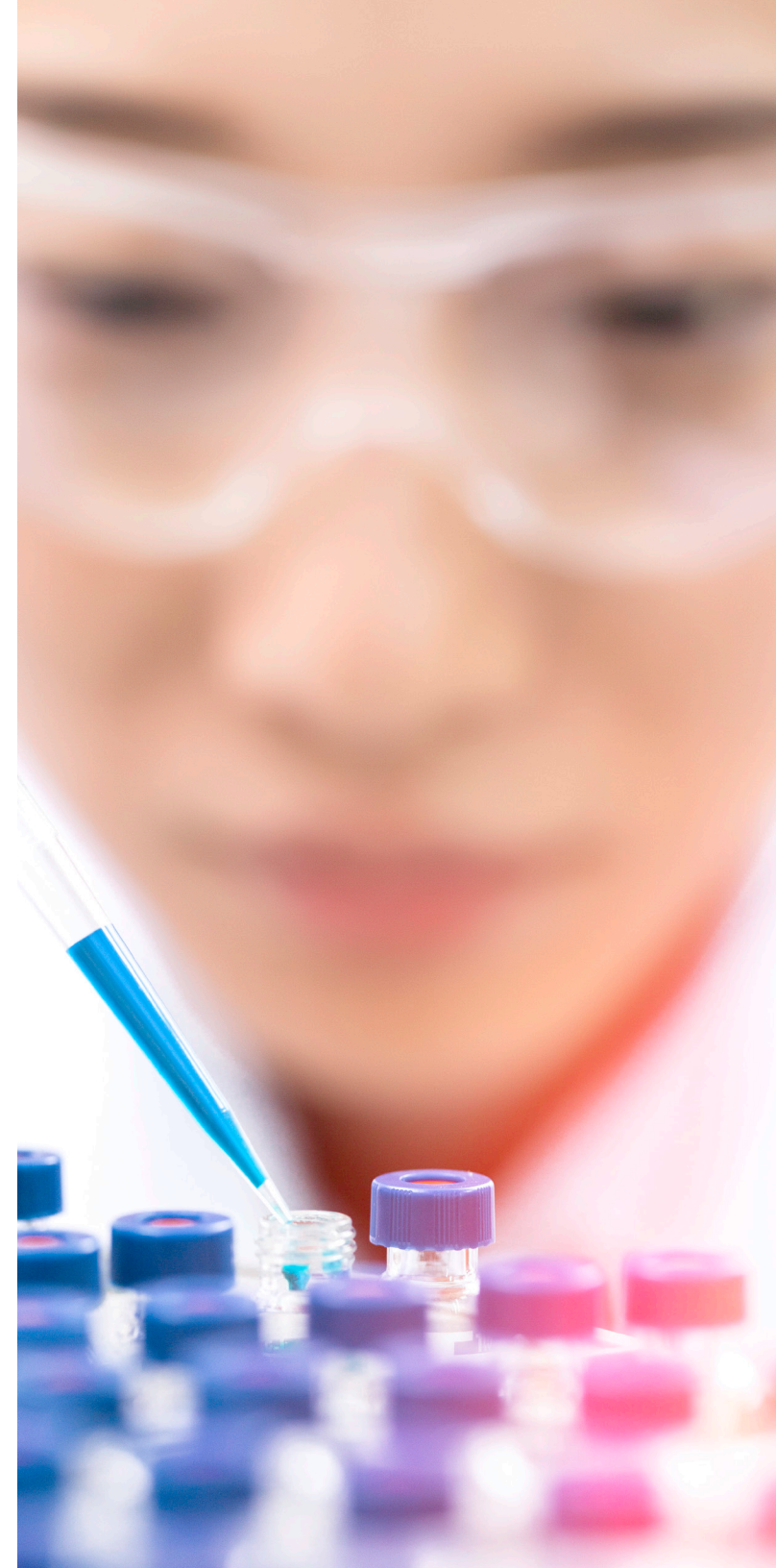
28 Grant RM, Lama JR, Anderson PL, et al for the iPrEx Study Team. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010 Dec 30; 363(27):2587-99.

29 PrEPWatch. *United States* (Accessed January 2021): prepwatch.org.

30 Wolters Kluwer. *Medispan Database* (Accessed January 2021): walterskluwer.com.

31 Decision Resources Group website: insights.decisionresourcesgroup.com (accessed November 2020; registration required)

32 Migraine Research Foundation. *About Migraine* (Accessed January 2021): migraineresearchfoundation.org.



Update on atopic dermatitis

The rapidly expanding atopic dermatitis pipeline

Atopic dermatitis (AD), the most common type of eczema, is an inflammatory skin disease that causes red, itchy, and sometimes painful rashes.³³ Disease severity ranges from mild, isolated flare-ups to severe, widespread disease that can significantly affect a patient's quality of life, including their ability to sleep.

Biologics have transformed the treatment space for several inflammatory diseases, like psoriasis and rheumatoid arthritis. The biopharma industry has similarly set its sights on AD. With a handful of late-stage agents in development, Dupixent®, the only biologic currently FDA-approved for patients 6 years of age and older with AD, will likely face competitors in the first half of 2021.

Prevalence of AD: Beginning as early as infancy for some, AD affects approximately 10% to 20% of children and 5% to 10% of adults.³⁴ Overall, 1 in 10 Americans are diagnosed with AD.³⁵

AD treatments: Topical steroids and emollients are the backbone of treatment for AD.³⁶ For mild disease, these agents are often used in combination with other topicals such as tacrolimus ointment, pimecrolimus cream, or Eucrisa® ointment.

When topicals are inappropriate or do not adequately control symptoms, patients may add on phototherapy and systemic agents.³⁷ Until the approval of Dupixent, systemic therapies were limited to off-label immunosuppressants such as cyclosporine, azathioprine, methotrexate, and oral steroids.

AD pipeline: With potential expansion in patients with AD as young as 6 months of age, Dupixent may continue to pave the way for biologic treatments for moderate-to-severe AD. Competitors in phase 3 development or higher are summarized in the table on the following pages.

33 National Institutes of Health. *Atopic dermatitis* (Accessed January 2021): niams.nih.gov.

34 U.S. National Library of Medicine. *Atopic dermatitis* (Accessed January 2021): medlineplus.gov.

35 American Academy of Dermatology Association. *Eczema Types: Atopic Dermatitis Overview* (Accessed January 2021): aad.org.

36 Eichenfield L, Tom W, Berger T, et al. Guidelines of care for the management of atopic dermatitis. Section 2: Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. Published Online May 7, 2014.

37 Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014 Aug; 71(2):327-49.



Key:**AD:** atopic dermatitis**JAK:** janus kinase inhibitor**SC:** subcutaneous injection**IL:** interleukin**Dupixent** is an IL-4/IL-13 inhibitor administered SC every 2 weeks

Update on atopic dermatitis (continued)

Drug or biologic manufacturer	Route/target	Place in therapy	Estimated approval (phase of development)
Dupixent competitors			
Abrocitinib Pfizer	Oral/JAK inhibitor	Competing to be first oral, once-daily JAK inhibitor; seeking approval in patients 12 and older	April 2021 (submitted)
Rinvoq™ (upadacitinib) AbbVie	Oral/JAK inhibitor	Competing to be first oral, once-daily JAK inhibitor; seeking approval in patients 12 and older; currently FDA-approved for select adults with rheumatoid arthritis	April 2021 (submitted)
Olumiant® (baricitinib) Eli Lilly	Oral/JAK inhibitor	Competing to be first oral, once-daily JAK inhibitor; seeking approval in adults; currently FDA-approved for select adults with rheumatoid arthritis	2021 (submitted)
Tralokinumab AstraZeneca	SC/IL-13 inhibitor	Would be first selective IL-13 inhibitor; seeking approval in adults; administered every 2 weeks with potential every 4 weeks maintenance dosing in select patients	April 2021 (submitted)
Lebrikizumab Dermira	SC/IL-13 inhibitor	Would be second selective IL-13 inhibitor; seeking approval in patients 12 and older; administered every 2 weeks with potential every 4 weeks maintenance dosing in select patients	2022 (phase 3)
Nemolizumab Galderma	SC/IL-31 inhibitor	Would be first IL-31 inhibitor; seeking approval in patients 12 and older; every 4 weeks injection	2022+ (phase 3)





Update on atopic dermatitis (continued)

Drug or biologic manufacturer	Route/target	Place in therapy	Estimated approval (phase of development)
Topical competitors			
IDP-124 (pimecrolimus) Bausch Health Companies	Topical/calcineurin inhibitor	Would be first lotion formulation; would compete with generically available topical calcineurin inhibitors, tacrolimus ointment, and pimecrolimus cream	Late 2021 to 2022 (phase 3)
Ruxolitinib Incyte	Topical/JAK inhibitor	Would be first topical JAK inhibitor; seeking approval in patients 12 and older with mild-to-moderate AD	June 2021 (submitted)

Sources:

Silverberg JI, Pinter A, Pulka G, et al. Phase 2B randomized study of nemolizumab in adults with moderate-to-severe atopic dermatitis and severe pruritus. *J Allergy Clin Immunol* 2020 Jan; 145(1):173-182.

Silverberg JI, Simpson EL, Thyssen JP, et al. Efficacy and Safety of Abrocitinib in Patients With Moderate-to-Severe Atopic Dermatitis: A Randomized Clinical Trial. *JAMA Dermatol* 2020; 156(8):863-873.

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The future of AD treatments: Four agents have been submitted to the FDA with potential approval in 2021, with others on the horizon. Three are janus kinase (JAK) inhibitors competing to be the first oral, once-daily option, providing a dosing advantage compared to Dupixent, a subcutaneous injection given every other week. While efficacy may appear similar to Dupixent, differences in safety profiles may curb enthusiasm and reduce uptake. JAK inhibitors seeking approval for AD will likely carry the same class warning as currently approved JAK inhibitors for rheumatoid arthritis, a black box warning for serious infections, malignancy, and thrombosis. With uncertainties regarding safety, the oral JAK inhibitors' impact on shifting utilization from Dupixent remains unclear. Similar to what was seen within the treatment landscape for other inflammatory conditions, additional approvals will provide alternatives and inevitably create competition for AD treatments.

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