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# A Standard September Ahead Thanks To Light US FDA User Fee Calendar With Few Expedited Reviews

by Bridget Silverman

Twelve applications with September goal dates include six novel agents but only one breakthrough designation.

The most unusual aspect of the dozen applications with September 2023 goal dates at the US FDA is how unusual they aren't. Standard reviews are the rule, even for the lone breakthrough therapy-designated NDA.

Six novel agents are among the September goal dates, along with four 505(b)(2) NDAs. A new formulation and a significant new indication round out the PDUFA calendar. (*See table at the end of the story for details on each application*.)

*Novo Nordisk A/S*'s small interfering RNA therapy nedosiran holds the only breakthrough therapy designation in the group, awarded in July 2019 for patients with primary hyperoxaluria. The drug was the centerpiece of Novo's 2021 acquisition of *Dicerna Pharmaceuticals, Inc.*. (Also see "*RNAi Returns To Spotlight As Novo Nordisk Swoops For Dicerna*" - Scrip, 18 Nov, 2021.)

*Alnylam Pharmaceuticals Inc.*'s Oxlumo (lumasiran) beat nedosiran to market thanks to a 6 October 2022 approval for primary hyperoxaluria type 1. Nedosiran, however, holds the potential for a broader label.

## Itching And Sweating Relief

*Eli Lilly and Company* has *Sanofi*'s commercial behemoth Dupixent (dupilimumab) in its sights as the company's lebrikizumab approaches an FDA decision for treatment of moderate to severe atopic dermatitis.

Lilly paid $1.1bn for *Dermira Inc.* in 2020 to get access to lebrikizumab, an interleukin-13

inhibitor being developed for inflammation and immunology conditions. Lebrikizumab has the potential for maintenance dosing every four weeks, while IL-13 and IL-4 inhibitor Dupixent is dosed every other week for atopic dermatitis.

In addition to the dosing advantage, Lilly has noted that lebrikizumab showed an effect on itching that could differentiate it on the market. (Also see "*Lilly's Paying $1.1bn For Itch Advantage With Dermira's Lebrikizumab*" - Scrip, 10 Jan, 2020.)

Dupixent, of course, continues to seek new indications. Next up is a chronic spontaneous urticaria claim with a 22 October goal date.

A direct competitor to another former Dermira product, *Journey Medical Corp.*'s Qbrexza (glycopyrronium), is up for FDA approval in primary axillary hyperhidrosis, or excessive underarm sweating, in September. The goal date for Botanix's sofpironium bromide is likely near the end of the month.

Like Qbrexza, *Botanix Pharmaceuticals Limited*'s sofpironium bromide is an anticholinergic. But while Qbrexza is provided as medicated cloths, sofpironium bromide topical gel 15% is delivered by a "patented applicator similar to a roll on commonly used in antiperspirants," the company said. (Also see "*Keeping Track: Orphans Headline FDA Approvals; Gene Therapies Stand Out Among Submissions*" - Pink Sheet, 7 Oct, 2022.)

The development of primary axillary hyperhidrosis therapies has been impacted by the FDA's Patient-Focused Drug Development initiative. The International Hyperhidrosis Society convened a patient-focused drug development meeting on all forms of hyperhidrosis in November 2017. (Also see "*Brickell's Phase III Data Sets Up NDA Filing In Axillary Hyperhidrosis*" - Scrip, 7 Oct, 2021.)

Sofpironium's pivotal Cardigan I and II trials used a proprietary validated patient-reported outcome, HDSM-Ax score, as the primary endpoint.

## Tecentriq Is Up For Enhanze-ment

*Halozyme Therapeutics, Inc.*'s Enhanze technology is marching through mature monoclonal antibody blockbusters, turning IV products into subcutaneous formulations that require much shorter administration time. The next could be *Roche Holding AG*'s anti-PD-(L)1 antibody Tecentriq (atezolizumab), with a 15 September user fee goal date for a subcutaneous formulation using the Enhanze platform.

Halozyme's Enhanze technology is based on recombinant human hyaluronidase (rHuPH20). The enzyme temporarily increases the permeability of the tissue under the skin. For Tecentriq, the subcutaneous formulation can be administered in seven minutes, compared with 30-60 minutes

for the approved IV infusion.

Roche has been one of the most energetic of Halozyme's customers. The company markets Phesgo (pertuzumab, trastuzumab and hyaluronidase-zzxf), Herceptin Hylecta (trastuzumab and hyaluronidase-oysk) and Rituxan Hycela (rituximab and hyaluronidase [human, recombinant]).

Tecentriq SC recently won its first regulatory nod in the UK for all indications in which IV Tecentriq has been approved. (Also see "*Roche's Seven-Minute Tecentriq Jab Wins First Ever Regulatory Approval*" - Pink Sheet, 29 Aug, 2023.)

If approved in the US, Tecentriq would be the first PD-1/L1 inhibitor to add subcutaneous administration, but development is underway for subcutaneous formulations of *Merck & Co., Inc.*'s Keytruda (pembrolizumab) and *Bristol Myers Squibb Company*'s Opdivo (nivolumab).

## Mixing It Up In Hematology

*GSK plc* is awaiting the 16 September goal date for its novel myelofibrosis candidate momelotinib, a JAK1/2 and ACVR1/ALK2 inhibitor.

The momelotinib NDA is based on the Phase III MOMENTUM trial, which compared the new drug with danazol in symptomatic and anaemic subjects who have previously received an approved Janus kinase inhibitor therapy for myelofibrosis.

European Union action on an MAA for momelotinib is expected by year-end.

The Isreali biopharma *BioLineRx Ltd.* is seeking an indication for stem cell mobilization for autologous bone marrow transplantation for multiple myeloma patients for its selective CXCR4 chemokine receptor inhibitor Aphexda (motixafortide).

On a 30 August 2023 earnings call, BioLineRx CEO Philip Serlin said the drug was "on track" for its 9 September goal date.

The company has emphasized the high success rate in the Phase III GENESIS study, highlighting the approximately 90% of patients who went directly to transplantation after mobilizing the optimal number of stem cells following a single motixafortide administration and G-CSF and one apheresis session. In the placebo arm, which received G-CSF alone, less than 10% of patients met that standard. (Also see "*Keeping Track: Terliprez, Sotyktu Keep Up US FDA's Novel Approvals Pace; Submissions By Pfizer, Chiesi And BioLineRx*" - Pink Sheet, 16 Sep, 2022.)

## Busy Days For UCB

*UCB S.A.* is expecting FDA action on two applications by the time the end of September closes out the third quarter, but only one of them is scheduled.

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UCB's zilucoplan, a second generation subcutaneous C5 inhibitor, would be offer the "first and only self-administration" for myasthemia gravis. Zilucoplan was designed for at-home administration as a daily injection.

Zilucoplan would be UCB's second novel agent for myasthenia gravis in a year. The FcRn-targeting antibody Rystiggo (rozanolixizumab-noli) cleared the FDA on 26 June for adults with generalized myasthenia gravis (gMG) who are anti-acetycholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive. (Also see "*UCB's Rystiggo Becomes Second FcRn Inhibitor Treatment For gMG*" - Scrip, 28 Jun, 2023.)

"Zilucoplan provides an option for patients who prefer a quick, self-administered daily injection at home as opposed to the more cyclical treatment routine of Rystiggo," the company explained.

The company's long-pending Bimzelx (bimekizumab), an IL-17A and IL-17F inhibitor for moderate to severe plaque psoriasis, could also see an FDA decision. UCB has been predicting action in the third quarter 2023 after a missed first cycle goal date due to COVID-19 and a second cycle that likely had a May 2023 goal date, but has not seen a decision since a facility inspection was carried out in April 2023.

On UCB's 27 July earnings call, Executive Vice-President and Chief Medical Officer Iris Loew-Friedrich confirmed "that there has been no extension of the PDUFA date and that we currently do not have an action date by FDA."

"Our estimate of the third quarter action that we have shared with you is based on our knowledge and experience of the process and the dynamics of the interaction with the agency," she said.

If approved by the FDA, "you can imagine that we have the supplemental biologics license applications for psoriatic arthritis and axSpA and now also HS [hidradenitis suppurativa] sitting ready," Loew-Friedrich commented. "We currently believe that the fastest path for these indications to be approved in the US is to submit them immediately after or shortly after the approval of the original biologics license application for psoriasis."

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