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Upcoming events – Portola approval and headache data from Lilly

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Welcome to your weekly digest of approaching regulatory and clinical readouts. By August 17 Portola could get its first ever FDA approval, for andexanet alfa, which it is looking to become the first universal factor Xa inhibitor antidote; a nod could attract a buyer.

Meanwhile Lilly expects results of a galcanezumab study in chronic cluster headaches before the end of the year, followed by data in episodic headaches in 2017. This project is also being tested in the competitive migraine space, but could become the first anti-CGRP antibody marketed for cluster headaches.

First to market

Portola's andexanet alfa, now branded Andexxa, gained breakthrough therapy designation in 2013 and received orphan drug status last year. It directly reverses the effects of factor Xa inhibitors in patients who suffer an uncontrolled bleed or who require emergency surgery.

It reversed the anticoagulant activity of Eliquis and Xarelto in two small phase III trials in healthy volunteers *(Portola and Boehringer lead bleeding antidote charge, June 23, 2015).*

An ongoing phase IV study called Annexa-4 is testing it in patients receiving Eliquis, Xarelto, Lixiana or enoxaparin – a heparin and indirect factor Xa inhibitor. It is looking to recruit 270 patients who present with an acute major bleed, and interim data are expected at the ESC Congress on August 30.

The BLA filing included efficacy and safety data from initial patients enrolled in Annexa-4, and Portola plans to file in Europe in the third quarter.

Use of factor Xa inhibitors such as Xarelto has been limited by the lack of available reversal agents. A dose of vitamin K can reduce warfarin's blood-thinning action, which alongside cost has kept use of the old drug popular in spite of its safety drawbacks. Andexxa's approval could boost the factor Xa space – analysts currently forecast sales of these products to grow 14% a year to reach $15.1bn in 2022.

Since its 2013 float Portola is up 59%. Andexxa is its lead asset, and 2022 sales are forecast to reach $864m, according to *EvaluatePharma* sellside consensus. Of this forecast $129m is from partnering outside the US; Bristol-Myers Squibb and Pfizer have rights in Japan.

Targeting CGRP

Lilly's galcanezumab, also known as LY2951742, is an anti-calcitonin gene-related peptide (CGRP) monoclonal antibody. Its two phase III trials are recruiting 162 patients each, one in subjects with chronic cluster headache and the other episodic disease, comparing activity against placebo on the primary measure of change in headache frequency.

In the chronic and episodic trials galcanezumab is given subcutaneously every 30 days, for 12 weeks and 8 weeks respectively. The chronic trial should read out first.

Cluster headaches involve severe pain in one side of the head, and bouts separated by a remission period of one month or more are classified as episodic; those separated by under a month, or present for at least 12 months without remission, which account for 20-30% of cases, are called chronic.

Galcanezumab is also being tested in migraine, last year meeting the primary endpoint in a phase IIb episodic study. The migraine space is pretty crowded, with antibodies targeting CGRP including Alder's ALDR403, Teva's TEV-48125 and Amgen/Novartis's erenumab *(Marginal migraine benefit puts Amgen and Novartis in pole position, June 9, 2016).*

However, Lilly looks like it could be first in cluster headaches, with potential submission next year. According to *EvaluatePharma* consensus 2022 sales could reach $484m.

The group's oral anti-CGRP project will enter human studies by the end of the year, but with the oral class previously linked to liver toxicities safety will be closely watched.

Study setting	Trial ID
Episodic	NCT02397473
Chronic	NCT02438826

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