Evaluate Vantage

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Upcoming events – Rare disease decisions for Ultragenyx and GW

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Welcome to your weekly digest of approaching regulatory and clinical readouts. Ultragenyx's burosumab is due a US approval decision in the US by April 17. It was green-lit in Europe for young patients with a rare form of rickets, but the company is looking at a broader population in the US, including adults, where it is on shakier ground.

Two days later GW Pharmaceuticals' Epidiolex will go before an FDA panel. The cannabinoid project performed well in two rare forms of childhood epilepsy, and the panel will likely concentrate on safety as there could be concerns over the use of this type of product in children.

Across the pond

Ultragenyx's burosumab received a positive verdict from the European Medicines Agency in February in children and adolescents with X-linked hypophosphataemia. The rare condition, also known as vitamin D-resistant rickets, is characterised by low blood levels of phosphorus that lead to bowed or bent legs, short stature, bone pain and severe dental pain.

The approval of burosumab, tradenamed Crysvita in Europe, is conditional on the outcome of three ongoing studies, whose results are to be submitted by 2020. While the EMA green light is encouraging, in the US Ultragenyx is also seeking approval in adults, where phase III data were mixed.

The US filing includes two phase II trials in children and one phase III study in adults. The adult trial hit its primary endpoint, achieving serum phosphorus levels above the lower limit of normal versus placebo, but missed an important secondary measure looking at pain, something the regulators might scrutinise *(Ultragenyx bounces back, but painful questions remain, April 19, 2017).*

Burosumab is forecast to be Ultragenyx's biggest growth driver, with sales expected to reach $892 by 2022, according to sellside consensus from *EvaluatePharma.* $652m of the total is assigned to its originator, Kyowa Hakko Kirin, and the rest to Ultragenyx under the groups' 2013 co-development/co-promotion deal.

The MAb could be a moneyspinner for Ultragenyx in another way: it has rare paediatric disease designation from the FDA so the company could receive a priority review voucher if burosumab is approved. Ultragenyx sold its first voucher, which it received for the Sly syndrome therapy Mepsevii, to Novartis for $130m.

Study detail	Trial ID
134 adults with X-linked hypophosphataemia	NCT02526160

GW's panel date

GW's Epidiolex is an oral cannabidiol being tested as an adjunct therapy to treat seizures associated with Dravet and Lennox-Gastaut syndrome, two rare forms of childhood epilepsy in which resistance to anti-epileptic drugs is common.

An advisory committee will meet on April 19, and the PDUFA is set for June 27. It is likely the adcom will concentrate on safety, as there could be concerns about the use of cannabinoids in children.

DEA scheduling on Epidiolex's abuse potential should happen within 90 days of approval. The company's first cannabinoid product, Sativex, which is approved outside the US to treat spasticity in adult patients with multiple sclerosis, was designated schedule IV in the UK, indicating low abuse potential.

Epidiolex performed well in two phase III trials in Lennox-Gastaut and one phase III study in Dravet, significantly reducing the frequency of seizures versus placebo. The most common adverse events included somnolence, diarrhoea and decreased appetite *(GW defies Brexit blues with second epilepsy win, June 27, 2016).*

Epidiolex is expected to be GW's biggest growth driver, with 2022 consensus sales forecast to reach $1.6bn. Lennox and Dravet make up $293m and $114m of the forecasts respectively, with analysts assigning the majority to the wider indication of drug-resistant epilepsy, including possible off-label use in refractory paediatric patients.

The asset is unpartnered, but the company, long rumoured as an acquisition target, is now worth over $3bn and has £414.8m ($559.2m) in cash, which according to Leerink analysts should be sufficient to launch Epidiolex. The drug also has a rare paediatric disease designation, so again a potentially valuable priority review voucher could be in the offing.

Study	Indication	Trial ID
GWPCARE1	Dravet syndrome (120 patients)	NCT02091375
GWPCARE4	Lennox-Gastaut syndrome (171 patients)	NCT02224690
GWPCARE3	Lennox-Gastaut syndrome (225 patients)	NCT02224560

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