

## Upcoming events - Avadel takes on Jazz and Axovant awaits early results



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**Data will soon show whether Avadel's FT218 is more convenient than Jazz's Xyrem, while Axovant will be looking for a dose response with its Parkinson's gene therapy.**

Welcome to your weekly roundup of approaching clinical readouts. Data due in the second quarter will see whether Avadel's FT218 can take on the leading narcolepsy drug from Jazz Pharmaceuticals. Avadel's project is a once-nightly formulation of sodium oxybate, the same ingredient in Jazz's Xyrem and the Xyrem follow-on JZP-258.

Both of Jazz's drugs need to be taken twice nightly, so any improvement on administration, alongside comparable efficacy and safety, could give Avadel a boost.

Avadel's placebo-controlled [Rest-On study](#) has enrolled 212 narcolepsy patients aged 16 and older. They start on 4.5g, with titration up to 9.0g, given once nightly, and can continue to use stimulants at stable doses. The co-primary endpoints measure changes in excessive daytime sleepiness and cataplexy.

Looking at what FT218 is up against, in one of Xyrem's trials patients taking 9g had a [median reduction of 16 cataplexy attacks from baseline, versus four for placebo](#) ( $p=0.0016$ ). In another study patients taking 9g saw a significant median reduction of five points on the Epworth sleepiness scale, versus 0.5 points for placebo.

Xyrem has a black box warning for respiratory depression, and its potential for misuse means that it has a restricted REMS programme. Despite the restrictions Xyrem is the market leader in narcolepsy, but 2023 will see generic competition, and sales are forecast to drop from a peak of \$1.7bn this year to \$709m by 2024, according to *EvaluatePharma's* consensus.

Jazz's low-sodium follow-on project JZP-258 will pick up some of the slack, with sales forecast to reach \$329m by 2024. JZP-258 was filed last month, and [has shown comparable efficacy to Xyrem](#). Worryingly, two patients in JZP-258's randomised withdrawal study had serious adverse events deemed to be treatment related. If FT218 can show a safety advantage this could be highly positive, but how likely this is, given that it is essentially a reformulation of Jazz's product, is debatable.

FT218 is being developed under the abbreviated 505(b)2 pathway, so just the one phase III study is needed. Ultimately Avadel needs to get it in place before Xyrem generics hit, and to price FT218 accordingly.

## Axovant ups the dose

Further data on Axovant's Parkinson's disease gene therapy AXO-Lenti-PD, which aims to raise production of dopamine, are expected this month or next. Axovant [licensed AXO-Lenti-PD from Oxford Biomedica for \\$30m in 2018](#). the therapy is said to be tenfold more potent than Oxford's Prosavin, which disappointed in the clinic.

Six-month results from the second cohort of the [Sunrise-PD](#) trial will concern just two patients, each on a dose of  $1.4 \times 10^7$  transducing units, some threefold higher than that given to the first cohort, in whom encouraging, albeit early, data, have been reported.

The two patients [in cohort 1 showed an average 22-point change](#) from baseline in motor function as assessed by "off" score at 12 months, representing a 37% improvement. Earlier six-month data showed an average 17-point change from baseline, or 29% improvement. Investors will be looking for a clear dose-response with the second cohort.

In terms of the competition Voyager's VY-AADC is slightly ahead of Axovant's project. Across three cohorts VY-AADC has shown a [12 to 16-point change from baseline in "off" score](#), with three-year data from a [phase Ib](#) study due later this year. Voyager also has an ongoing phase II study, [Restore-1](#), in 42 patients.

According to *EvaluatePharma* the sellside forecasts 2024 sales of \$396m for AXO-Lenti-PD, but the disparity between analyst numbers is wide.

### Selected phase I/II gene therapies in Parkinson's disease

Product	Company	Mechanism	2024e indication sales (\$m)	Notes
AXO-Lenti-PD	Axovant Gene Therapies/ Oxford Biomedica	Aromatic-L-amino-acid decarboxylase gene transference; tyrosine hydroxylase gene therapy	396	Cohort 2 data from <a href="#">Sunrise-PD</a> due Q1; cohort 3 will test $4.2 \times 10^7$ TUs; Axovant to start sham-controlled part of the study this year
AAV-GAD	Meiragtx	Glutamic acid decarboxylase gene transference	48	<a href="#">Phase II data</a> reported, but few details on path forward
VY-AADC/NB1b-1817	Voyager/ Neurocrine Biosciences	Aromatic-L-amino-acid decarboxylase gene transference	43	Three-year data from <a href="#">PD-1101</a> and two-year results from <a href="#">PD-1102</a> (posterior delivery) due this year; phase II <a href="#">Restore-1</a> study has a primary completion in Dec 2020
PR001	Prevail Therapeutics/ Regenxbio	Delivers the <i>GBA1</i> gene, which encodes beta-glucocerebrosidase	-	<a href="#">Trial in Parkinson's disease with GBA1 mutation</a> started in Oct 2019 (NCT04127578)

Source: *EvaluatePharma*.