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Roivant May Take On AbbVie In Uveitis With Strong Phase II Efficacy

by Joseph Haas

Roivant's brepocitinib bests data Humira previously posted in non-infectious uveitis, a top cause of blindness. The TYK2/JAK1 inhibitor also is in Phase III for dermatomyositis.

Roivant Sciences Ltd. said it is poised to take on *AbbVie Inc.*'s Humira in non-infectious uveitis, a leading cause of blindness, after reporting Phase II data showing that brepocitinib met its primary endpoint in a trial design that the company intended to set a higher bar for efficacy than AbbVie met in its pivotal trials. With the successful data in hand, the company also announced 2 April a $1.5bn share buyback program involving reacquiring all equity held by *Sumitomo Pharma Co., Ltd.*

Roivant subsidiary *Priovant Therapeutics* is developing brepocitinib, a dual TYK2/JAK1 inhibitor, specifically for non-anterior NIU, a subset within the global NIU patient base, estimated at 400,000 overall, with the non-anterior segment comprising between 70,000-100,000 patients, which the company attributed to a *JAMA Ophthalmology* report. Uveitis is the fourth-leading cause of blindness globally, the biotech reported, accounting for 10% of blindness cases in the US. Priovant also has the candidate, licensed from *Pfizer Inc.*, in Phase III for dermatomyositis with data expected in 2025. (Also see "*Roivant Cuts Multiple R&D Programs As It Takes On Pfizer's TYK2/JAK1 Inhibitor*"

Roivant's Matthew Gline On Success, Failure And Finding An R&D Sweet Spot

By Andrew McConaghie

18 Dec 2023
Roivant achieved its greatest-ever success in selling RVT-3101 to Roche for $7.1bn – but not all investors are yet convinced by its unorthodox business model, and will be watching how it re-invests its new windfall.

Read the full article here

- Scrip, 28 Jun, 2022.)

It perceives a blockbuster sales opportunity for brepocitinib in a setting where steroids often are the first-line therapy, while AbbVie's Humira (adalimumab), typically used in second-line therapy, is the only drug with a US Food and Drug Administration label indication for the disease.

"Today is really the beginning of kind of the Roivant/Priovant brepocitinib era," Roivant CEO Matthew Gline told a same-day call, noting that this is the drug's first success in a Phase II study designed and initiated by Priovant. Pfizer began development in both dermatomyositis and in systemic lupus erythematosus before it and Roivant agreed to form Priovant to lead the oral drug's development in inflammation and immunology indications in 2022. Roivant/Priovant shelved development in SLE following a Phase II failure last November that it attributed mainly to a high placebo response. (Also see "*Roivant Won't Continue With Brepocitinib In Lupus After Phase II Failure*" - Scrip, 27 Nov, 2023.)

Key Takeaways

- Roivant's brepocitinib demonstrated strong Phase II efficacy in avoiding treatment failure in non-anterior non-infectious uveitis, a leading cause of blindness.
- The company is positioning the dual TYK2/JAK1 inhibitor for approval in NIU and dermatomyositis after Roivant ended development in lupus following a Phase II failure.
- Roivant also will undertake up to $1.5bn in share buybacks, including reacquiring a large ownership stake from Sumitomo.

In the 26-patient NEPTUNE study in non-infectious uveitis, Priovant randomized patients either to a daily 15mg or 45mg dose of brepocitinib, with no placebo arm. Patients were predosed with prednisone, but then tapered off the steroid entirely six weeks into the study in an effort to avoid any false signals of efficacy, Priovant CEO Ben Zimmer told the call. The higher dose yielded a 29% (5/17) rate of treatment failure at 24 weeks, while the smaller dose had a 44% (4/9) treatment failure rate.

Failure Rate Data Better Factoring Out Discontinuations

Treatment failure rate is a registrational endpoint in NIU that comprises multiple measures of disease activity including ocular inflammation and visual acuity, with a lower rate meaning better efficacy. Roivant noted that when discontinuations were factored out of the 45mg dosing arm, the treatment failure rate due to disease activity was 18%. The study also met multiple secondary endpoints at 24 weeks, including haze grade, visual acuity and macular thickness. Safety and tolerability were consistent with prior studies of brepocitinib.

Zimmer said the NEPTUNE efficacy data is significantly greater than that seen for Humira in its pivotal studies for NIU. In addition, Priovant designed the study to measure quickness of effect and tapered steroid therapy much sooner than the AbbVie studies, which ended concomitant steroid therapy at 15 weeks and measured treatment failure at 25 weeks, he noted.

"The study generated the strongest data that's been generated to date in any study on the registrational endpoint in NIU and we also had great results on a number of important secondary endpoints," Zimmer said. "We achieved these results in spite of an aggressive six-week steroid taper, which involves pulling patients off 60mg per day of steroids, [with patients] completely off prednisone more than twice as quickly as in precedent studies."

Roivant/Priovant are discussing Phase III plans with the FDA, with a goal of initiating a pivotal study during the second half of 2024, the exec said.

Leerink Partners analyst David Risinger called the data "extremely impressive" in a 2 April note, pointing out that a treatment failure rate lower than 70% with the 45mg dose would have been considered successful. "Results compare very favorably to Humira's Phase III NIU trial, which Roivant notes showed a 62% week 25 treatment failure rate among 110 patients with a slower steroid taper," he added.

Cantor Fitzgerald analyst Louise Chen called the efficacy data about twice-as-good as that of Humira, and better than expected by the Street in a same-day note. Positive but less impressed was Truist analyst Robyn Karnauskas who pointed out that the Phase II study lacked placebo control and enrolled a small number of patients. Still, Karnauskas said in her 2 April analysis that brepocitinib could bring in $1bn in sales if approved for both dermatomyositis and NIU.

Wolfe Research analyst Andy Chen increased brepocitinib's likelihood of approval in NIU from 50% to 65% and raised his global sales projection in that indication from $150m to $600m.

Roivant/Priovant management told the investor call that the drug could yield multi-billion-dollar revenue in NIU, noting that there is nothing in Phase III development for the disease and limited potential competition in Phase II.

Buying Out Sumitomo For $648m

Gline explained the $1.5bn share buyback as a way to help clarify its capital allocation and financial return strategies and also provide liquidity to Sumitomo, which has a complex relationship with Roivant dating back to 2019 when the Japanese pharma acquired five Roivant subsidiaries and conglomerated them into *Sumitovant Biopharma Ltd.* (Also see "*Gene Therapy 'Vant' Unveiled As Dainippon, Roivant Finalize $3bn Deal*" - Scrip, 6 Nov, 2019.)

Overall, Roivant will buy back up to $1.5bn of its stock, utilizing some of its $6.7bn in cash,

which ballooned after it sold subsidiary Televant and TLA1 antibody RVT-3101, seen as a potential best-in-class therapy for inflammatory bowel disease indications, to *Roche Holding AG* for $7.1bn up front last fall. (Also see "*Roche Makes Play For Bowel Disease Leadership With $7.1bn Roivant Deal*" - Scrip, 23 Oct, 2023.)

“We have the flexibility to think very carefully about our capital,” Gline told the call. “We have the tools in our toolkit to do what we need to do yesterday, today and tomorrow.”

The arrangement with Sumitomo will reacquire the Japanese firm’s entire ownership stake for an estimated $648m and reduce shares outstanding by 9%, Roivant said. Shareholders showed some enthusiasm for the twin announcements, as Roivant’s share price finished the 2 April trading day up nearly 5% to $10.92 a share.