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Protagonist Falls 50% On PN-943 Ulcerative Colitis Missed Endpoint

Queensland's Protagonist fell 49.95 percent to $US9.41 ($A13.12) on news that its 159-patient phase II trial of PN-943 for ulcerative colitis missed its primary endpoint.

Protagonist has traded as high as $US50.54 in July 2021, but has had several recent set-backs, including a US Food and Drug Administration hold on its rusfertide or PTG-300 for cancer, which was later lifted (BD: Sep 20, Oct 13, 2021).

Last week, Protagonist said the FDA intended to rescind breakthrough status for rusfertide for poly-cythaemia vera due to "observed malignancies" (BD: Apr 19, 2022).

Today, the company said the randomized, double-blinded, placebo-controlled, 'Ideal' phase II study missed its primary endpoint.

Protagonist said the study, to evaluate the safety and efficacy of PN-943 in patients with moderate-to-severe active ulcerative colitis found the 450mg dose "did not meet the … primary endpoint" of remission at week-12 compared to placebo; but the 150mg dose achieved a placebo versus treatment delta [or difference] of 13 percent ($p = 0.08$) in the modified intent-to-treat group, and a delta of 16 percent ($p = 0.04$) in the bio-naïve group.

The company said that the 150mg data "showed strong concordance across multiple parameters including statistically significant histological remission and endoscopic improvement".

Protagonist said that patients were randomized to either twice daily doses of 450mg or 150mg PN-943, or placebo, for 12 weeks and analyzed for outcome measures.

The company said that PN-943 achieved 27.5 percent clinical remission, with “strong concordance across all key proxies including histological and endoscopic endpoints for efficacy, in the twice daily 150mg dose arm”.

The company said that plans were underway for a registrational phase III study using a twice daily 150mg dose of PN-943, pending regulatory guidance.

Protagonist chief executive officer Dr Dinesh Patel said the company was “delighted with the strength of the results from the Ideal study and look forward to working with the regulatory agencies as we prepare for a phase III registrational program for PN-943 in moderate-to-severe ulcerative colitis”.

“Our oral, gut-restricted alpha-4-beta-7-integrin antagonist agent PN-943 has demonstrated clinical efficacy on par with the approved injectable antibody drug working through the same biological target,” Dr Patel said.

“We believe the results of the Ideal study may be paradigm-shifting and of broad scientific relevance in understanding [irritable bowel disease] pathogenesis and gut-restricted drug development via intervention of the integrin-MAdCAM pathway,” Dr Patel said.

“Based on its convenience of oral administration and the favorable efficacy and safety results observed to date, we believe that PN-943 has the potential to become a first-in-class, foundational oral medicine for individuals living with moderate-to-severe ulcerative colitis,” Dr Patel said.

Protagonist head of gastro-enterology Dr Scott Plevy said the study assessed two doses of PN-943, 150mg and 450mg twice daily, and showed “a very clear and consistent treatment effect at the lower 150mg [twice daily] dose across key endpoints”.

“The dose response demonstrated by this study is consistent with several other modalities in the integrin pathway,” Dr Plevy said. “The findings in the lower-dose arm provide consistent evidence of clinical efficacy and safety, and clear direction on the dosing regimen for the phase III registrational program.”

In 2016, the University of Queensland spin-out Protagonist said it raised $US90 million ($A117.1 million) and listed on the Nasdaq to develop peptide drugs (BD: Aug 12, 2016).

On the Nasdaq last night, Protagonist fell $US9.39 or 49.95 percent to $US9.41 ($A13.12) with 8.0 million shares traded.