

## Worm turns on Coronado as Crohn's disease trial fails



[Jonathan Gardner](#)

Coronado Biosciences investors must believe today that that the strategy of modulating immune response using parasite eggs was a pig in a poke. Readout of the phase II Trust-1 trial of *Trichuris suis* eggs in Crohn's disease failed to reduce disease activity, although executives offered hopeful consolation that the project appeared to be effective in treating more severe patients.

Shares plummeted by two thirds to \$1.91 on the news yesterday, a destruction of shareholder value that will have bullish sellside analysts tearing up price targets that were as high as \$24 in August. The Massachusetts group's backup asset is a phase II cancer immunotherapy, an area of oncology that has raised its profile but is still a risky proposition.

### Whipworm eggs over, easy

Trust-1 tested *Trichuris suis* ova (TSO), or the eggs of the pig whipworm, against placebo in 220 moderately to severely ill patients, trying to detect a 100-point decline in the Crohn's disease activity index. Coronado only disclosed that TSO failed to achieve the primary endpoint, but did not say how badly it missed; the company blamed a better-than-expected improvement in the placebo arm.

A pre-defined analysis of severely ill patients, those scoring between 290 and 450 on the Crohn's index, showed a non-significant improvement over placebo. In a call with investors, chief executive Harlan Weisman said the subgroup had not been powered to detect significant differences, suggesting that data-mining would serve as justification to continue trials in the severe population.

A second trial called Trust-2 run by European partner Dr Falk Pharma is under way in patients with a score of 220-350. The difference is that patients in the European trial will not be allowed to take background immunosuppressants, and multiple doses will be used, raising the possibility that efficacy could be detected when the German collaborator discloses data, which could happen very soon.

No matter what, should Coronado forge ahead in clinical development with the therapy it seems likely that more phase II work needs to be conducted, either in the sicker Crohn's disease patients or at a more effective dose. With \$100m in cash at September 30, Coronado is certainly in a position to soldier on with TSO, though some investors might not be keen to hear this.

### Where next?

Coronado had acquired the immunotherapy with the buyout of Asphelia Pharmaceuticals in 2011. The hypothesis behind using the pathogen was to stimulate an immunomodulatory reaction that would blunt the action of the overactive T-helper 1 cells that fuel autoimmune conditions like Crohn's disease.

Helminths like *Trichuris suis* stimulate T-helper 2 cells, which can downregulate T-helper-1 activity. The species was chosen for research because it is not a human pathogen, does not multiply nor is spread by contact in humans, and is cleared spontaneously.

Analysts admitted it was difficult to value the company, but this did not stop them trying; Oppenheimer's Boris Peaker applied a comparative methodology, using "comparable" companies such as hepatitis C specialist Achillion Pharmaceuticals and cancer company Oncolytics Biotech when he initiated coverage of the company in 2012. In August, Mr Peaker had a \$12 price target on Coronado - half of the exuberant, bubble-inflated goal set by Roth analyst Joseph Pantginis.

Of course, failure in Crohn's disease does little to validate the effectiveness of the approach, and with trials under way in ulcerative colitis, plaque psoriasis and autism spectrum disorders, the group could be throwing good money after bad.

Scrapping the project does not leave it with promising options. The second-string product is CNDO-109, a natural-killer (NK) cell activator that US regulators have designated an orphan drug for acute myeloid leukaemia. A Phase I/II trial is due to report later this year.

Cancer immunotherapies have improved their profile of late, with work in the programmed death pathway. However, analysts from Summer Street Research Partners, in analysing the value of Coronado in the event of a TSO failure, wrote last month that the NK strategy “reminds us of the previous failed work with other immune cell therapies” and called it “a financial drain with little chance of success”.

The Trust-1 results scrambled the helminth egg therapy, but unfortunately for some shareholders the results were not decisive enough for Coronado to call time. Given glimmers of efficacy, the executive team has incentive to persist rather than looking for more promising uses for its healthy cash pile.

<b>Trial</b>	<b>Setting</b>	<b>ID</b>
Trust-1	Single dose of TSO in moderate to severe Crohn's disease patients	NCT01576471
Trust-2	Three doses of TSO in moderate Crohn's disease patients	NCT01279577

To contact the writer of this story email Jonathan Gardner in London at [jonathang@epvantage.com](mailto:jonathang@epvantage.com) or follow [@JonEPVantage](https://twitter.com/JonEPVantage) on Twitter