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THE BERNSTEIN REPORT

ON BIOBUSINESS

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Product Development

A more subtle shock

While anti-TNF drugs have revolutionized the inflammatory/autoimmune space, their activity is not subtle. CBio Ltd. is following what it hopes will be a more nuanced approach with its lead compound, Chaperonin 10 (Cpn10). Last week, data from a Phase IIa trial published in *The Lancet* showed the compound reduced disease activity scores in rheumatoid arthritis patients.

Cpn10 (XToll) is a naturally occurring member of the heat-shock protein family (Hsp10) that elevates anti-inflammatory cytokines. It also interacts with activated toll-like receptors (TLRs) to reduce the production of pro-inflammatory cytokines and chemokines. "Cpn10 downregulates the inflammatory cytokines, such as TNF alpha, and upregulates anti-inflammatory cytokines, such as interleukin-10," said Richard Willis, VP of business development at CBio (Brisbane, Australia).

The compound has been shown to interact with TLR2, TLR4, TLR7 and TLR9, although its exact mechanism of action is not known. But according to CBio, unlike existing TNF drugs, Cpn10 does not eliminate pro-inflammatory cytokines from the body completely. Instead, it brings the activated innate immune system back to normal levels.

"We have a very broad effect that doesn't knock out any part of the immune system," said CEO Wolf Hanisch. "Cpn10 turns down the volume on an over-activated immune response, instead of wiping it out."

Completely removing production of TNFs has been shown to have adverse effects, including increased infections and certain cancers, he noted. "A certain level of production of TNF is important to the maintenance of an intact immune surveillance network."

The *Lancet* data are from a double-blind Australian Phase IIa study in 23 patients with moderate to severe RA. The primary endpoint of disease activity score (DAS28) significantly im-

proved by day 14 versus baseline in all groups (5 mg: $p=0.0449$; 7.5 mg: $p=0.0126$; and 10 mg: $p=0.0182$) and continued to improve through day 84. In three out of 23 patients, clinical remission was achieved by the end of the study.

Patients received intravenous Cpn10 twice weekly for 12 weeks. There was no evidence of a difference in DAS28 response between the three groups ($p=0.1538$). The company said the compound was probably dosed too low and that the doses were bunched together too closely.

DAS28 measures include tenderness and swelling in 28 joints. The index is similar to the ACR log scale score, which is primarily used in the U.S.

The company measured ACR as a secondary endpoint. Other secondary endpoints included tender and swollen joint counts, mean duration of morning joint stiffness and physician and patient assessment of overall disease activity. All secondary endpoints improved from baseline to day 14 and

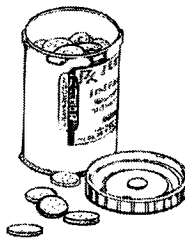
continued to show improvement across the study period to day 84.

"When we compared the ACR responder rate data from one-arm trials of marketed RA drugs like Remicade, Enbrel and Humira, Cpn10 clearly had a faster onset and much greater efficacy," said Willis. "Only 10% of the patients achieved ACR70 with the competitors, while Cpn10 achieved 30% efficacy."

The company plans to start Phase IIb testing in about 1,000 RA patients in early 2007. CBio also has completed Phase IIa safety studies in multiple sclerosis (MS) and psoriasis. Data will be published by year end, according to the company.

CBio plans to conduct studies in additional autoimmune and inflammatory indications, including ulcerative colitis (UC) and Crohn's disease. The company has an exclusive worldwide license to Cpn10 from the University of Queensland.

— Urooj Muftaba



This week's briefing

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