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Equillium tell: Fast track for itolizumab shows FDA faith that CD6 targeter could hit mark in lupus nephritis

By Randy Osborne, Staff Writer

Shares of Equillium Inc. (NASDAQ:EQ) closed at $4.75, up 69 cents, or 17%, after trading as high as $5.25 as Wall Street hailed the FDA's granting of fast track status to itolizumab – the first clinical-stage anti-CD6 therapy – for the treatment of lupus nephritis (LN).

CD6, a tightly regulated co-stimulatory receptor, is expressed on T effector cells but not on those of the regulatory type, noted Equillium's chief scientific officer, Stephen Connelly, whose firm Equillium has benefited from research on CD6 as well as its ligand, ALCAM. La Jolla, Calif.-based Equillium acquired rights to itolizumab through an exclusive partnership with Biocon Ltd., of Bangalore, India. "We're able to modulate not just the activity of these T cells but the trafficking of those T cells into the organs," he told *BioWorld*. Activated T effector cells are known to drive immuno-inflammatory diseases across therapeutic areas that include transplant science, systemic autoimmunity, pulmonary, neurologic, gastrointestinal, renal, vascular, ophthalmic and dermatologic disorders.

In September, Equillium started the phase Ib study called Equalise with itolizumab, also known as EQ-001, in patients with lupus and LN. The trial has two cohorts: type A is open-label and will treat patients with systemic lupus erythematosus for four weeks; type B is a double-blind, placebo-controlled cohort in patients with active proliferative LN for 12 weeks.

Along with Equalise, Equillium has itolizumab in a phase Ib/II trial dubbed Equate, which in March began testing its mettle in acute graft-vs.-host disease. First data are expected in the second half of next year. There's also the phase Ib Equip study, launched in June, trying the compound against uncontrolled moderate to severe asthma.

Krishna Polu, chief medical officer, commenting on the Equate trial, noted that transplants in the U.S. are largely done in academic centers, which are "very slow at getting activated. Now, with more centers on board, we're seeing an uptick in the number of patients that are coming through on screening," he said. The phase Ib portion of the study is enrolling more severe patients and the phase II less severe ones. As for Equip, it's "going well" in Australia and New Zealand, he said. "We knew that we could move a lot faster in those countries from a regulatory process perspective. All the centers there are quite experienced," and researchers face less competition for enrollees. The study is signing up "all types of uncontrolled asthma patients. Those clinical criteria tend to enrich for patients who have very high levels of CD6-prominent T cells that are a prominent part of the biology," he said, and the experiment is not excluding patients based on eosinophil thresholds.

The Equalise push in lupus has "gone off very quickly," Polu said. The study is focused on LN but also dosing and studying non-nephritis disease to enable what amounts to "an active control, as we evaluate a set of biomarkers from a personalized medicine approach." The effort also may turn up differences in pharmacokinetics among nephritis vs. non-nephritis patients. "A key strategy for this program is to think about a patient-selection approach" that will allow the most efficient evaluation. "In early development, we're going to study all patients. As we keep going, if what we see is a differential response, then we can stratify with that biomarker diagnostic." That the drug might work in all patients seems a long shot, "given the heterogeneity of the disease," he said. "That's the journey that we're starting."

Down the road, Equillium may probe itolizumab combinations in autoimmune disease, using the drug with other compounds or sequentially. He cited research exploring Rituxan (rituximab, Roche Holding AG / Biogen Inc.) followed by Benlysta (belimumab, Glaxosmithkline plc). "I think that's where the puck is going," he said. "We're going to get there."

Itolizumab has already been approved for psoriasis in India and launched under the trade name Alzumab. Biocon generated positive clinical data across multiple late-stage trials, and Alzumab has been available since 2013. "While Biocon is not actively promoting the drug because it has only been made available in an infusion-based formulation, resulting in negligible sales in India, Equillium aims to deploy itolizumab in a far more convenient subcutaneous injection format," Wainwright analyst Raghuram Selvaraju pointed out in a July report. He started coverage of the company with a buy rating and a $14

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price target. The firm is pursuing "a differentiated take on the underlying cause of autoimmunity and inflammation in various chronic diseases, which could allow the company to assume a leadership position in targeting conditions driven by effector T cells and neutrophils," in his view.

In October 2018, Equillium priced its IPO of about 4.6 million shares at $14 each, for gross proceeds of about $65.4 million. Selvaraju said the decline in share price since the company went public "does not reflect the company's fundamentals. In particular, we note that Equillium has not generated any negative data with itolizumab, and that there have not been any contextual clinical failures in the space that would have impacted itolizumab's positioning or likelihood of success. Rather, we believe the stock came under pressure due to the downturn in the markets that occurred in late 2018 and has not yet recovered because the company has yet to report top-line data" from its experiments.

Earlier this month, the Lupus Foundation of America cheered a "monumental breakthrough" in lupus kidney disease after Victoria, British Columbia-based Aurinia Pharmaceuticals Inc. disclosed positive efficacy and safety results from its pivotal Aurora phase III trial of voclosporin in combination with mycophenolate and low-dose corticosteroids for LN. The global study enrolled 357 patients with active LN and met its primary endpoint of renal response rates of 40.8% for voclosporin vs. 22.5% for the control. Voclosporin is a calcineurin inhibitor with clinical data in more than 2,600 patients across indications, Aurinia said.