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Novartis Phase III Study Shows ACZ885 Helped Substantially Reduce Steroid Use in 45% of Patients With Serious Form of Childhood Arthritis

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- - Chronic steroid use to treat the symptoms of systemic juvenile idiopathic arthritis (SJIA) can contribute to slowed growth and delayed puberty[2],[3]
- - The new pivotal Phase III data also showed SJIA patients treated with ACZ885 were nearly three times less likely to suffer a new flare vs. placebo[1]
- - ACZ885 regulatory submissions on track for 2012 in SJIA, a rare, disabling and potentially fatal auto-inflammatory disease, with spiking fever and arthritic pain[2],[4]

EAST HANOVER, N.J., Nov. 7, 2011 /PRNewswire/ -- Novartis announced today new pivotal Phase III data showing 45% of children with active systemic juvenile idiopathic arthritis (SJIA) were able to substantially reduce their use of oral corticosteroids (often described as steroids) within 28 weeks of commencing treatment with ACZ885 (canakinumab) ($p<0.0001$)[1].

The results of the study, which met both primary endpoints, will be presented on November 9th at the American College of Rheumatology's (ACR) Annual Scientific Meeting in Chicago, US[1].

"The treatment of SJIA is a challenge given our current treatment options. Despite our best efforts, optimal disease control is often times elusive. We still must use steroids in the treatment of these children with SJIA. Steroids help manage many SJIA symptoms, such as fever and inflammation, but doctors try to minimize their use because of the potential negative impact on bones and growth," said Daniel Lovell, M.D., one of the study investigators and Professor of Pediatrics at the Cincinnati Children's Hospital Medical Center. "These data are exciting because they show that patients on ACZ885 were able to reduce their steroid use, and also experienced excellent disease control."

In addition, patients with SJIA on ACZ885 were nearly three times (0.37 hazard ratio) less likely to suffer a new flare. Therefore, only 27% of ACZ885-treated patients experienced a new flare, vs. 75% of patients on placebo during the study ($p=0.0043$)[1].

Data from this trial supports the safety and efficacy profile of ACZ885 in the study population. These results, along with data from a second pivotal study, are planned to form the basis for worldwide regulatory submissions in 2012. Side effects observed in this study were similar to those already seen for ACZ885's approved indication, including infections and neutropenia[1]. In addition, cases of macrophage activation syndrome (MAS) were reported in this study[1].

"These data demonstrate the significant benefits that ACZ885 may provide this young population, both in steroid reduction and in extending the period these children can live free from SJIA flares," said David Epstein, Head of the Pharmaceuticals Division of Novartis. "Novartis is committed to helping improve the health of patients with SJIA and other inflammatory diseases, which is why we are delighted to be sharing these results."

ACZ885 is an investigational fully human monoclonal antibody which neutralizes the key inflammatory

mediator, interleukin-1 beta (IL-1 beta), which plays an important role in a number of diseases including SJIA[5].

The incidence of SJIA is estimated to be less than 1 in 100,000 children[6]. It is called 'systemic' because the inflammation affects the whole body, as well as most of the joints[4]. The condition is characterized by potentially life-long, recurrent and painful arthritis flares, skin rashes and daily spiking fevers[2],[4].

Novartis is also presenting a number of other studies at ACR, including a second pivotal Phase III trial of ACZ885 in SJIA, which was previously presented at the 2011 European Pediatric Rheumatology Congress in Bruges, Belgium, in September.

About the Study

The Phase III, two-part study had an open-label, single-arm active treatment in Part I followed by a randomized, double-blind, placebo-controlled, event-driven withdrawal design in Part II[1]. A total of 177 patients between the ages of 1 and 19 years with active SJIA were enrolled in the study[1]. In Part I, patients received a subcutaneous (s.c.) dose of ACZ885 (4 mg/kg, up to 300 mg) every 4 weeks. After 8 weeks, patients who met the adapted ACR Pediatric 30 criteria began tapering (reducing) their steroid use until either: a) the dose had been decreased to less than or equal to 0.5 mg/kg[7] while maintaining the adapted ACR Pediatric 30 Criteria (successful tapering of steroids); or b) a maximum of 20 weeks passed without reaching this goal (unsuccessful tapering of steroids)[1]. In Part II of the study, patients were randomized to either continue receiving ACZ885, or to receive placebo every 4 weeks, until a pre-specified number (37) of flare-events ("flares") had occurred[1].

The primary endpoints were to: a) assess if ACZ885 allows tapering of steroids in at least 25% of SJIA patients (Part I); and b) demonstrate that time to next flare is extended with ACZ885 vs. placebo (Part II)[1].

In Part I of the study (representing 58 patient years), 138 of 177 patients (78%) reported an adverse event (AE), with the most common being nasopharyngitis, headache and cough. Serious adverse events (SAEs) were reported in 15 patients, with the most common being infections, MAS (four cases) or flare-associated events[1]. Five SAEs led to discontinuation, and one patient died of MAS[1]. During Part II, AEs (the most common being arthralgia, cough, nasopharyngitis and pyrexia) were reported by 40 of 50 (80%) ACZ885-treated patients (vs. 35 of 50 [70%] placebo patients previously treated with ACZ885)[1]; and six patients in each arm experienced one or more SAE, which mainly included infections, MAS and flare-associated events[1]. Six patients, all in the placebo arm, discontinued the study due to AEs or SAEs during Part II[1]. One patient died from MAS after study discontinuation in the placebo group.

MAS is a potentially fatal condition known to be associated with SJIA and is characterized by liver abnormalities, bleeding disorders, central nervous system dysfunction and multiple organ failure[4]. Approximately 10% of SJIA patients are diagnosed with MAS, some of whom suffer repeated episodes[4].

About ACZ885

ACZ885 is a fully human monoclonal antibody that inhibits IL-1 beta, which is an important part of the body's immune system defenses. Excessive production of IL-1 beta plays a major role in certain inflammatory diseases, including SJIA[5]. ACZ885 works by neutralizing IL-1 beta for a sustained period of time, therefore inhibiting inflammation.

ACZ885 is currently approved in the US and other countries for a different disease state.

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The foregoing release contains forward-looking statements that can be identified by terminology such as "can," "on track," "potentially," "will," "planned," "may," "committed," "potential," or similar expressions, or by express or implied discussions regarding potential new indications or labeling for ACZ885 or regarding potential future revenues from ACZ885. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with ACZ885 to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that ACZ885 will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that ACZ885 will achieve any particular levels of revenue in the future. In particular, management's expectations regarding ACZ885 could be affected by, among other things, unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; competition in general; government, industry and general public pricing pressures; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; unexpected manufacturing issues, the impact that the foregoing factors could have on the values attributed to the Novartis Group's assets and liabilities as recorded in the Group's consolidated balance sheet, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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References

1. ACZ885 G2305 SJIA presentation (both G2305 and G2301) Brunner H, Ruperto N, Horneff G, et al. Efficacy and safety of canakinumab, a fully human anti-interleukin-1beta antibody, in active systemic juvenile idiopathic arthritis: Results from two Phase III studies. Presented on 9 November: The 2011 ACR Annual Scientific Meeting; November 5-9, 2011, Chicago, US. 2011.
2. Woo P. Systemic juvenile idiopathic arthritis: diagnosis, management, and outcome. Nat Clin Pract

Rheumatol 2006; 2(1):28-34
3. Bailey KM, McDonagh JE, Prieur AM. Systemic juvenile idiopathic arthritis presenting in a young child with long term disability as an adolescent. Ann Rheum Dis 2004; 63(12):1544-8.
4. Mellins ED, Macaubas C, Grom AA. Pathogenesis of systemic juvenile idiopathic arthritis: some answers, more questions. Nat Rev Rheumatol 2011; 7(7):416-26.
5. Church LD, Cook GP, McDermott MF. Primer: inflammasomes and interleukin 1beta in inflammatory disorders. Nat Clin Pract Rheumatol 2008; 4(1):34-42.
6. Ramanan AV, Grom AA. Does systemic-onset juvenile idiopathic arthritis belong under juvenile idiopathic arthritis? Rheumatology (Oxford) 2005; 44(11):1350-3.
7. Novartis data on file. Abrams K, Dimitrov-Kuhl M, Doerr T et al. Clinical Study Protocol (CACZ885G2301): beta-SPECIFIC 2: Study of Pediatric EffiCacy wIth FIrst-line use of Canakinumab [A randomized, double-blind, placebo controlled, withdrawal study of flare prevention of canakinumab (ACZ885) in patients with Systemic Juvenile Idiopathic Arthritis (SJIA) and active systemic manifestations]. 23 May 2011.

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