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## **ACZ885 Phase III data show rapid, sustained clinical remission in children and adults suffering from a group of rare, potentially life-threatening autoinflammatory diseases**

- *Patients with rare autoinflammatory syndromes achieved remission after a single ACZ885 dose – treatment needed only every two months to maintain response<sup>1</sup>*
- *ACZ885 demonstrated potential to rapidly control Systemic Juvenile Idiopathic Arthritis, the most severe form of arthritis in children<sup>2</sup>*
- *Orphan drug status granted to ACZ885 in the EU and US, filing on track in the EU and US*
- *Studies of ACZ885 currently under way in rheumatoid arthritis and gout using an innovative tailored approach with biomarkers*

Basel, October 27, 2008 – New Phase III data demonstrate that ACZ885 (canakinumab), a biological drug in development, achieved rapid and long-lasting clinical remission after just one dose in children and adults with a group of rare but potentially life-threatening autoinflammatory diseases called Cryopyrin-Associated Periodic Syndromes (CAPS)<sup>1</sup>. Due to the long duration of response, patients only needed further treatment every two months<sup>1</sup>.

In addition, preliminary results of a Phase I/II study in Systemic Juvenile Idiopathic Arthritis (SJIA), the most severe form of arthritis in children, showed that most patients treated with ACZ885 achieved substantial clinical improvement within 15 days<sup>2</sup>.

The data, presented at the American College of Rheumatology (ACR) meeting in San Francisco, confirm the potential of ACZ885 to fulfill an unmet medical need in the treatment of autoinflammatory diseases, which can cause life-long debilitating symptoms and potentially fatal complications<sup>3</sup>.

“The results for ACZ885 are exciting for patients and for the medical community,” said Professor Philip Hawkins of the National Amyloidosis Centre at the Royal Free and University College Medical School, London. “Current treatments are not always effective, and are also short-acting and often poorly tolerated by patients. The rapid and long-lasting remission induced by ACZ885 is an important and much-needed development for both children and adults with CAPS.”

The significant findings are based on the selective mechanism of action of ACZ885, a fully human monoclonal antibody. Unlike other agents, ACZ885 solely blocks interleukin-1 $\beta$  (IL-1 $\beta$ ), the form of the interleukin-1 protein that sustains autoinflammatory diseases such as CAPS.

CAPS, including Muckle-Wells Syndrome, are characterized by a single gene mutation that activates excessive production of IL-1 $\beta$ . This leads to symptoms such as fever, fatigue, skin

rash, painful joints and muscles, and severe headache. In addition, patients can suffer from more debilitating complications like hearing loss and amyloidosis, which may lead to accumulations of amyloidosis (a protein) in kidneys causing dialysis or transplantation<sup>3</sup>.

IL-1 $\beta$  is also thought to play a pivotal role in Systemic Juvenile Idiopathic Arthritis (SJIA)<sup>4</sup>, causing symptoms such as destructive arthritis, fever and rash. Suboptimal treatment can lead to growth retardation and joint and bone disability, as well as developmental and social consequences and life-threatening complications such as Macrophage Activated Syndrome, mostly caused by infections and requiring immediate intensive care<sup>4</sup>.

“Children and adults affected by these inflammatory diseases have to cope daily with very distressing and debilitating symptoms,” said Trevor Mundel, MD, Head of Global Development Functions at Novartis Pharma AG. “We are extremely encouraged by these results that highlight the potential of ACZ885 to address the enormous unmet need in patients with these conditions.”

The potential of ACZ885 is reflected in its broad development program. In addition to the studies in CAPS and SJIA, it is also being investigated in more common inflammatory diseases such as rheumatoid arthritis (RA), which affects up to 1% of the world’s population<sup>5</sup>. Studies are currently under way in RA using an innovative tailored approach with biomarkers to predict response to treatment. If successful, these will give suitable patients a personalized approach to the treatment of their disease.

The six-month CAPS clinical trial presented at ACR involved patients aged nine to 74 years old and was divided into three parts. In the first part lasting two months, 35 patients received a single dose of ACZ885 by subcutaneous injection. All but one patient (97.1%) showed a rapid and long-lasting clinical and biochemical response<sup>1</sup>.

After this, 31 patients who maintained their response proceeded to part two, a randomized six-month, double-blind, placebo-controlled withdrawal design study. Patients were treated every two months and if a relapse occurred, they discontinued and entered part three<sup>1</sup>.

Part two of the study included the primary endpoint, a comparison between the number of patients treated every two months with ACZ885 who experienced disease outbreaks or ‘flares’ vs. those on placebo. Results showed that no patients in the ACZ885 group experienced a disease flare compared to 81% (13 out of 15 patients) in the placebo group ( $p < 0.001$ ). Markers of inflammation (C-reactive protein and serum amyloid A) were normalized in patients treated with ACZ885, but increased significantly for those on placebo.

The study is being concluded with a four-month open-label, active-treatment period to provide further efficacy and safety data. All patients are subsequently being offered the chance to take part in an additional Phase III study to provide long-term information about the efficacy and safety of ACZ885.

The most common adverse event reported was upper respiratory tract infection. No deaths or serious adverse events were reported, and there were no discontinuations due to adverse events in the overall study<sup>1</sup>.

Preliminary data from the Phase I/II study in SJIA<sup>2</sup> demonstrated that patients aged four to 19 years treated with ACZ885 achieved substantial clinical improvement (measured by the pediatric ACR50 scale) within 15 days. Importantly, four patients achieved complete remission of the disease, i.e. no arthritis inflammation in joints, no fever, and no disease activity according to the physicians’ assessment<sup>2</sup>.

Orphan drug status has been granted to ACZ885 in the European Union and US for treating CAPS and SJIA, and filing is on track in CAPS in the EU and US. Orphan drugs

are those designed to treat serious or life-threatening diseases affecting fewer than 200,000 people (in the US)<sup>6</sup> or fewer than five out of 10,000 people (in the EU)<sup>7</sup>.

## Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as “may”, “potential”, “potentially”, “can”, “predict”, “will”, or similar expressions, or by express or implied discussions regarding potential future regulatory filings or marketing approvals 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 the Company 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 approved for sale in any market. Nor can there be any guarantee that ACZ885 will achieve any 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; the company’s ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry and general public pricing pressures; the impact that the foregoing factors could have on the values attributed to the 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. Lachmann H.J. et al. Efficacy and Safety of Canakinumab (ACZ885), a Fully Human Anti-Interleukin-1 $\beta$  Antibody, in Cryopyrin Associated Periodic Fever Syndrome: Results of a Multicenter, Randomized, Double-blind, Phase III Study. Poster presentation at ACR Congress, October 27, 2008, San Francisco, California, US.
2. Ruperto, N. et al. ACZ885 (canakinumab), a new IL-1 $\beta$  blocking monoclonal antibody has a beneficial effect in children with Systemic Juvenile Idiopathic Arthritis (SJIA). Oral presentation at ACR Congress, October 29 2008, San Francisco, California, US.
3. <http://www.capscommunity.com/index.html>, last accessed October 21, 2008.  
<http://www.orpha.net/consor/cgi-bin/index.php>, last accessed October 21, 2008.
4. Dinarello C.A. Blocking IL-1 in systemic inflammation. JEM Vol. 201, No. 9, May 2, 2005 1355–1359.
5. Datamonitor Report, 2007.
6. <http://www.fda.gov/orphan>, last accessed October 21, 2008.
7. [http://ec.europa.eu/health/ph\\_threats/non\\_com/rare\\_6\\_en.htm](http://ec.europa.eu/health/ph_threats/non_com/rare_6_en.htm), last accessed October 21, 2008.

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## **Novartis Media Relations**

### **Eric Althoff**

Novartis Global Media Relations  
+41 61 324 7999 (direct)  
+41 79 593 4202 (mobile)  
eric.althoff@novartis.com

### **Irina Ferluga**

Novartis Pharma Communications  
+41 61 324 2422 (direct)  
+41 79 824 1121 (mobile)  
irina.ferluga@novartis.com

e-mail: [media.relations@novartis.com](mailto:media.relations@novartis.com)

## **Novartis Investor Relations**

**Central phone:** +41 61 324 7944

Ruth Metzler-Arnold +41 61 324 9980

Pierre-Michel Bringer +41 61 324 1065

John Gilardi +41 61 324 3018

Thomas Hungerbuehler +41 61 324 8425

Isabella Zinck +41 61 324 7188

### **North America:**

Richard Jarvis +1 212 830 2433

Jill Pozarek +1 212 830 2445

Edwin Valeriano +1 212 830 2456

e-mail: [investor.relations@novartis.com](mailto:investor.relations@novartis.com)

e-mail: [investor.relations@novartis.com](mailto:investor.relations@novartis.com)