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Novartis first IL-17A Phase III results show AIN457 (secukinumab) significantly improves psoriatic arthritis in patients

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- - Secukinumab met primary endpoints demonstrating statistically significant improvements versus placebo in signs and symptoms of active psoriatic arthritis (PsA) in two pivotal Phase III studies
- - FUTURE 1 and FUTURE 2 are the first Phase III studies of a selective IL-17A inhibitor in PsA, a painful, debilitating condition causing inflammation of joints and skin
- - In FUTURE 1, secukinumab patients had significantly less progression of joint structural damage compared to placebo, as evaluated by erosion and joint narrowing scores
- - FUTURE 1 showed majority of secukinumab patients achieving ACR20 responses at Week 24 also maintained the response at Week 52 with continued treatment; inhibition of joint structural damage was also sustained with secukinumab, in exploratory analyses

EAST HANOVER, N.J., Nov. 16, 2014 /PRNewswire/ -- Novartis announced today results from the pivotal Phase III FUTURE 1 and FUTURE 2 studies showing AIN457 (secukinumab) met primary endpoints demonstrating statistically significant improvement of the signs and symptoms of psoriatic arthritis (PsA) versus placebo. PsA is part of a spectrum of long-term diseases impacting joints, known as spondyloarthritis (SpA). There is a high unmet need for new treatment options for patients with PsA and approximately 45% of people are dissatisfied with their treatments. Secukinumab binds to and neutralizes interleukin-17A (IL-17A), which has been shown to play an important role in the development of inflammatory diseases. These results are being presented today at the American College of Rheumatology (ACR) Annual Meeting in Boston.

"We are thrilled to present the Phase III results of secukinumab in psoriatic arthritis, a painful and debilitating condition, with a significant unmet treatment need for patients," said Vasant Narasimhan, Global Head of Development, Novartis Pharmaceuticals. "We are committed to bringing innovative and effective therapies to rheumatology patients, and these important data are expected to form the basis of our regulatory filing submission in psoriatic arthritis planned in 2015."

About the Data at ACR
Statistically significant improvements in signs and symptoms of PsA were achieved with secukinumab versus placebo at Week 24, as measured by a 20% reduction in the American College of Rheumatology (ACR20) response criteria, a standard tool used to assess improvement. Between 50% to 54% of secukinumab patients achieved ACR20 in both FUTURE 1 ($p<0.0001$) and FUTURE 2 ($p<0.0001$). This is in comparison to 17.3% and 15.3% of placebo patients who achieved ACR20, respectively.

Exploratory analyses in FUTURE 1 showed more secukinumab-treated patients in the 75 mg (20.3%) and 150 mg (20.8%) dose groups experienced ACR20 responses by Week 1 versus placebo (5.4%) ($p<0.0001$). In FUTURE 2, more secukinumab-treated patients in the 150 mg (42.0%) and 300 mg (37.0%) dose groups

experienced ACR20 responses by Week 3 (150 mg p<0.0001;300 mg p<0.001) versus placebo (15.3%); secukinumab-treated patients who received the 75 mg (23.2%) dose did not achieve a statistically significant response.

In an additional exploratory analysis in FUTURE 1, a majority of secukinumab-treated patients achieving ACR20 responses at Week 24 also maintained the response at Week 52 with continued treatment. Additional analyses evaluated clinical benefits in patients who had not been previously treated with anti-TNF therapies (anti-TNF naïve) and also in patients who had an inadequate or no response to anti-TNFs. Those who had prior exposure to anti-TNFs included 29.5% (FUTURE 1) and 35.0% (FUTURE 2) of study participants. In FUTURE 1, patients on secukinumab had significantly less progression of joint structural damage compared to placebo, as evaluated by erosion and joint narrowing scores. Improvements in joint damage were shown in both anti-TNF naïve patients and in the patients with inadequate or no response to anti-TNFs. Additionally, secukinumab demonstrated significant improvements in skin psoriasis in both FUTURE 1 and FUTURE 2 compared to placebo.

Secukinumab was well tolerated in both studies, with a safety profile generally consistent with that observed in the psoriasis clinical trial program involving nearly 4,000 patients. In FUTURE 1, the most common adverse events (AEs) were nasopharyngitis, headache, upper respiratory tract infection, hypercholesterolaemia (increased lipid levels), and nausea. In FUTURE 1, 60.4% (75 mg), 64.9% (150 mg) and 58.4% (placebo) of patients reported an AE. Serious adverse event (SAE) rates were 2.5%, 4.5%, and 5.0%, respectively. In FUTURE 2, the most common AEs were upper respiratory tract infection, nasopharyngitis, headache, nausea, diarrhea, and urinary tract infection. In FUTURE 2, 53.8% of patients in the pooled secukinumab group and 58.2% in the placebo group reported an AE. SAE rates were 3.3% and 2.0%, respectively.

"We are encouraged by the results of the FUTURE studies which suggest treatment with secukinumab significantly reduced clinical signs and symptoms of psoriatic arthritis," said Philip Mease, MD, clinical professor at the University of Washington School of Medicine in Seattle, director of the Rheumatology Clinical Research Division of Swedish Medical Center, and an investigator in the secukinumab clinical trial program. "These results add to our growing understanding of psoriatic arthritis and indicate the IL-17 pathway may be a promising target for the treatment of this debilitating disease."

About Secukinumab Psoriatic Arthritis Phase III Trials
FUTURE 1 and FUTURE 2 are multi-center, randomized, placebo-controlled Phase III studies to evaluate the efficacy of IL-17A inhibition with secukinumab in PsA. In FUTURE 1, patients received an intravenous loading dose of 10 mg/kg every two weeks for the first four weeks of treatment, followed by monthly subcutaneous dose of 75 mg or 150 mg compared to placebo. FUTURE 2 patients received a subcutaneous loading dose of 75 mg, 150 mg, or 300 mg of secukinumab every week for the first four weeks of treatment, followed by the same monthly subcutaneous maintenance dose compared to placebo. The intravenous loading period used in FUTURE 1 was designed to provide high systemic exposure for induction of response, in keeping with the initial proof of concept study in PsA with secukinumab. FUTURE 2 utilized an administration route (subcutaneous loading dose) and dose range (up to 300 mg) that is more consistent with the psoriasis program. A combined total of more than 1,000 patients were enrolled in the studies.

Both studies met their primary endpoint of ACR20 at Week 24:

- FUTURE 1, 50.5% for secukinumab 75 mg and 50.0% for secukinumab 150 mg versus 17.3% for placebo; p<0.0001
- FUTURE 2, 29.3% for secukinumab 75 mg (p<0.05); 51.0% and 54.0% for secukinumab 150 mg and 300 mg, respectively, versus 15.3% for placebo; p<0.0001

Full results of secondary endpoints will be presented at ACR. Secondary endpoints at Week 24 in FUTURE 1 and FUTURE 2 included:

- 75% and 90% improvement in Psoriasis Area-and-Severity Index score (PASI 75 and PASI 90)
- Change from baseline in 28-joint Disease Activity Score using C-reactive protein (DAS28 – CRP)
- Physical function assessed using the Medical Outcome Short Form (36) Health Survey physical component summary scores (SF-36 PCS)
- Physical function assessed using the Health Assessment Questionnaire Disability Index (HAQ-DI)
- ACR50 response
- Proportion of subjects with dactylitis and enthesitis
- Overall safety and tolerability of each secukinumab regimen compared with placebo

Additional secondary endpoint at Week 24 in FUTURE 1:

- Radiographic progression assessed using the van der Heijde modified total Sharp score (mTSS)

About Psoriatic Arthritis (PsA)
Closely associated with psoriasis, psoriatic arthritis (PsA) is part of a spectrum of long-term diseases impacting joints, known as spondyloarthritis (SpA), which also includes ankylosing spondylitis (AS); approximately 30% of patients with psoriasis have psoriatic arthritis. It is a debilitating, long-lasting inflammatory disease linked with significant disability, poor quality of life and reduced life expectancy. PsA is associated with joint pain and stiffness, skin and nail psoriasis, swollen toes and fingers, persistent painful tendonitis, and irreversible joint damage. Between 0.3% and 1% of the general population may be affected by PsA and as many as one in four people with psoriasis may have undiagnosed PsA.

About Secukinumab (AIN457)
Secukinumab (AIN457) is a human monoclonal antibody (mAb) that selectively binds to and neutralizes IL-17A. Secukinumab is the first IL-17A inhibitor with positive Phase III results for the treatment of PsA. Research shows IL-17A plays an important role in driving the body's immune response in psoriasis and certain inflammatory arthritic diseases, including PsA.

In addition to PsA, secukinumab is also in clinical trials for the treatment of AS and rheumatoid arthritis (RA). Following the presentation of the first moderate-to-severe plaque psoriasis Phase III results of secukinumab in October 2013, US regulatory filings were submitted at the end of 2013. Joint regulatory applications of secukinumab in PsA and AS are planned to be submitted in 2015.

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The foregoing release contains forward-looking statements that can be identified by words such as "thrilled," "committed," "expected," "planned," "encouraged," "suggest," "indicate," "may," "promising," "will," or similar terms, or by express or implied discussions regarding potential marketing authorizations for AIN457, or regarding potential future revenues from AIN457. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that AIN457 will be submitted in AS or PsA in any market, or approved for any indication, or at any particular time. Nor can there be any guarantee that AIN457 will be commercially successful in the future. In particular, management's expectations regarding AIN457 could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the

company's ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected manufacturing issues, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. 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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