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Novartis AIN457 (secukinumab) showed significant symptom improvement in two pivotal Phase III ankylosing spondylitis studies

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- - Secukinumab is the first selective IL-17A inhibitor to significantly improve signs and symptoms of ankylosing spondylitis (AS) versus placebo in Phase III studies
- - Exploratory analyses showed improvements in AS symptoms with secukinumab were seen at Week 1 and sustained through one year of treatment
- - Up to 40% of AS patients do not respond well to standard of care biologic medicines. Secukinumab is the first non anti-TNF biologic to show significant efficacy in AS patients
- - AS is painful and often progressively debilitating, caused by spine inflammation that can result in irreversible damage reducing patients' mobility and quality of life

EAST HANOVER, N.J., Nov. 15, 2014 /PRNewswire/ -- Novartis announced today results from the MEASURE 1 and MEASURE 2 pivotal Phase III studies of AIN457 (secukinumab) in ankylosing spondylitis (AS). In the studies, secukinumab met the primary endpoint demonstrating statistically significant improvements versus placebo in the signs and symptoms of AS. AS is a common type of spondyloarthritis (SpA), a spectrum of long-term inflammatory diseases impacting joints. Detailed study results will be presented during a plenary session (MEASURE 1) and in a poster presentation (MEASURE 2) at the American College of Rheumatology (ACR) Annual Meeting in Boston.

"Ankylosing spondylitis is a debilitating condition that severely impacts patients' mobility, ability to work, and overall quality of life," said Vasant Narasimhan, Global Head of Development, Novartis Pharmaceuticals. "As part of our commitment to addressing the significant unmet patient needs, we are proud to present positive Phase III results of secukinumab in ankylosing spondylitis, which marks a potential new treatment option for these patients. These data are expected to form the basis of joint regulatory submissions planned for 2015, which also include results from the FUTURE 1 and FUTURE 2 psoriatic arthritis studies."

Statistically significant improvements in signs and symptoms of AS were achieved with secukinumab versus placebo at Week 16, as measured by at least 20% improvement in the Assessment of Spondyloarthritis International Society criteria (ASAS20), a standard tool used to assess clinical improvement in AS. More than 60% of secukinumab 150 mg treated patients achieved an ASAS20 response in MEASURE 1 ($p<0.0001$) and MEASURE 2 ($p<0.001$). This is in comparison to 28.7% and 28.4% of placebo patients who achieved an ASAS20 response in MEASURE 1 and MEASURE 2, respectively.

In exploratory analyses, secukinumab 150 mg treated patients experienced ASAS20 responses at Week 1 in both studies ($p<0.01$, MEASURE1; $p<0.05$, MEASURE 2) and were sustained through 52 weeks of treatment, according to data from MEASURE 1. Additionally, statistically significant improvements in ASAS20 at Week 16 with secukinumab 150 mg were observed, compared to placebo ($p<0.05$) in patients who had not been previously treated with anti-TNF therapies (anti-TNF naïve) and also in patients who had an inadequate response or intolerance to anti-TNFs. In both studies, treatment with secukinumab 150 mg resulted in significant improvements in physical function and quality of life at Week 16 versus placebo ($p<0.05$), as

measured by the SF-36 Physical Component Summary (PCS) and ASQoL (AS quality of life), with improvements sustained through 52 weeks of treatment in MEASURE 1.

Secukinumab was well tolerated in both studies, with a safety profile consistent with that observed in the psoriasis clinical trial program involving nearly 4,000 patients. In MEASURE 1, the most common adverse events (AEs) were nasopharyngitis, dyslipidemia (imbalance of fats circulating in the blood stream), headache, nausea, and leukopenia (low white blood cell count). In MEASURE 1, 66.9% of secukinumab 75 mg patients and 69.6% of secukinumab 150 mg patients experienced an AE compared to 55.7% of placebo patients. Serious adverse event (SAE) rates were 1.6% (75 mg), 2.4% (150 mg), and 4.1% (placebo). In MEASURE 2, the most common AEs were nasopharyngitis, headache, and influenza. In MEASURE 2, 57.5% of secukinumab 75 mg patients and 62.5% of secukinumab 150 mg patients experienced an AE compared to 63.5% of placebo patients. SAE rates were 5.5% (75 mg), 5.6% (150 mg), and 4.1% (placebo).

"The MEASURE results suggest secukinumab may offer a novel therapeutic approach for ankylosing spondylitis and add to our understanding of the key role the IL-17 pathway plays in the disease," said Dr. Atul Deodhar, professor of medicine and medical director of Rheumatology Clinics at Oregon Health & Science University, and an investigator in the secukinumab clinical trial program. "Ankylosing spondylitis is a painful, debilitating chronic disease and effective new treatment options are needed as not every patient responds to existing therapies."

About Phase III Secukinumab AS Studies at ACR
MEASURE 1 and MEASURE 2 are multi-center, randomized, placebo-controlled Phase III studies to evaluate the efficacy of IL-17A inhibition with secukinumab in AS compared to placebo, and to assess the safety, tolerability, and effectiveness in patients with AS. Both MEASURE 1 and MEASURE 2 evaluated secukinumab 75 mg and 150 mg versus placebo. In the MEASURE 1 study patients received an intravenous loading dose of 10 mg/kg every two weeks for the first four weeks of treatment followed by monthly subcutaneous doses that aimed to provide high exposure for induction of response in order to confirm the clinical benefit observed in an initial proof-of-concept study. MEASURE 2 evaluated subcutaneous loading regimens. Both studies met their primary endpoint of ASAS20 (a ≥20% improvement of at least one unit in each of three domains, with no worsening in the fourth domain) in at least one study dose arm of secukinumab:

- MEASURE 1: 60.8% and 59.7% for secukinumab 150 mg and 75 mg, respectively, versus 28.7% for placebo; $p<0.0001$
- MEASURE 2: 61.1% and 41.1% for secukinumab 150 mg and 75 mg, respectively, versus 28.4% for placebo; $p<0.001$ for 150 mg, $p=0.0967$ for 75 mg

Full results of secondary endpoints will be presented at ACR. Secondary endpoints at Week 16 for MEASURE 1 and MEASURE 2 included:

- ASAS40 response (a ≥40% improvement of at least two units in each of three domains, with no worsening in the fourth domain)
- High sensitivity C-reactive protein (hs-CRP)
- ASAS 5/6 responses (≥20% improvement in five of six domains, adding spinal mobility and C-reactive protein [CRP], with no worsening in the sixth domain)
- Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), ASAS partial remission (a score of <2 units in each domain)
- BASDAI, quality of life assessed using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) and the ASQoL, and ASAS partial remission

About Ankylosing Spondylitis (AS)

Ankylosing spondylitis (AS) is a common type of spondyloarthritis (SpA), a spectrum of long-term diseases of joints (inflammatory disease), which also includes psoriatic arthritis (PsA). AS is a painful, progressively debilitating condition caused by inflammation of the spine. Up to 70% of patients with severe AS can develop spinal fusion (bones grow together), significantly reducing mobility and quality of life. Patients with AS can become progressively disabled and unable to work, which may add to their reduced quality of life.

AS occurs in up to 1% of the general population and typically affects young men and women aged 25 or older. Certain genetic factors increase a person's risk of developing AS by more than 50%.

Up to 40% of patients do not respond well to anti-tumor-necrosis-factor (anti-TNF) medicines, and there are few therapeutic options available to those people.

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 AS. Research shows IL-17A plays an important role in driving the body's immune response in psoriasis and certain inflammatory arthritic diseases, including AS.

In addition to AS, secukinumab is also in clinical trials for the treatment of psoriatic arthritis (PsA) and rheumatoid arthritis (RA). US regulatory applications for secukinumab in AS and PsA are planned for 2015. This follows the secukinumab US regulatory application for moderate-to-severe plaque psoriasis which was filed in October 2013 with approval anticipated in early 2015.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as "will," "commitment," "potential," "expected," "suggest," "may," "planned," "anticipated," 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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