

News Release

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Evotec AG Schnackenburgallee 114 22525 Hamburg Germany www.evotec.com Evotec Announces the Successful Completion of the First Phase I Study with EVT 401, an Oral P2X<sub>7</sub> Receptor Antagonist - Very Good Safety Profile and Confirmed "On Target Activity"

**Hamburg, Germany** – Evotec AG (Frankfurt Stock Exchange: EVT; NASDAQ: EVTC) today announced the successful completion of the first Phase I study with its P2X<sub>7</sub> receptor antagonist EVT 401. EVT 401 is a small molecule drug candidate and a potentially novel approach to orally treat inflammatory conditions such as Rheumatoid Arthritis.

The study was a double-blind, placebo controlled study investigating the safety, tolerability, pharmacokinetics and pharmacodynamics of EVT 401. A total of 96 healthy male volunteers received single oral ascending doses of the compound as a suspension or capsule.

The compound was very safe and well tolerated and there were no serious adverse events or withdrawals. In addition, the pharmacodynamic assay used in this study demonstrated the ability of EVT 401 to block ATP-stimulated IL-1 $\beta$  release in whole blood samples taken from subjects, thereby proving "on target" activity at well tolerated oral doses.

In Rheumatoid Arthritis, the first potential indication for EVT 401, there is a significant need for new oral therapies. Oral drugs can be used both as alternatives to and in combination with existing agents to increase the responder rates and potentially reduce or delay the need for expensive biological therapies.

**Dr Werner Lanthaler, Chief Executive Officer of Evotec, commented**: "We are encouraged that EVT 401 showed positive results in its first human trial. It was well tolerated and demonstrated the desired pharmacodynamic activity in healthy volunteers. We are now focusing our efforts on optimizing the oral dose formulation, completing the Phase I studies, and preparing Phase II studies in Rheumatoid Arthritis."

### Notes to the editor

#### About P2X<sub>7</sub> antagonists

The P2X<sub>7</sub> receptor is an ATP-gated ion channel primarily expressed on cells of the immune system and is thought to play an important role in inflammatory processes through the regulation of a number of proinflammatory cytokines such as IL-1 $\beta$ . P2X<sub>7</sub> receptor antagonism may therefore provide a novel approach to the treatment of rheumatoid arthritis and other inflammatory conditions.

Release of IL-1β is stimulated by ATP activation of P2X<sub>7</sub> receptors expressed on monocytes in the blood. The pharmacodynamic assay used in this study demon-



## News Release

strated the ability of EVT 401 to block ATP-stimulated IL-1 $\beta$  release in whole blood samples taken from subjects, thereby confirming "on target" activity following oral dosing.

#### **About Rheumatoid Arthritis (RA)**

RA is a chronic autoimmune disease that causes pain, stiffness, swelling and limitations in the motion and function of multiple joints. Current treatment guidelines for RA focus on preventing or slowing joint damage with the use of disease modifying anti-rheumatic drugs (DMARDs). Typical first line treatment is with older oral DMARDs such as methotrexate. Biological therapies, predominantly anti-TNF agents such as etanercept, are used in patients with significant disease who fail to respond adequately to first line treatment. While more effective than older oral DMARDs these biological treatments are expensive, cannot be administered orally and have certain drawbacks, including an increased risk of serious infections. In addition, around 30% of patients fail to respond adequately to a first-line TNF-alpha inhibitor.

#### About the RA market

It is estimated that over 5 million patients in the 7 major markets suffer from RA (US 2.2 million, EUR 2.3 million, Japan 0.6 million). The TNF-alpha inhibitors dominate this market by value, with their use in RA generating over \$6 billion in sales 2008 across these markets. However, only around 17% of RA patients are prescribed TNF-alpha inhibitors, in part due to their high cost resulting in reimbursement restrictions. (source: DecisionResources).

#### **About Evotec AG**

Evotec is a leader in the discovery and development of novel small molecule drugs. The Company has built substantial drug discovery expertise and an industrialized platform that can drive new innovative small molecule compounds into the clinic. In addition, Evotec has built a deep internal knowledge base in the treatment of diseases related to neuroscience, pain, and inflammation. Leveraging these skills and expertise the Company intends to develop best-in-class differentiated therapeutics and deliver superior science-driven discovery alliances with pharmaceutical and biotechnology companies.

Evotec has long-term discovery alliances with partners including Boehringer Ingelheim, CHDI, Novartis, Ono Pharmaceutical and Roche. The Company's has a  $P2X_7$  antagonist for the treatment of inflammatory diseases in clinical development and a series of preclinical compounds and development partnerships, including a strategic alliance with Roche for EVT 101, a subtype selective NMDA receptor antagonist, for use in treatment-resistant depression.

## Forward-Looking Statements

Information set forth in this press release contains forward-looking statements, which involve a number of risks and uncertainties. Such forward-looking statements include, but are not limited to, statements about our expectations and assumptions concerning regulatory, clinical and business strategies, the progress of our clinical development programs and timing of the results of our clinical trials, strategic collaborations and management's plans, objectives and strategies. These statements are neither promises nor guarantees, but are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in these forward-looking statements. In particular, the risks and uncertainties include, among other



## News Release

things: risks that the Company may be unable to reduce its cash burn through recent restructuring and cost containment measures; risks that product candidates may fail in the clinic or may not be successfully marketed or manufactured; risks relating to our ability to advance the development of product candidates currently in the pipeline or in clinical trials; our inability to further identify, develop and achieve commercial success for new products and technologies; the risk that competing products may be more successful; our inability to interest potential partners in our technologies and products; our inability to achieve commercial success for our products and technologies; our inability to protect our intellectual property and the cost of enforcing or defending our intellectual property rights; our failure to comply with regulations relating to our products and product candidates, including FDA requirements; the risk that the FDA may interpret the results of our studies differently than we have; the risk that clinical trials may not result in marketable products; the risk that we may be unable to successfully secure regulatory approval of and market our drug candidates; and risks of new, changing and competitive technologies and regulations in the U.S. and internationally.

The list of risks above is not exhaustive. Our most recent Annual Report on Form 20-F, filed with the Securities and Exchange Commission, and other documents filed with, or furnished to the Securities and Exchange Commission, contain additional factors that could impact our businesses and financial performance. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any such statements to reflect any change in our expectations or any change in events, conditions or circumstances on which any such statement is based.