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Evotec's EVT 101 Shown to Penetrate the Brain in Man and to Modulate Brain Activity during the Performance of Cognitive Tasks

- **Single-dose, volunteer fMRI study completed and reported today**
- **Dosing in four week higher repeat dose study completed**

Hamburg, Germany | Oxford, UK – Evotec (Frankfurt Stock Exchange: EVT) is pleased to announce the preliminary findings of a double-blind, single-dose, 3-way cross-over study with its orally active NR2B subtype selective NMDA receptor antagonist, EVT 101. The study was performed in 19 healthy young subjects and was conducted at the Centre for Neuroimaging Sciences of the Institute of Psychiatry at King's College London using functional magnetic resonance imaging techniques (fMRI) to investigate short-term effects of two doses of EVT 101 and placebo. The effects of the compound on cognitive endpoints, changes in local cerebral blood flow, reflecting neuronal activation or deactivation during the performance of cognitive tasks, as well as base-line regional cerebral blood flow, were explored.

All treatments were well tolerated confirming previous observations in healthy subjects.

While there was no evidence of acute improvement in cognitive function, an observation not unexpected in healthy young subjects who frequently perform at an optimum level, the activity of a number of brain regions, known for their role as a memory retrieval network, were selectively modified during the performance of certain tasks, as assessed by analysis of the changes in local cerebral blood flow.

Analysis of the changes in basal regional cerebral blood flow indicated a selective increase in blood flow in one specific region of the cortex, an area rich in NMDA receptors which is considered to be significant for indications such as pain and depression. Basal blood flow in other brain areas was unaffected.

These findings represent the first demonstration of effects of EVT 101 on human brain function at doses that are well tolerated and predicted to be clinically relevant.

In addition, Evotec has satisfactorily completed dosing of its four week higher repeat dose study conducted in France. Encouragingly, initial findings regarding the cerebrospinal fluid (CSF) penetration of EVT 101 assessed in a subgroup receiving EVT 101 showed that the compound demonstrated penetration into the CSF at levels predicted to inhibit NR2B re-

ceptors to a significantly higher amount than memantine at its therapeutic dose in Alzheimer's Disease.

"These data are extremely encouraging. They demonstrate EVT 101 penetrates the brain at doses that are well tolerated in man and expected to be clinically relevant, shows activity in areas relevant to pain and, importantly, modulates the activity of specific brain regions during the performance of cognitive tasks relevant to Alzheimer's disease", **commented Dr Tim Tasker, Executive Vice President Clinical Development, Evotec AG.**

Dr Mitul Mehta, academic lead for the project at the Centre for Neuroimaging Sciences at the Institute of Psychiatry at King's College London stated: "We have clearly visualised not only a direct, dose dependent effect of the compound on the brain but also an interaction of the drug with tasks pertinent to cognitive performance and dysfunction in Alzheimer's disease. These exciting new data also bode well for future studies in several indications of neurological and psychiatric ill health."

About Evotec AG

Evotec is a leader in the discovery and development of novel small molecule drugs. Both through its own discovery programmes and through research collaborations, the Company is generating the highest quality research results to its partners in the pharmaceutical and biotechnology industries.

In proprietary projects, Evotec specialises in finding new treatments for diseases of the Central Nervous System. Evotec has three programmes in clinical development: EVT 201, a partial positive allosteric modulator (pPAM) of the GABA_A receptor complex for the treatment of insomnia, EVT 101, a subtype selective NMDA receptor antagonist for the treatment of Alzheimer's disease and/or pain, and EVT 302, a MAO-B inhibitor in development for smoking cessation.

On 19 September 2007, Evotec announced that it has entered into a definitive agreement to acquire Renovis, a biopharmaceutical company focused on the discovery and development of drugs for major medical needs in the areas of pain and inflammatory diseases. The acquisition is subject to Renovis' stockholder vote, anti-trust clearance and other customary closing conditions.

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Forward looking statements

Information set forth in this report contains forward-looking statements, which involve a number of risks and uncertainties. Such forward-looking statements include, but are not limited to, statements about the anticipated benefits of Evotec's products, the timing of the completion of the transaction between Evotec and Renovis, the anticipated benefits of the business combination transaction involving Evotec and Renovis, including future financial and operating results, the combined company's plans, objectives, expectations and intentions, the anticipated timing and results of the combined company's clinical and preclinical programs, and other statements that are not historical facts. Evotec cautions readers that any forward-looking information is not a guarantee of future performance and that actual results could differ materially from those contained in the forward-looking information. These include risks and uncertainties relating to: the ability to obtain regulatory approvals of the transaction on the proposed terms and schedule; the parties' abil-

ity to complete the transaction because conditions to the closing of the transaction may not be satisfied; the failure to successfully integrate the businesses; unexpected costs or liabilities resulting from the transaction; the risk that synergies from the transaction may not be fully realized or may take longer to realize than expected; disruption from the transaction making it more difficult to maintain relationships with customers, employees or suppliers; competition and its effect on pricing, spending, third-party relationships and revenues; the need to develop new products and adapt to significant technological change; implementation of strategies for improving internal growth; use and protection of intellectual property; general worldwide economic conditions and related uncertainties; future legislative, regulatory, or tax changes as well as other economic, business and/or competitive factors; and the effect of exchange rate fluctuations on international operations. The risks included above are not exhaustive.