News Release

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# Evotec Successfully Completes Phase I for Potential Alzheimer's Disease and Neuropathic Pain Treatment, EVT 101

**Hamburg, Germany | Oxford, UK** – Evotec AG (Frankfurt Stock Exchange: EVT, TecDAX 30, "Evotec") today announced the successful completion of Phase I with EVT 101, an NR2B subtype-specific NMDA receptor antagonist for the treatment of Alzheimer's disease and/or neuropathic pain. A total of 90 healthy, young and elderly subjects received single and multiple ascending doses of the compound. In all subjects EVT 101 was well absorbed, achieved good exposure levels, and was very well tolerated with no significant adverse events. In both the young and elderly subjects, the compound had a good pharmacokinetic profile, with an eleven hour half-life consistent with once or twice daily oral dosing.

The good tolerability of EVT 101 is significant given the unfavourable side-effect profile of non-selective NMDA antagonists.

## Notes to the editor

### About EVT 101

EVT 101 is being developed for the treatment of Alzheimer's disease and/or neuropathic pain. It is a highly potent and selective antagonist of NR2B subunit containing NMDA receptors. In preclinical models, the compound has potent beneficial effects and an improved side effect profile compared to non-selective NMDA receptor antagonists and has good oral bioavailability and *in vivo* pharmacokinetics.

### NMDA background

Apart from their normal physiological role in nerve-to-nerve cell communication NMDA receptors are important players in certain pathological disease states such as Alzheimer's disease, Parkinson's disease, neuropathic pain and epilepsy. The hypothesis is that when NMDA receptor over-activation is reduced in these conditions with an "antagonist", disease symptoms are reduced. Extensive studies over the last 15 years have indicated a potential for NMDA receptor antagonists in the treatment of these diseases. However, the clinical development of non-selective antagonists has been limited by unfavourable side-effects, such as hallucinations. In the early 1990's it was found that multiple NMDA receptor subtypes exist which contain different NR2(A-D) subunits. In preclinical studies, compounds selectively targeting NR2B subunit-containing receptors retain many of the beneficial effects of earlier non-selective compounds but have much improved side effect profiles. Separating side effects from beneficial effects by selectively targeting the NR2B-subunit could allow higher dosing and hence the potential to increase efficacy of the drug.

### 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 contract research partnerships, 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 neuropathic pain and EVT 301, a selective and reversible inhibitor of MAO-B for the treatment of Alzheimer's disease.
In contract research, Evotec has established itself as the partner of choice for pharmaceutical and biotechnology companies worldwide. The Company provides innovative and often integrated solutions from drug target to clinic through an unmatched range of capabilities, including early stage assay development and screening through to medicinal chemistry and drug manufacturing.
In 2005, Evotec has generated sales of EUR 80 million with 600 employees located in Hamburg, Germany and near Oxford and in Glasgow, UK.
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