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Evotec Reports Positive Top-Line Results in Phase II Study with EVT 201 in Elderly Insomniacs with Daytime Sleepiness

- Statistical significance in primary and key secondary endpoints at both doses
- Data confirm robust sleep onset and sleep maintenance effects seen in the first Phase II study in the adult population

Hamburg, Germany | Oxford, UK – Evotec AG (Frankfurt Stock Exchange: EVT) announced today positive top-line results from its second phase II trial of EVT 201 in elderly primary insomnia patients with daytime sleepiness. These top-line results are from the pre-specified intention-to-treat analysis from the 149 patients who were randomized into the study.

The study showed a highly significant improvement between both doses of EVT 201 and placebo on the primary endpoint of polysomnography (PSG) derived Total Sleep Time (TST); compared to placebo, mean TST increased by 30.9 minutes (9%) on EVT 201 1.5 mg and 56.4 minutes (17%) on EVT 201 2.5 mg; p=0.0001 and p=<0.0001 respectively.

Significant improvements were also seen across key PSG-derived secondary endpoints including Wake After Sleep Onset (WASO) and Latency to Persistent Sleep (LPS). Although the study was not powered to show this, the 2.5 mg dose also showed a significant effect on TWT (Total Wake Time) during the second half of the night, indicating that EVT 201 is highly effective in maintaining sleep throughout the night. This was further confirmed by the hour-by-hour analysis of TWT. Treatment with EVT 201 produced a statistically significant reduction in TWT for all hours of the night apart from hour 7.

A randomized, double-blind, placebo-controlled parallel group design was used to assess the hypnotic efficacy of EVT 201 1.5 mg and 2.5 mg following 7 nights dosing. The study was conducted in 20 sleep labs in the US using both objective and subjective measures. PSG data were collected on nights 1, 6 and 7 and results are based on the mean data from these three nights.

The table below shows the results for the primary and key secondary PSG endpoints.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo</th>
<th>EVT 201 1.5 mg</th>
<th>EVT 201 2.5 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted mean TST (mins) / % change from placebo</td>
<td>338.6</td>
<td>369.5 / 9% p=0.0001</td>
<td>395 / 17% p=&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted mean WASO (mins) / % change from placebo</td>
<td>101.4</td>
<td>86.2 / 15% p=0.0140</td>
<td>65.3 / 36% p=&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted mean LPS (mins) / % change from placebo</td>
<td>46.5</td>
<td>30.5 / 34% p=0.0091</td>
<td>26.5 / 43% p=0.0014</td>
</tr>
</tbody>
</table>

The PSG analysis also showed that EVT 201 generally preserved sleep architecture.

These PSG results were supported by patient reported measures including subjective Total Sleep Time (sTST), subjective Sleep Onset Latency (sSOL) and subjective Wake After Sleep Onset (sWASO).

Subjectively, sleep quality was improved on all nights and there was no residual sedation assessed 30-minutes post wake time (approximately 9 hours post dose).
An additional element of the study design was to assess daytime function on Day 8. This included the Multiple Sleep Latency Test (MSLT), an objective assessment of daytime sleepiness. Initial analyses showed that both doses of EVT 201 produced a statistically significant overall improvement in the MSLT compared to placebo, indicating that patients were less sleepy during the day following treatment with EVT 201.

Daytime function was further assessed objectively using the Rey Auditory Verbal Learning Test (RAVLT), a short-term verbal memory test, and Psychomotor Vigilance Task (PVT), a measure of sustained attention and reaction time and subjectively using the Karolinska Sleepiness Scale (KSS). Initial analyses suggest overall that there was no significant difference between EVT 201 and placebo. Further analyses of these endpoints are ongoing.

EVT 201 was well tolerated. No serious treatment emergent adverse events were reported during the study. The majority of adverse events reported were mild and infrequent. The most common adverse events were dizziness, headache and somnolence and the percentage of patients reporting these events is shown in the table below:

<table>
<thead>
<tr>
<th>Treatment emergent adverse events</th>
<th>Placebo (n=44)</th>
<th>EVT 201 1.5 mg (n=53)</th>
<th>EVT 201 2.5 mg (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>5.7%</td>
<td>9.6%</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
<td>9.4%</td>
<td>5.8%</td>
</tr>
<tr>
<td>Somnolence</td>
<td>2.3%</td>
<td>1.9%</td>
<td>11.5%</td>
</tr>
</tbody>
</table>

No significant difference was seen between either dose of EVT 201 and placebo in the Benzodiazepine Withdrawal Questionnaire.

The results of this study confirm the effects of EVT 201 on sleep onset and sleep maintenance seen in the adult population in Study 2004 and indicate that the same doses 1.5 mg and 2.5 mg have hypnotic efficacy in the elderly with no significant residual effects.

Further analysis of the remaining secondary and exploratory endpoints is ongoing.

"We’re delighted that these results in elderly insomniacs again confirm the excellent profile of EVT 201 as a potential treatment that helps patients to fall asleep quickly, maintains their sleep throughout the night and yet enables them to wake in the morning without hangover effects and feeling like they’ve had a good night’s sleep," said Dr John Kemp, Chief Research & Development Officer, Evotec AG. "Due to its partial positive allosteric modulation of GABA\textsubscript{A} receptors, EVT 201 provides a novel approach to the treatment of insomnia, yet since the GABA\textsubscript{A} system is a well understood pathway, the risk of unexpected side effect findings are low compared to completely novel mechanisms."

Jörn Aldag, President and Chief Executive Officer, Evotec AG, said: "The positive outcome of this second clinical Phase II trial with EVT 201 is particularly encouraging as elderly patients are particularly underserved by current treatments. The study’s confirmation of our earlier Phase II data in adults underscores the finding that EVT 201 has hypnotic efficacy in both adults and elderly primary insomniacs and we believe that these data make EVT 201 an extremely attractive partnering opportunity."

"We now have two sets of data which robustly demonstrate the same profile of EVT 201 in both adults and the elderly – effects upon sleep onset and sleep maintenance throughout the night with minimal residual effects. This is exceptional for a compound at this stage of development", added Dr Tim Tasker, Executive Vice President Clinical Development, Evotec AG. "The results also show that elderly patients with insomnia and daytime sleepiness were significantly less sleepy during the day following seven nights treatment measured using the objective MSLT test. The size of this effect was clinically significant, and has not been demonstrated in other recent hypnotic studies. This exciting headline finding will now be fully investigated in further analysis of the 2005 data."

Principal Investigator Dr James Walsh, Executive Director of the Sleep Medicine and Research Center, St John’s Mercy Medical Center, Chesterfield, Missouri, US, said: “In this second Phase II study with EVT 201 the robust efficacy seen previously in the adult population was duplicated with the same doses in elderly insomnia patients. It is exciting that the sleep-promoting effects seen throughout the night, coupled with no significant sedative activity of the drug during the daytime, allowed the improvement of sleep to be accompanied by significantly improved alertness during the day. This
Combination gives the compound a very attractive profile as a sleep promoting agent which improves both night-time and daytime symptoms of insomnia in the elderly.

R&D Update in London
Webcast Presentation and Conference Call

Evotec has scheduled an R&D Update in London at 13.00 pm BST (14.00 pm CET, 08.00 am US time East Coast) today which will be broadcast live on the internet. Evotec will also present details on this positive Phase II study in insomnia at that meeting.

For those who prefer to listen to the presentation via phone, please dial:

From Europe:
+49.(0)69.5007 1308 (Germany)
+44.(0)20.7806 1956 (UK)

From the US: +1.718.354 1388
Pass Code: 2793143

The on-demand version of the webcast will be available on our website: www.evotec.com - Investors – Webcasts.

Notes to the editor

Study design
This US, multi-centre, randomized, double-blind, placebo-controlled, parallel group design trial was designed to evaluate the hypnotic efficacy of EVT 201 in the treatment of primary insomnia in elderly patients with daytime sleepiness. Patients were screened for entry into the study and the eligibility criteria included: age ≥ 65 years; a diagnosis of primary insomnia according to DSM (Diagnostic and Statistical Manual of Mental Disorders) IV; mean TST 240-410 minutes inclusive determined during two consecutive nights polysomnography (PSG) evaluation; mean MSLT ≥ 4 and ≤ 16. Patients were randomized to receive EVT 201 1.5 mg or EVT 201 2.5 mg or placebo for seven consecutive nights. PSG data was collected for two nights at Screening and on nights 1, 6 and 7 during the Treatment Period. The primary endpoint of this trial was to assess Total Sleep Time (TST) determined by PSG. The secondary endpoints included additional PSG-based measures such as latency to persistent sleep, wake after sleep onset and effects on sleep architecture. In addition, subjective sleep quality and quantity were assessed, along with the Profile of Mood State (POMS). Daytime function was assessed objectively by using the Multiple Sleep Latency Test (MSLT), the Psychomotor Vigilance Task (PVT), a measure of sustained attention and reaction time, the Rey Auditory Verbal Learning Test (RAVLT), a short-term verbal memory test and subjectively using the Karolinska Sleepiness Scale (KSS). Residual sedation was assessed 30 minutes post wake time subjectively using a categorical rating scale. Safety measures included adverse events, laboratory data and the Benzodiazepine Withdrawal Questionnaire.

About EVT 201
EVT 201 is a partial positive allosteric modulator (pPAM) of the GABA_A receptor complex. Acting on GABA_A receptors it addresses the gold standard mechanism for insomnia with more than 90% of current insomnia drugs using this mechanism. Importantly, however, its close to ideal half life of 3 to 4 hours and its partial agonist activity gives EVT 201 a differentiated preclinical profile and mechanism of action. The results of the first Phase II study with EVT 201 in adult primary insomnia patients were very positive in terms of all key aspects of the problems faced by insomniacs, i.e. sleep onset and sleep maintenance and yet the patients didn’t feel any drug hang-over effects after waking in the morning. Furthermore, in two previous Phase I/II proof-of-principle studies in subjects with induced insomnia, EVT 201 significantly reduced Wake After Sleep Onset (WASO) while significantly increasing the Total Sleep Time (TST) and quality of sleep with no subjective residual effects. The studies were conducted in a sleep laboratory setting using the traffic noise model of insomnia in healthy male volunteers. In this setting an average of 52 decibels of recorded traffic noise is played throughout the night thereby provoking insomnia. This model has been used to evaluate several insomnia treatments currently in development and on the market. EVT 201 showed no tolerance/dependence liabilities in pre-clinical studies and no interaction with alcohol.

About Insomnia
Good quality and refreshing sleep is a prerequisite for continued good health and daily functioning. Insomnia patients suffer from a) difficulty falling asleep; b) difficulty maintaining sleep due to waking up frequently during the night with difficulty returning to sleep or due to waking up at early hours and c) unrefreshing sleep. In 2005, the Sleep in America poll found that 54% of the adult population reported
symptoms of insomnia at least a few nights a week. However, only a fraction of patients are diagnosed, with even fewer using a sleep aid. The insomnia market is estimated to be worth US$ 6.1 billion across the major markets in 2007, and is set to be impacted by the launch of new drug classes (Datamonitor, Pipeline Insight: Insomnia, April 2007). Physicians highlight that the ideal insomnia drug has the ability to induce, maintain and improve the quality of sleep without causing next day hang-over and the absence of addiction liabilities. Key unmet needs include improvements in sleep maintenance and more effective treatments in the elderly population. The entry of novel treatments with differentiated profiles in terms of dosage, mode of action and clinical profile are expected to accelerate growth within the market.

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 under which Evotec will 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. www.evotec.com

Forward looking statements
Information set forth in this communication 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 anticipated timing and results of Evotec’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 as a result of risks and uncertainties relating to: the need to adapt to significant technological change; use and protection of intellectual property; 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. Evotec expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any such statements to reflect any change in the parties’ expectations or any change in events, conditions or circumstances on which any such statement is based.

Additional Information
Renovis filed a Current Report on Form 8-K with the Securities and Exchange Commission on September 24, 2007, that includes as an exhibit the Agreement and Plan of Merger between Evotec and Renovis. Evotec intends to file a Registration Statement on Form F-4 with the Securities and Exchange Commission in connection with the proposed merger. Evotec and Renovis expect to mail a joint proxy statement/prospectus, which will form part of the Registration Statement on Form F-4, to shareholders of Renovis in connection with the proposed merger. This document will contain important information about the merger and should be read before any decision is made with respect to the merger. Investors and stockholders will be able to obtain free copies of this document and any other documents filed or furnished by Evotec or Renovis through the website maintained by the Securities and Exchange Commission at www.sec.gov. Free copies of these documents may also be obtained from Evotec, by directing a request to Evotec’s Investor Relations department at Schnackenburgallee 114, 22525 Hamburg, Germany, or from Renovis, by directing a request to Renovis’ Investor Relations department at Two Corporate Drive, South San Francisco, California 94080.

In addition to the documents referenced above, Renovis files or furnishes annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any reports, statements or other information filed or furnished by Renovis at the SEC’s Public Reference Room at Station Place, 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the Public Reference Room. Renovis’s SEC filings are also available to the public at the SEC’s web site at www.sec.gov, or at their web site at www.renovis.com.

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