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## **Aeolus Pharmaceuticals Reports Positive Safety Results from Completed Phase 1 Single Dose Study of AEOL 10150 in 25 Patients with ALS (Lou Gehrig's Disease).**

*All six single doses (3, 12, 30, 45, 60 and 75 mg) were well tolerated with no serious adverse events, no significant laboratory abnormalities and no cardiovascular issues related to AEOL 10150. Phase 1 multiple dose study in patients diagnosed with ALS, using 40, 70 and 100 mg doses, twice-daily for seven days, anticipated to be started and completed within the fourth quarter of 2005.*

SAN DIEGO, CA., September 7, 2005 /PRNewswire/ -- Aeolus Pharmaceuticals, Inc. (OTC Bulletin Board: AOLS.OB), a developer of a potential new class of disease-modifying compounds that have evidenced efficacy in pre-clinical models of central nervous system diseases, today announced results for its multi-center, double-blind, randomized, placebo-controlled, Phase 1 clinical trial. This escalating single dose study was conducted to evaluate the safety, tolerability and pharmacokinetics of AEOL 10150 administered by subcutaneous injection in patients with amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease).

"We are very pleased with the results from our Phase 1 single dose study of AEOL 10150 and we are looking forward to moving this exciting and potential therapeutic into multiple dose evaluation" noted Richard P. Burgoon, Jr., Aeolus' chief executive officer. Mr. Burgoon further stated that "Although the Phase 1 single and multiple dose studies are being conducted in patients diagnosed with ALS, these Phase 1 safety studies can also support human efficacy studies of AEOL 10150 in other clinical indications for which AEOL 10150 has shown pre-clinical efficacy." On this point, Mr. Burgoon noted that in addition to efficacy in the scientifically recognized ALS model, AEOL 10150 also has demonstrated efficacy in models of other neurodegenerative disorders, autoimmune diabetes, stroke, chronic obstructive pulmonary disease, pancreatic islet cell preservation, radiation-induced lung fibrosis, and inflammation.

### ***Phase 1 Single Dose Clinical Trial Details***

In the study, 4-5 patients diagnosed with ALS were utilized in each dosage cohort (3 or 4 receiving AEOL 10150 and 1 receiving placebo). Each dose cohort was evaluated at a separate clinical center. In total, seven separate cohorts were evaluated for the study, and 25 ALS patients received AEOL 10150.

Based upon an analysis of the data, it was concluded that single doses of AEOL 10150 ranging from 3 mg to 75 mg were well tolerated. In addition, no serious adverse clinical events were reported, nor were there any significant laboratory abnormalities. Based upon extensive cardiovascular monitoring (*i.e.* frequent electrocardiograms and continuous Holter recordings for up to 48 hours following dosing), there were no compound-related cardiovascular abnormalities.

Following administration of single doses of AEOL 10150 (3, 12, 30, 45, 60 and 75 mg), pharmacokinetic analysis demonstrated plasma area under the curve (AUC) values ranging from 354 ng•hr/mL in the 3 mg group to 12,167 ng•hr/mL in the 75 mg group. Correspondingly, C<sub>max</sub> ranged from 114.8 ng/mL to 1584 ng/mL, and T<sub>max</sub> ranged from 1 to 2 hours in these same groups. The mean half-life of AEOL 10150 ranged from 2.6 (3 mg cohort) to 6.4 hours (75 mg cohort). Linear dose response, and dose proportionality, were documented. A summary of these results is provided below in table form below.

The most frequently reported adverse events were injection site reactions, followed by dizziness and headache. Adverse events were primarily mild in severity, and approximately one-half of the events were considered to have a possible relationship to the study medication. In addition, no clinically meaningful findings were noted in the safety, laboratory, vital sign, UPDRS, functional ALS, or ECG data. All cohorts exhibited dose-related peak plasma drug concentrations and consistent disappearance half-lives.

Taken together, the pharmacokinetic data indicate that accumulation of AEOL 10150 with multiple dosing is unlikely.

### ***Launch of Phase 1 Multi-dose Clinical Trial***

Based on these data, and in consultation with the Phase 1 single dose principal investigators, Aeolus will initiate a multiple dose study of AEOL 10150 in patients diagnosed with ALS in the fourth quarter of this year. The dosing study is expected to be completed in the fourth quarter of this year.

Under the multiple dose protocol, three groups of six ALS patients (four receiving AEOL 10150; two receiving placebo, 18 total patients) will be recruited, based upon patients who meet the El Escorial criteria for Clinically Definite ALS, Clinically Probable ALS, Clinically Probably-Laboratory-Supported ALS, or Definite Familial-Laboratory Supported ALS (*i.e.*, Clinically Possible ALS with an identified SOD gene mutation). Each patient will receive twice daily subcutaneous injections of AEOL 10150 or placebo for six days, followed by a single subcutaneous administration on the seventh day, for a total of 13 injections. In the first cohort, each injection will be 40 mg (*i.e.*, 80 mg daily for six days and 40 mg on the seventh day). In the second cohort, each injection will be 70 mg (*i.e.*, 140 mg daily for six days and 70 mg on the seventh day). In the third cohort, each injection will be 100 mg (*i.e.*, 200 mg daily for six days and 100 mg on the seventh day). Each patient will complete follow-up evaluation by 14 days.

The study is planned to be conducted at six clinical ALS centers, with each center enrolling three patients. Male and female ALS patients, 18 to 70 years of age, will be eligible for study participation. Patients must be ambulatory (with the use of a walker or cane, if needed) and capable of orthostatic blood pressure assessments. Clinical signs/symptoms, laboratory values, cardiac assessments, and pharmacokinetics (PK) will be performed.

***About Aeolus Pharmaceuticals.***

Aeolus is developing a variety of therapeutic agents based on its proprietary small molecule catalytic antioxidants, with AEOL 10150 being the first to enter human clinical evaluation. AEOL 10150 is a small molecule catalytic antioxidant that has shown the ability to scavenge a broad range of reactive oxygen species, or free radicals. As a catalytic antioxidant, AEOL 10150 mimics and thereby amplifies the body’s natural enzymatic systems for eliminating these damaging compounds. Because oxygen-derived free radicals are believed to have an important role in the pathogenesis of many diseases, Aeolus’ catalytic antioxidants are believed to have a broad range of potential therapeutic uses. The Aeolus Pipeline Initiative, begun in the third calendar quarter of this year, is an internal development initiative focused on advancing, in addition to AEOL 10150, several of the most promising catalytic antioxidant compounds from Aeolus’ proprietary library of 200 compounds. The initial therapeutic focus areas for the Aeolus Pipeline Initiative are: Parkinson’s disease; Autoimmune disorders (arthritis and ulcerative colitis); Chronic Obstructive Lung Disease; Biodefense/Radioprotection; Tumor Suppression/Bone Marrow Transplantation; and Stroke. These therapeutic focus areas were selected based upon preliminary data developed using Aeolus catalytic antioxidant compounds.

**Pharmacokinetic Parameters for AEOL 10150:  
Result Summary, Phase I Single Dose Evaluation**

Pharmacokinetic Parameter	AEOL 10150						
	3 mg N = 3	12 mg N = 4	30 mg N = 3	45 mg N = 4	45 mg N = 4 (repeat, different patients)	60 mg N = 4	75 mg N = 3
<b>AUC(0-∞) (hr•ng/mL)</b>	354 ±100	1,494 ±386	4,580 ± 1828	7,116 ±1010	5,922 ±1307	9,087 ±2180	12,167 ±1543
<b>Tmax (0-48) (hr)</b>	1 ±0	1 ±1	1 ±0	1 ±0	2 ±1	2 ±0	2 ±1
<b>Cmax (0-48) (ng/mL)</b>	115 ±38	267 ±40	733 ±166	1,245 ±247	962 ±333	1,330 ±226	1,584 ±378
<b>T1/2 (hr)</b>	2.61 ±0.60	3.97 ±1.09	5.25 ±1.65	6.31 ±2.54	5.28 ±1.00	5.93 ±0.90	6.36 ±0.47

The statements in this press release that are not purely statements of historical fact are forward-looking statements. Such statements include, but are not limited to, those relating to Aeolus’ product candidates, as well as its proprietary technologies and research programs. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause Aeolus’ actual results to be materially different from historical results or from any results

expressed or implied by such forward-looking statements. Important factors that could cause results to differ include risks associated with uncertainties of progress and timing of clinical trials, scientific research and product development activities, difficulties or delays in development, testing, obtaining regulatory approval, the need to obtain funding for pre-clinical and clinical trials and operations, the scope and validity of intellectual property protection for Aeolus' product candidates, proprietary technologies and their uses, and competition from other biopharmaceutical companies. Certain of these factors and others are more fully described in Aeolus' filings with the Securities and Exchange Commission, including, but not limited to, Aeolus' Quarterly Report on Form 10-Q for the quarter ended June 30, 2005. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof.

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