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## **Concordia Pharmaceuticals Reports Encouraging Clinical Data in Patients with K-Ras Mutations Treated with First-in-Class Ras Antagonist, Salirasib**

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### **Data on Patients with Advanced Pancreatic and Non-Small Cell Lung Cancer to be Presented at American Society of Clinical Oncology Annual Meeting**

FORT LAUDERDALE, Fla., May 14, 2009 – Concordia Pharmaceuticals today reported encouraging new clinical data for salirasib, its novel small-molecule direct Ras antagonist, from two ongoing clinical trials – one in patients with advanced pancreatic cancer, and another in patients with advanced non-small cell lung cancer (NSCLC). The results in pancreatic cancer and NSCLC were reported in two abstracts (#4529 and 8012 respectively) released in advance of the American Society of Clinical Oncology 2009 Annual Meeting, and will be presented by investigators in two separate poster presentations.

In a phase 1/2 trial in patients with advanced pancreatic cancer, salirasib treatment resulted in median survival of >10.8 months and one-year survival of 50%. Of significant note, biopsies of human tumors showed consistent and substantial reductions in Ras levels, which the company believes to be the first such reductions ever demonstrated.

In a separate phase 2 study of salirasib monotherapy in NSCLC, 38% of evaluable patients in the treatment naïve group were classified as having stable disease following salirasib treatment, while 26% in the previously treated group achieved stable disease, and the compound was well tolerated.

These results underscore salirasib's potential as a first-in-class treatment of a wide range of solid tumors in K-Ras mutated patients, where multiple reports have indicated that certain drugs (such as EGFR inhibitors) are not effective. Ras, a protein vital to cell signaling, is a critically important target for drug development due to its role in the etiology of a wide variety of tumors. Mutant forms of Ras are found in approximately 70-90% of pancreatic cancers, 20-25% of non-small cell lung cancers, and 35-40% of colorectal cancers.

Concordia is developing salirasib as the first direct Ras antagonist, and believes it is unique in its ability to potentially overcome limitations of other Ras inhibition

mechanisms. Salirasib is distinct from other classes of drugs such as EGFR inhibitors and farnesyltransferase inhibitors (FTIs), in that it inhibits all of the Ras isoforms from binding to the cell membrane, a critical point in the signaling pathway. The clinical results reported at ASCO are consistent with a large body of preclinical data demonstrating salirasib's potential – in cell culture, animal xenograft models, and transgenic mouse models.

“The data presented at ASCO demonstrate salirasib's potential in two very challenging cancers where K-Ras mutations play a significant role,” said Victor J. Bauer, PhD, chief scientific officer at Concordia Pharmaceuticals. “Salirasib's demonstrated ability to inhibit mutated Ras could translate into an important clinical advance for the treatment of diseases where there are very few treatment options. We are highly encouraged by the results to date, and are now working with two major cancer centers to design follow-up trials in both indications, including a registration trial evaluating salirasib in combination with gemcitabine in pancreatic cancer, and a randomized trial of salirasib in combination with a chemotherapy agent in NSCLC.”

Details on the abstracts presented at ASCO:

#### **Abstract #4529 – Phase 1/2 Study in Advanced Pancreatic Cancer**

This ongoing study is evaluating gemcitabine plus salirasib in patients with previously untreated advanced pancreatic cancer. Study objectives include determining the compound's safety and tolerability, seeking preliminary evidence of antitumor activity and clinical benefit, and assessing salirasib's effect on intratumor Ras levels. At time of analysis, thirteen patients were enrolled; each received standard dosing and schedule of gemcitabine plus oral salirasib at doses between 200-800 mg twice daily for 21 days of a 28-day cycle. Results showed salirasib was well tolerated: the study did not reach a conventional maximum tolerated dose (MTD). The most common adverse event associated with salirasib was diarrhea, which was managed effectively using standard protocols. Progression-free survival for patients receiving gemcitabine plus 400-800 mg salirasib twice daily was 4.7 months, with median survival of >10.8 months and one-year survival of 50%. Ras inhibition was confirmed by reduction of tumor Ras as measured through tissue biopsy. These data will be presented in a poster session on May 31 from 5-6 pm.

#### **Abstract #8012 – Phase 2 Study in Advanced Lung Cancer**

This ongoing, open-label study evaluates salirasib in two groups of patients with stage III/IVB non-small cell lung cancer: previously treated patients with K-Ras mutations, and treatment-naïve patients. The company believes that this is the first study in which a K-Ras mutant population has been recruited and studied prospectively, making it important from a clinical perspective. The primary objective is measurement of rate of disease non-progression at 10 weeks, with objective response rate, time to disease progression, survival, and correlation of outcome with K-Ras as secondary endpoints. After 10 weeks of treatment, 5 of 19

(26%) evaluable patients in the previously treated group, and 3 of 8 (38%) evaluable patients in the treatment-naïve group, were classified as stable disease. The median time to progression was one month for patients in the previously treated group, and 2 months in the treatment-naïve group. Median overall survival was not reached in the previously treated group, and was 13 months for the treatment naïve-group. Salirasib was well tolerated by both groups, with grade 3 diarrhea and grade 3 fatigue the most common toxicities. These data will be presented in a poster session on June 1 from 8-11 am, and have been chosen for discussion after the session.

### **About Salirasib**

Salirasib is a first in class direct Ras antagonist being developed for potential use in a wide range of solid tumors where Ras signaling is known to play a role. Mutant forms of Ras are found in approximately 35-40% of colorectal cancers, 70-90% of pancreatic cancers, and 20-25% of non-small cell lung cancers. The first compound to be categorized as a Ras inhibitor, salirasib has demonstrated a consistent ability to reduce Ras levels in a wide array of established laboratory and animal models and in human tumor tissue. Recently completed trials of salirasib include a phase 1/2 study in advanced pancreatic cancer and a phase 2 study in advanced lung cancer.

### **About Concordia Pharmaceuticals**

Founded in 2003, Concordia is a pharmaceutical development company focused on the acquisition, in-licensing and development of innovative cancer therapies. The company's lead compound is salirasib, a novel, orally available small molecule therapeutic that acts to inhibit cancer by significantly inhibiting the effects of overexpressed farnesylated wild-type Ras and mutated Ras, both widely believed to be contributing factors in the growth of many tumors. Concordia is led by seasoned pharmaceutical executives, and is based in Fort Lauderdale, Florida. For additional information, please visit [www.concordiapharma.com](http://www.concordiapharma.com).

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