

## News Release

Nektar Therapeutics 201 Industrial Road San Carlos, CA 94070 650-631-3100 Phone 650-631-3150 Fax www.nektar.com

### **Significant Anti-Tumor Activity and Extended Half-Life of NKTR-102 (PEG-irinotecan) Highlighted in Phase 1 Data Presented at EORTC-NCI-AACR Symposium**

*Active metabolite concentrations of NKTR-102 significantly more sustained in between doses than possible with irinotecan*

**Geneva and San Carlos, Calif., October 24, 2008** – Nektar Therapeutics (Nasdaq: NKTR) today reported positive Phase 1 data for its lead proprietary oncology product candidate, NKTR-102 (PEG-irinotecan). The data were presented at the 20<sup>th</sup> EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Geneva, Switzerland, and highlighted the significant anti-tumor activity and superior pharmacokinetic profile of NKTR-102. NKTR-102 leverages Nektar's innovative small molecule PEGylation platform and is currently in Phase 2 clinical development.

"NKTR-102 is an excellent example of how our proprietary PEGylation platform allows us to precisely modify an oncolytic with sub-optimal pharmacokinetics and enhance its therapeutic profile," said Randall Moreadith, M.D. Ph.D., Chief Development Officer and Senior Vice President of Drug Development of Nektar. "In our Phase 1 study, we established our desired pharmacokinetic profile with NKTR-102 - and in particular - a substantially prolonged half-life relative to standard irinotecan. These Phase 1 data underscore the importance of our clinical development strategy, which includes additional indications for which irinotecan was never developed, such as ovarian, cervical, and breast cancers. We are excited about the potential of NKTR-102 to dramatically expand therapeutic options for oncologists and improve survival rates for patients with a variety of cancers."

Of the 57 patients in total from all dose schedules, 13 reported significant anti-tumor activity. Seven patients had confirmed partial responses (greater than 30 percent tumor regression per RECIST). Of these seven partial responses, all responses ranged from a 40% reduction to as high as a 58% reduction in tumor size. Six patients in the study had minor responses (tumor regression by more than 15 percent but less than 30 percent per RECIST, or demonstrated significant cancer biomarker reduction). Responders were seen in a variety of tumor settings, including breast, ovarian, and cervical. Nektar plans to initiate Phase 2 studies to evaluate NKTR-102 in these tumor types in the fourth quarter of 2008.

The observed plasma half life of the active metabolite (SN38) of NKTR-102 was 50 days; this is significantly longer than the observed half-life of 30-50 hours with irinotecan dosing.<sup>1</sup> Increased SN38 levels, the active metabolite of irinotecan responsible for its

anti-tumor activity, were also observed with administration of NKTR-102, with exposures up to 4.4-fold higher than predicted with irinotecan at equivalent doses.

“The high number of responses observed with NKTR-102 in a Phase 1 study following only a few courses of treatment highlights the exceptional promise of this optimized investigational cancer drug,” said Daniel D. Von Hoff, M.D., lead author of today’s presentation of the Phase 1 trial, Chief Medical Officer for the Scottsdale Clinical Research Institute at Scottsdale Healthcare and Clinical Professor of Medicine, University of Arizona. “Additionally, the drug’s activity in a number of tumor types, particularly in extremely aggressive tumor settings such as triple-negative breast, strongly supports the expanded development of NKTR-102.”

Patients enrolled in the NKTR-102 Phase 1 study had failed all prior established treatment regimens. The majority of patients had progressive disease despite three or more previous regimens. All partial responses were observed following the first or second course of treatment, highlighting the value of an oncolytic with an extended half-life and sustained delivery of the active metabolite.

### **Clinical Trial Summary**

In this Phase 1 dose-escalation trial, the safety, pharmacokinetics and anti-tumor activity of NKTR-102 monotherapy were evaluated in 57 patients with advanced solid tumors who had failed prior treatments or had no standard treatment available to them. Patients were enrolled in one of three dose schedules and received 90-minute infusions of NKTR-102 (PEGylated irinotecan) as follows: weekly for three weeks with the fourth week off (n=32); q14 days (n=10); or q21 days (n=15). Tumor responses were evaluated according to RECIST (Response Evaluation Criteria in Solid Tumors) criteria.

Doses ranged from 58 mg/m<sup>2</sup> to 230 mg/m<sup>2</sup> in the weekly dose schedule (weekly x3 Q4 weeks). In the every two week dose schedule (q14 days) and every three week dose schedule (q21 days), doses ranged from 145 mg/m<sup>2</sup> up to 245 mg/m<sup>2</sup>. Tumor regression, other anti-tumor activity or prolonged disease stabilization was observed in a broad spectrum of cancer types, including triple-negative breast, ovarian, cervical, bladder, non-small cell lung cancer, small cell lung cancer, adrenocortical, esophageal, maxillary sinus and Hodgkins lymphoma.

The Phase 1 study, sponsored by Nektar Therapeutics includes clinical sites at Translational Genomics Clinical Research Services at Scottsdale Healthcare and the Louisville Oncology Clinical Research Program. Nektar expects to present complete results from this ongoing Phase 1 trial at additional scientific forums later this year.

### **Data Presentation for NKTR-102**

The poster presentation from today’s session entitled ‘Topoisomerase inhibitors’ can be found on Nektar’s website at <http://www.nektar.com/wt/page/nktr102media> .

2008 EORTC-NCI-AAACR Symposium - Poster #595, “First Phase I Trial of NKTR-102 (PEG-irinotecan) Reveals Early Evidence of Broad Anti-Tumor Activity in Three Different Schedules” – Authors: D.D. Von Hoff, G.S. Jameson, M.J. Borad, L.S. Rosen, J. Utz, M. Basche, C. Alemany, S. Dhar, L. Acosta, T. Barker, J. Walling, J.T. Hamm.

## **About NKTR-102**

Nektar is developing NKTR-102, a PEGylated form of irinotecan, which was invented by Nektar using its small molecule PEGylation technology platform. NKTR-102 is the first PEG-oncolytic that leverages Nektar's innovative small molecule PEGylation chemistry. Using a proprietary approach that directly conjugates the drug to a unique PEG structure, Nektar is the first company to have created a PEGylated small molecule with a unique pharmacokinetic profile that has demonstrated therapeutic activity in patients.

NKTR-102 is entering Phase 2 clinical development in breast, ovarian and cervical cancers in the fourth quarter of 2008. A Phase 2b randomized trial evaluating NKTR-102 monotherapy versus irinotecan in second-line colorectal cancer patients with the KRAS mutant gene is also planned to begin by the end of 2008. A Phase 2a study evaluating NKTR-102 in combination with cetuximab is ongoing.

## **About Nektar**

Nektar Therapeutics is a biopharmaceutical company developing novel therapeutics based on its unique and proprietary PEGylation and advanced polymer conjugate technology platforms. Nektar's technologies and drug development expertise have enabled eight approved products for partners, which include leading biopharmaceutical companies. Nektar has a robust pipeline of high-value therapeutics in development, including two programs in Phase 2 development, NKTR-102 (PEG-irinotecan) for solid tumors and NKTR-118 (oral PEG-naloxol) for opioid-induced constipation.

This press release contains forward-looking statements that reflect the company's current views regarding the potential, progress, and clinical plans for the company's proprietary and partnered product pipeline, and the value and potential of the company's technology platforms. These forward-looking statements involve risks and uncertainties, including but not limited to: (i) the company's proprietary product candidates and those of its partners are in various stages of clinical development and the risk of failure is high and can occur at any stage prior to regulatory approval; (ii) the timing or success of the commencement or end of clinical trials and commercial launch of partnered products may be delayed or unsuccessful due to slower than anticipated patient enrollment, drug manufacturing challenges, changing standards of care, clinical trial design, clinical outcomes, or delay or failure in obtaining regulatory approval in one or more important markets; (iii) clinical trials are long, expensive and uncertain processes and the risk of failure of any product that is in clinical development and prior to regulatory approval remains high and can occur at any stage due to efficacy, safety or other factors; (iv) the company's patent applications for its proprietary or partner product candidates may not issue, patents that have issued may not be enforceable, or intellectual property licenses from third parties may be required in the future; and (v) the outcome of any existing or future intellectual property or other litigation related to the company's proprietary product candidates. Other important risks and uncertainties are detailed in the company's reports and other filings with the Securities and Exchange Commission, including its most recent Quarterly Report on Form 10-Q. Actual results could differ materially from the forward-looking statements contained in this press release. The company undertakes no obligation to update forward-looking statements, whether as a result of new information,

future events or otherwise. For more information on Nektar Therapeutics, please visit [www.nektar.com](http://www.nektar.com)

Stephan Herrera, 415-488-7699  
[sherrera@nektar.com](mailto:sherrera@nektar.com)

Jennifer Ruddock, 650-631-4954  
[jruddock@nektar.com](mailto:jruddock@nektar.com)

1 Diederik F. S. Kehrer et al., Factors Involved in Prolongation of the Terminal Disposition Phase of SN-38: Clinical and Experimental Studies, *Clinical Cancer Research* 2000; 6; 3451–3458.

**###**