

# News Release

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## **New Positive Data Announced for NKTR-102 (PEG-irinotecan), Highlights Promise of Nektar's Innovative Small Molecule PEG-Oncolytics**

**San Carlos, Calif., June 2, 2008** -- Nektar Therapeutics (Nasdaq: NKTR) announced new positive data today from a Phase 1 clinical study for NKTR-102 (PEG-irinotecan) in advanced cancer patients whose tumors had progressed on other therapies. Significant anti-tumor activity was observed in all dose schedules of the study for NKTR-102 with partial responses observed in seven out of 44 total patients (16 percent) in the trial. The data highlights the potential of Nektar's innovative 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.

A total of 44 patients were evaluated in the NKTR-102 single-agent Phase 1 study. Patients were enrolled in one of three dose schedules: weekly x3 Q4 weeks, every two weeks (q14 days), and every three weeks (q21 days). Of the 44 patients in total from all dose schedules, 13 patients exhibited anti-tumor activity. Seven patients, or 16 percent, had partial responses (greater than 30 percent tumor regression per RECIST), and six patients, or 12 percent, had other evidence of anti-tumor activity (tumor regression by more than 15 percent but less than 30 percent per RECIST, or significant biomarker evidence). Repeat evidence of anti-tumor activity was observed in a number of tumor settings, including breast and ovarian.

The comprehensive results from this study will be discussed by Dr. Daniel D. Von Hoff, the lead clinical investigator for the NKTR-102 Phase 1 trial, at an event to be held on June 2, 2008 at 6:30 PM Central time during the ASCO 2008 Annual Meeting in Chicago, Illinois. Dr. Von Hoff serves as Physician-in-Chief at the Translational Genomics Research Institute and Chief Scientific Officer for the Scottsdale Clinical Research Institute at Scottsdale Healthcare.

"The high activity of NKTR-102 in multiple tumor settings greatly exceeds expectations for a single oncolytic agent in a classic Phase 1 study," said Dr. Von Hoff. "A typical response rate observed with a single agent in Phase 1 is about four percent. With NKTR-102, we observed an overall response rate considerably higher than that. This rate, combined with the drug's activity in a number of tumor settings, strongly supports the aggressive development of this drug."

The company previously reported preliminary results for 32 patients in the study that were on the weekly dose schedule (weekly x3 Q4 weeks).<sup>1</sup> These interim results showed partial responses in a total of three patients (10 percent) and other evidence of anti-tumor activity in four patients. Increased SN38 levels, the active metabolite of irinotecan, was also observed with administration of NKTR-102 (PEG-irinotecan), with exposures up to six-fold higher than predicted with irinotecan at equivalent doses.

Nektar's proprietary PEGylation technology can enhance the properties of therapeutic agents by increasing drug circulation time, improving pharmacokinetics, decreasing immunogenicity and dosing frequency, increasing bioavailability and improving drug solubility and stability. Using our proprietary technology, Nektar is the first company to create a PEGylated small molecule with a unique pharmacokinetic profile that has demonstrated therapeutic activity in patients.

## Clinical Trial Summary

In the Phase 1 dose-escalation trial, the safety, pharmacokinetics and anti-tumor activity of NKTR-102 monotherapy was evaluated in 44 patients with advanced solid tumors who had failed prior treatments or had no standard treatment available to them. Patients received 90-minute infusions of NKTR-102 (PEGylated irinotecan) as follows: weekly for three weeks with the fourth week off (n=32); q 14 days or every two weeks (n=6); and q 21 days or every three weeks (n=6). Tumor responses were evaluated according to RECIST (Response Evaluation Criteria in Solid Tumors) criteria. The q14 and q21 day dose schedules in the study are ongoing.

Doses ranges 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> to 170 mg/m<sup>2</sup>. Tumor regression, anti-tumor activity or prolonged disease stabilization was observed in a broad spectrum of cancer types, including breast, ovarian, cervical, bladder, non-small cell lung cancer, small cell lung cancer, adrenocortical, esophageal, maxillary sinus and Hodgkins lymphoma.

Side effects of clinical significance observed in the first and second dose schedules were diarrhea and neutropenia, with diarrhea being the dose-limiting toxicity associated with NKTR-102. There was no significant diarrhea and neutropenia observed in the every three week (Q21 days) dose schedule.

NKTR-102 exhibited extended pharmacokinetics in this Phase 1 trial. Serial plasma concentrations of NKTR-102, irinotecan, active metabolite SN38 and SN38-glucuronide were quantified by LC-MS/MS. Nektar's small molecule PEGylation technology produced an increase in cumulative SN38 exposure that was up to six-fold higher than the exposure previously reported with irinotecan. SN38, a topoisomerase I inhibitor, is the active metabolite of irinotecan.

The Phase 1 trial, 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.

## Webcast Replay Information

A Webcast replay of the data presentation made by Dr. Von Hoff is available on Nektar's website at [www.nektar.com](http://www.nektar.com), or can be accessed using the following url:

<http://phx.corporate-ir.net/phoenix.zhtml?p=ir-ol-eventDetails&c=72130&eventID=1851169>

## About NKTR-102

Nektar is developing NKTR-102, a PEGylated form of irinotecan, which was invented by Nektar using its world-leading small molecule PEGylation technology platform. The product is currently in Phase 2 clinical development. Irinotecan is an important chemotherapeutic agent used for the treatment of solid tumors, including colorectal and lung cancers. By applying Nektar's small molecule PEGylation technology to irinotecan, NKTR-102 may prove to be a more powerful and tolerable anti-tumor agent. Preclinical studies show that treatment with NKTR-102 results in significant suppression of tumor growth in an irinotecan-resistant mouse colorectal tumor model and in similar models of breast and lung cancer. Administration of NKTR-102 in an animal model also results in a markedly improved time-concentration profile for SN38, the active metabolite of irinotecan, as compared to treatment with irinotecan.

Nektar PEGylation technology can enhance the properties of therapeutic agents by increasing drug circulation time in the bloodstream, decreasing immunogenicity and dosing frequency, increasing bioavailability and improving drug solubility and stability. It can also be used to modify pharmaceutical agents to preferentially target certain systems within the body. It is a technique in which non-toxic polyethylene glycol (PEG) polymers are attached to therapeutic agents, and it is applicable to most major drug classes, including proteins, peptides, antibody fragments, small molecules, and other drugs. Nektar PEGylation technology is also used in eight additional approved partnered products in the U.S. or Europe today, including UCB's Cimzia® for Crohn's Disease, Roche's PEGASYS® for hepatitis C and Amgen's Neulasta® for neutropenia.

## About Nektar

Nektar Therapeutics is a biopharmaceutical company that develops and enables differentiated therapeutics with its industry-leading PEGylation and pulmonary drug development technology platforms. Nektar PEGylation and pulmonary technology, expertise, manufacturing capabilities have enabled eight approved products for partners, which include the world's leading pharmaceutical and biotechnology companies. Nektar also develops its own products by applying its PEGylation and pulmonary technology platforms to existing medicines with the objective to enhance performance, such as improving efficacy, safety and compliance.

This press release contains forward-looking statements regarding the potential of NKTR-102 and the company's PEGylation technology platform. These forward-looking statements involve important risks and uncertainties, including but not limited to: (i) preclinical testing and clinical trials for NKTR-102 are long, expensive and uncertain processes, (ii) because the NKTR-102 product development programs are in the early phases of clinical development, the risk of failure is high and can occur at any stage of development, (iii) the company may fail to obtain regulatory approval of NKTR-102, (iv) the timing or success of the commencement or conclusion of NKTR-102 clinical trials is subject to a number of uncertainties including but not limited to clinical design, patient enrollment, regulatory requirements and clinical outcomes (v) potential competition from existing approved products (branded or generic) or product candidates under development by other companies could negatively impact the commercial potential of NKTR-102 due to such common industry competitive factors as efficacy and safety profiles, pricing, and reimbursement by third party payers, and (vi) the company's patent applications for NKTR-102 may fail to issue; patents that have issued may not be enforceable; or unanticipated intellectual property licenses from third parties may be required in the future. Other important risks and uncertainties are detailed in the company's reports and other filings with the SEC including its most recent Quarterly Report on Form 10-Q filed with the SEC on May 9, 2008. 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. No information regarding or presented at the scientific meetings referred to above (or contained at the Internet links provided) is intended to be incorporated by reference in this press release.

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## References

<sup>1</sup> Nektar press release dated May 16<sup>th</sup> 2008 "Significant Anti-Tumor Activity of NKTR-102 in Patients with Refractory Solid Tumors; Interim Data Published in ASCO 2008 Proceedings" and Borad, M.J., Hamm, J.T., Rosen, L.S., Jameson, G., Utz, J., Mulay, M., Eldon, M., Dhar, S., Acosta, L., Von Hoff, D.D., "Phase 1 Dose-finding and pharmacokinetic study of NKTR-102 (Pegylated irinotecan): early evidence of anti-tumor activity"; *J Clin Oncol* 26: 2008 (May 20 suppl; abstr 13518).

Additional references are Horstmann, E, McCabe, M, Grochow, L, Yamamoto, S, Rubinstein, L, Budd T, Shoemaker, D Emanuel, E., and Grady, Christine. "*Risks and Benefits of Phase 1 Oncology Trials, 1991 through 2002. Table 1. Rates of Response to Treatment in Phase 1 Oncology Trials,*" N Engl J Med, 352;9; March 3, 2005.