# NKTR-102 Shows High Response Rate and Sustained Duration of Response in Women with Platinum-Resistant/Refractory Ovarian Cancer Previously Treated with Doxil®

## Phase 2 Data Highlighted in Presentation at 2011 American Society of Clinical Oncology Annual Meeting

CHICAGO, June 5, 2011 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced positive results from a subpopulation of patients in a Phase 2 clinical study evaluating single-agent NKTR-102 in women with platinum-resistant/refractory ovarian cancer. A total of 33 women in the study with prior Doxil® (pegylated liposomal doxorubicin or PLD) treatment were evaluable for response rate using either RECIST 1.0 criteria (response by tumor imaging) or Gynecologic Cancer InterGroup (GCIG) criteria, which is a combination of RECIST and/or ovarian cancer biomarker (CA-125) criteria.(1) Confirmed and unconfirmed objective response rates using RECIST were 25 percent (4/16) and 29 percent (4/14) for the q14d and q21d dose schedules, respectively. Confirmed objective response rates using RECIST were 19 percent (3/16) and 21 percent (3/14) for each dose schedule, respectively. GCIG (confirmed and unconfirmed) response rates were 50 percent (8/16) in the once every 14 days (q14d) dose schedule and 35 percent (6/17) for the once every 21 days (q21d) dose schedule. Confirmed objective GCIG response rates were 38 percent (6/16) and 35 percent (6/17) in the q14d and q21d dose schedules, respectively.

Median progression-free survival for all 33 patients in the subpopulation previously treated with PLD was 5.4 months and median overall survival was 13.9 months. The median duration of confirmed response was 4.2 months in the q14d schedule and 4.4 months in the q21d schedule.

"NKTR-102 exhibits an exceptionally high response rate and long median survival compared to what would be expected in this group of heavily pre-treated women with platinum-resistant and refractory ovarian cancer," said Dr. Agustin Garcia, Associate Professor of Clinical Medicine at USC Norris Comprehensive Center. "Women whose cancer has progressed following treatment with PLD represent a very high unmet medical need as there are currently no good treatment options available for these women. These results demonstrate that NKTR-102 holds great therapeutic potential for women battling ovarian cancer. We look forward to the continued late-stage development of NKTR-102."

NKTR-102 was generally well tolerated in the subset of women with prior PLD treatment, particularly in the q21 dose schedule. The most common Grade 3 and 4 side effects were diarrhea, hypokalemia, and nausea, with most side effects being Grade 3 in severity. [Table 3.]

### NKTR-102 Phase 2 Data Presentation in Ovarian Cancer

- *The role of NKTR-102 in women with platinum resistant/refractory ovarian cancer and failure on pegylated liposomal doxorubicin (PLD).*
  Abstract #5047, Poster Board #15C
  General Poster Session: Gynecologic Cancer
  Session Date and Time: Sunday, June 5, 2011, 8:00 AM — 12:00 PM, Central Time
  Location: Hall A

The NKTR-102 Phase 2 Study was an international, multicenter, open-label, randomized, two-stage study to evaluate NKTR-102 when given either on a q14d or q21d regimen in women with platinum-resistant/refractory disease to any line of platinum-based chemotherapy (platinum-free interval ≤6 months). 46 percent (33/71) of the women in the study had failed prior treatment with PLD. Median lines of prior therapy for this subpopulation of women enrolled in the study were 4. The primary endpoint of the study was objective response rate (based on RECIST and GCIG response criteria). Secondary endpoints were safety, progression-free survival and overall survival.

**TABLE 1. Patient Demographics: Prior Therapies in Subpopulation Receiving Prior Treatment with PLD**

| | NKTR-102 145 mg/m2 q14d (N=16) | NKTR-102 145 mg/m2 q21d (N=17) | Total (N=33) |
|---|---|---|---|
| Prior Lines of Therapy (median) | 4 | 4 | 4 |
| Previous Platinum Regimens | | | |

| | | | |
|---|---|---|---|
| 1 | 13% | 35% | 24% |
| 2 | 56% | 24% | 39% |
| 3 | 25% | 18% | 21% |
| 4+ | 6% | 24% | 15% |
| Prior bevacizumab | 6% | 24% | 15% |
| Prior gemcitabine | 56% | 59% | 58% |
| Prior taxane | 100% | 100% | 100% |

**TABLE 2. Efficacy Results: Objective Response Rates by RECIST and GCIG in Subpopulation Receiving Prior Treatment with PLD**

| | **NKTR-102 145 mg/m2 q14d** | **NKTR-102 145 mg/m2 q21d** |
|---|---|---|
| **RECIST** | | |
| N (evaluable) | 16 | 14 |
| Confirmed + Unconfirmed | 4 (25%) | 4 (29%) |
| Confirmed | 3 (19%) | 3 (21%) |
| Duration of Confirmed Response (months, range) | 4.2 (3-14) | 4.4 (3-9) |
| **GCIG** | | |
| N (evaluable) | 16 | 17 |
| Confirmed + Unconfirmed | 8 (50%) | 6 (35%) |
| Confirmed | 6 (38%) | 6 (35%) |
| **CA-125** | | |
| N (evaluable) | 15 | 14 |
| Confirmed | 6 (40%) | 5 (36%) |

*Only patients with measurable disease/CA-125 at baseline were considered evaluable.

**TABLE 3. Safety Results in Subpopulation Receiving Prior Treatment with PLD**

| Most Common Drug-related Grade 3 and 4 Adverse Events > 5% or event of interest N (%) | NKTR-102 145 mg/m2 q14d N=16 | | NKTR-102 145 mg/m2 q21d N=17 | |
|---|---|---|---|---|
| | Grade 3 | Grade 4 | Grade 3 | Grade 4 |
| Diarrhea | 5 (31%) | 0 | 3 (18%) | 0 |
| Hypokalemia | 5 (31%) | 1 (6%) | 0 | 0 |
| Nausea | 5 (31%) | 0 | 1 (6%) | 0 |
| Dehydration | 3 (19%) | 0 | 1 (6%) | 0 |
| Fatigue | 1 (6%) | 0 | 3 (18%) | 0 |
| Vomiting | 4 (25%) | 0 | 0 | 0 |
| Neutropenia | 1 (6%) | 0 | 1 (6%) | 1 (6%) |
| Anaemia | 2 (12.5%) | 0 | 0 | 0 |
| Decreased appetite | 1 (6%) | 0 | 1 (6%) | 0 |
| Hyponatraemia | 2 (13%) | 0 | 0 | 0 |
| Lymphophenia | 1 (6%) | 0 | 1 (6%) | 0 |

Note: There was one death in the q14d schedule due to renal failure from dehydration, possibly related to treatment.

## About Ovarian Cancer

Nearly all ovarian cancers will become resistant or refractory to platinum-based therapy over time. Ovarian cancer is the fifth leading cause of cancer deaths among women, accounting for more deaths than any other cancer of the female reproductive system.(2) Approximately 22,000 new cases of ovarian cancer will be diagnosed and 15,000 deaths are expected to be caused by ovarian cancer in the United States this year.(2) Initial response rates to treatment with platinum-based agents can be as high as 80 percent, but most patients recur. Treatment options following relapse are limited and overall long-term survival among ovarian cancer patients has not changed significantly in nearly 40 years.(3) Agents currently approved by the

U.S. Food & Drug Administration to treat women with platinum-resistant ovarian cancer have modest overall response rates of between 6.5 to 13.8 percent.(4,5)

**About NKTR-102**

Nektar is developing NKTR-102, a next-generation topoisomerase I inhibitor with reduced peak concentrations and a continuous concentration profile. NKTR-102 was invented by Nektar using its advanced polymer conjugate technology platform, and is the first oncology product candidate to leverage Nektar's releasable polymer technology platform.

In addition to the fully-enrolled Phase 2 studies in platinum-refractory/resistant ovarian cancer and metastatic breast cancer, NKTR-102 is also being tested in a separate Phase 2 clinical trial in patients with second-line colorectal cancer and a Phase 1 clinical trial evaluating NKTR-102 in combination with 5-FU therapy. An expansion arm of the Phase 2 study of single-agent NKTR-102 in platinum-refractory/resistant ovarian cancer in women who failed prior Doxil therapy is also currently enrolling. A Phase 3 study of single-agent NKTR-102 is planned in metastatic breast cancer.

**About Nektar**

Nektar Therapeutics is a biopharmaceutical company developing novel therapeutics based on its PEGylation and advanced polymer conjugation technology platforms. Nektar's technology and drug development expertise have enabled nine approved products in the U.S. or Europe for leading biopharmaceutical company partners, including UCB's Cimzia(R) for Crohn's disease and rheumatoid arthritis, Roche's PEGASYS(R) for hepatitis C and Amgen's Neulasta(R) for neutropenia.

Nektar has created a robust pipeline of potentially high-value therapeutics to address unmet medical needs by leveraging and expanding its technology platforms to improve and enable molecules. In addition to the releasable polymer technology, Nektar is the first company to create a permanent small molecule-polymer conjugate with enhanced oral bioavailability and restricted entry into the CNS. Nektar is currently conducting clinical and preclinical programs in oncology, pain and other therapeutic areas. Nektar entered into an exclusive worldwide license agreement with AstraZeneca for its oral NKTR-118 program to treat opioid-induced constipation and its NKTR-119 program for the treatment of pain without constipation side effects. NKTR-102 is being evaluated in Phase 2 clinical studies for the treatment of ovarian, breast and colorectal cancers. NKTR-105 is in a Phase 1 clinical study in cancer patients with refractory solid tumors.

Nektar is headquartered in San Francisco, California, with additional R&D operations in Huntsville, Alabama and Hyderabad, India. Further information about the company and its drug development programs and capabilities may be found online at http://www.nektar.com.

This press release contains forward-looking statements that reflect Nektar's current views regarding the potential of its technology platform, the potential of NKTR-102 for ovarian cancer patients, results from a subpopulation of patients from the Phase 2 clinical study of NKTR-102 in ovarian cancer patients, and the potential of certain other drug candidates in Nektar's pipeline. These forward-looking statements involve substantial risks and uncertainties, including but not limited to one or more of the following: (i) NKTR-102 is in mid-stage clinical development and the risk of failure remains high and failure can unexpectedly occur at any stage for one or more of the cancer indications being studied (i.e. ovarian cancer, breast cancer, and colorectal cancer) due to efficacy, safety or other unpredictable factors even after earlier clinical results have been positive; (ii) the data package required and the timing for regulatory approval of a new drug application (NDA) is very uncertain and difficult to predict due to broad regulatory discretion, changing standards of care, available approved therapies, the size of the completed clinical trials and the statistical significance of the results, the potential need for comparative clinical studies against approved therapies, and other important factors that are not within the control of Nektar; (iii) the results from the expanded Phase 2 clinical study for NKTR-102 in platinum-resistant/refractory ovarian cancer patients are unlikely to result in a review or an approval of an NDA by the United States Food and Drug Administration; (iv) the timing or success of the commencement or end of clinical trials and commercial launch of new drugs may be delayed or unsuccessful due to commercial and funding considerations, regulatory delays, clinical trial design, slower than anticipated patient enrollment, drug manufacturing challenges, changing standards of care, clinical outcomes, or delay or failure in obtaining regulatory approval in one or more important markets; (v) the Phase 2 results for NKTR-102 in ovarian cancer patients previously treated with PLD set forth in this press release remain subject to audit and confirmation procedures, and therefore the results may change materially and adversely after such procedures are completed; (vi) the data in this press release is not necessarily predictive of the outcome of the expansion arm of the Phase 2 study of NKTR-102 in patients with platinum resistant/refractory ovarian that have received prior treatment with PLD—therefore the results from this expanded Phase 2 study population could be materially and adversely different than the results described in this press release; (vii) additional important data will be reported by Nektar in the future regarding the Phase 2 NKTR-102 clinical study in ovarian cancer (including without limitation the expansion arm of the study) and therefore the future results from this ongoing Phase 2 ovarian cancer study may differ materially and adversely from the preliminary interim results presented in this press release; (viii) Nektar's patent applications for its proprietary or partner product candidates may not issue, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required in the future; (ix) the uncertain outcome of any future intellectual property, commercial or other litigation related to Nektar's proprietary product candidates, including without limitation NKTR-102; and (x) certain other important risks and uncertainties set forth in Nektar's Quarterly Report on Form 10-Q for the quarter ended March

31, 2011, filed with the Securities and Exchange Commission on April 29, 2011. Actual results could differ materially from the forward-looking statements contained in this press release. Nektar undertakes no obligation to update forward-looking statements, including but not limited to any clinical, FDA or other regulatory information, whether as a result of new information, future events or otherwise.


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(1) 2005 International Gynecologic Cancer Society. Gynecological Cancer Intergroup, http://www.gcig.igcs.org/CA-125.html and Therasse P, Arbuck SG, Eisenhauer EA, et al. *New guidelines to evaluate the response to treatment in solid tumors*. J Natl Cancer Inst. 2000; 92:205-216)

(2) *American Cancer Society*, 2009.

(3) Ovarian Cancer National Alliance

(4) Gordon et al., *Journal of Clinical Oncology* 2001, 19: 3312-3322

(5) Doxil US Package Insert, 2008. http://www.doxil.com/


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