Nektar Therapeutics

Hold

NKTR: $11.23
Price Target: $11.00

Biotechnology

NKTR: Shifting NKTR-102 Catalysts & Adjusting Market size; Downgrade To Hold

THINK ACTION:
Based on due diligence with KOLs regarding potential development paths forward for NKTR-102 in Breast Cancer (BC) we believe the BC opportunity for NKTR-102 may be smaller than we previously estimated. While fundamentals remain strong, NKTR has decided to not partner NKTR-102 and recent management guidance call for us to readjust expected mid-11 catalysts to YE11. We remain positive on NKTR longer term but are decreasing our 12 month price target to $11 (prev. $17) and moving to a Hold rating (prev. Buy). We would take advantage of weakness if shares drift below $8 in the future.

KEY POINTS:
Docs on NKTR-102 Data: Overall, our KOLs suggest NKTR-102 is a more active therapeutic candidate than most at its stage of development. On the positive side, consultants believe patients evaluated in the NKTR-102 BC Phase 2 trial were more homogenous than the first 70 patients in the Phase 2 ovarian study, increasing potential longer-term predictive therapeutic value.
NKTR-102 BC Development Path ahead: Given the importance of BC to the overall NKTR-102 market opportunity in conjunction with management enthusiasm to not partner the compound, we have been keenly interested in understanding the optimal clinical risk/peak sales revenue development path forward including associated funding expenses. Available NKTR guidance provides these details for the Phase 3 BC program ahead: 1) planning underway with KOLs; 2) likely to enroll ~800 patients in a randomized controlled study of single-agent NKTR-102; 3) final design target in 2Q11; 4) initiation target in 4Q11; 5) include high populations such as Anthracyclin (A)/Taxane (T) failures, AT/C (Capecitabine) failures or triple negative BC. While impressed with the NKTR-102 BC data, our consultants believe a clear regulatory strategy and path ahead in BC is complicated by competitive approved therapies in a crowded market. The most promising designs recommended by KOLs are: 1) NKTR-102 vs. Xeloda (capecitabine) or Xeloda w/wo NKTR-102 in AT failure patient with residual signs of serious neuropathy post AT therapy (we est. 20% of AT failures), and 2) NKTR-102 vs. Best Investigator Choice in Triple Negative BC patients (we also ets. 20% of patients). Based on these suggested designs we are decreasing our projected peak NKTR-102 sales to $1.5B from $1.8B previously.Please see our doc call transcript on pages 2-11.
Financials: NKTR recently completed a 19M share offering (2.8M share overallotment) that we estimate results in a current cash position of over $500M (near $4.66 per share). Without clarity on the NKTR-102 development program ahead, especially for BC but also colorectal cancer (CRC), we are unsure what these resources will fund but they could be utilized to retire $215M in outstanding convertible debt due Sept-12 (3.25%, $21.69 strike).

2011 Potential Catalysts: Recent presentations by NKTR management suggest to us that catalysts we expected starting in mid-11 will not be available until YE11. For 2011, potential drivers include: 1) maturing NKTR-102 Breast and Ovarian data sets beginning toward YE11, and, 2) NKTR-118 Phase 3 trial initiations in 1H11. We currently do not believe NKTR-102 Phase 2 Colorectal data will be available until 2012.
New Hold Rating and $11PT: We are decreasing our price target to $11 (prev. $17) and moving to a Hold rating (prev. Buy). We foresee a number of potential positive drivers starting toward YE11 and would take advantage of

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Changes	Current	Previous
Rating	Hold	Buy
Price Target	$11.00	$17.00
FY11E REV (M)	$76.7E	--
FY12E REV (M)	$99.2E	--
FY11E EPS	($1.12)E	--
FY12E EPS	($0.94)E	($1.03)E

52-Week High:	$16.06
52-Week Low:	$10.38
Shares O/S-Diluted (M):	115.4
Market Cap (M):	$1,295.9
Average Daily Volume:	1,025,628
Short Interest:	17.7%
Debt/Total Cap:	0.7%
Net Cash Per Share:	$4.66
P/E (12-month forward):	NA
Est. Long-Term EPS Growth:	NA
P/E/G:	NM
Fiscal Year-End:	Dec

REV (M) $	2010E	2011E	2012E
Mar	33.2A	34.9E	NA
Jun	42.6A	13.1E	NA
Sep	37.9A	14.6E	NA
Dec	41.6E	14.2E	NA
FY	155.3E	76.7E	99.2E
CY	NA	NA	NA
FY P/S	8.3x	16.9x	13.1x
CY P/S	8.3x	16.9x	13.1x

EPS $	2010E	2011E	2012E
Mar	(0.07) A	(0.06) E	NA
Jun	(0.01) A	(0.34) E	NA
Sep	(0.09) A	(0.38) E	NA
Dec	(0.18) E	(0.35) E	NA
FY	(0.31) E	(1.12) E	(0.94) E
CY	NA	NA	NA
FY P/E	NM	NM	NM
CY P/E	NM	NM	NM

ThinkEquity NKTR-102 Breast & Ovarian Cancer KOL Conference Call Transcript:

Format of Call: 30 minutes of interview followed by a Q&A session.

Consultant Background:

Consultant: I am a Medical Oncologist, I specialize on breast and ovarian cancer, I've been in practice for a little over ten years, half of my time is in clinical care and the other half of the time is teaching and research. For instance, my research and clinical practice interests are breast and ovarian cancer, I participate mostly in drug development and clinical trials for both tumor types, and am informed of drugs and development even though we might not be participating in those trials.

Marko Kozul: Can you describe for us, which clinical stage, or recently-approved breast and ovarian cancer agents you might be most familiar with?

Consultant: Well in terms of recently-approved agents, these are the ones that I am most familiar with. For ovarian cancer, I don't think we have approved anything on ovarian cancer in a long time, but I'm very familiar with Avastin for ovarian cancer, and familiar also with PARP Inhibitors in both tumors, (HER-2) Inhibitors, most of them such as TDM1, Labatinib, which was recently approved. For ovarian cancer I am familiar with Yondelis, NKTR-102 for both tumors, EC145 for ovarian cancer, and so on.

Marko Kozul: I will have more questions on some of those later on in the call. For now, can you briefly describe which of these agents you consider the most promising for breast or ovarian?

Consultant: For ovarian cancer, I think more in terms of how closely they would be to getting approved. It's still Avastin, PARP-Inhibitors, NKTR-102, and I think I'm also fairly excited with EC-145. For breast cancer, obviously we are very excited about BSI-201 until a week ago, but I still think that the PARP Inhibitors are important agents and promising agents for breast cancer. TDM-1, Neratinib (HKI-272), I think those are the ones that are more relevant right now.

BREAST CANCER OVERVIEW:

Marko Kozul: Thanks, maybe we can move the discussion a little more onto breast cancer, and then the same with ovarian after. Maybe just a quick review first on how you treat some of your metastatic breast cancer patients and then onto ovarian therapies.

Consultants: So for the frontline treatment, or initial treatment for breast cancer always has to be divided in a couple of molecular feature of a tumor with HER-2+ and the counterpart negative for one or the other. If patients have shown which of the positive tumors, their initial treatment will be with hormonal manipulations, eventually all of them will become resistant to hormonal therapy and they will start chemotherapy.

In HER-2+ tumors it implies that all patients will receive a HER-2 targeted agent as part of their treatment, most frequently in combination with chemotherapy. Then the patients who are either hormone receptive positive will become resistant to hormonal therapy, or those patients that are the so-called Triple-Negative, those patients will be focused and their treatment chemotherapy.

I think the common ground, that everybody will agree, is that treatment of Metastatic Cancer is an incurable disease. So there are then different philosophies in terms of how to approach that. Our approach is to say, well if we can cure patients, we should try to maintain their quality of life (QoL), for as long as we can, and that in our opinion implies also using a drug that has a better or a more favorable toxicity profile. So we are big believers of having our initial treatment being with Xeloda (capecitabine) as the loader, because of the toxicity profile and convenience of administration, etc.

But I think that happens more in the academic centers where we are not so influenced by the business of administering chemotherapy drugs than in private practices. Probably the agent I have used most commonly, besides Xeloda (capecitabine) as frontline treatment for metastatic breast cancer are the taxols, either weekly paclitaxel or docetaxel. In between the taxols and Xeloda, I think that covers the vast majority of initial chemotherapies for breast cancer.

And then there is a whole laundry list of other agents that can be used for 2nd, 3rd line and so on. Probably the only little exception or difference is for Triple Negative tumors which are frequently more resistant in general to chemotherapy. There was and still exists, a push for using platinum-based regimens in that subset. I think that's part of the reason some

of the ongoing trials looking into Triple Negative have used platinum, and they thought they were going to be better agents. I personally don't think they are any better than any other chemotherapy drugs.

Once a patient receives either Xeloda (capecitabine) or a Taxane as their initial treatment, the second-line treatment will include using agents or other drugs such as Gemcitabine, Navelbine, Ixempra (ixabepilone), Eribulin now, and probably those are the most commonly-used drugs.

Marko Kozul: For some of these commonly-used chemotherapies you mentioned, the Anthracyclins, Xeloda (capecitabine), Eribilin etc, could you just briefly, maybe discuss some of the strengths and weaknesses or pros and cons of using these therapies?

Consultant: Well of all these agents, at the end I think they have similar activity, and that's why you will get different opinions from different physicians in terms of which ones to start with, and they all are overall similar and most them don't improve overall survival, so in terms of the efficacy, they are similar. Physicians will be biased in favor of one or the other, but I think if push comes to shove, we would all admit at the end they're probably similar. What that means is none of them is wonderful, if there was a clear winner and a model we could use to discover this, the use of Herceptin for HER-2+ breast cancer is still by far the most commonly utilized agent, because everybody acknowledges the setting is clear or a very effective drug when combined with chemotherapy.

But chemotherapy alone is not a highly effective, so the median survival of patients is around 2 years. In general, with single agents you have response rate of around 20%. What they have is different treat scales for administration and different toxicities. Capecitabine has the advantage that it is an oral agent, and therefore more convenient and easy to administer to the patient. It does not have the hair loss and vomiting that patients are usually concerned about. A disadvantage is also that it is an oral agent, so you have to rely on the patient on being compliant with the drug. We know that with many drugs and medicines, patients are not as compliant as we would like them to be.

Taxanes are very important agents, probably one of the limitations is that many patients with breast cancer now have received a taxane as part of their initial treatment when they had early disease. The implication of that is that the taxane are associated with development of peripheral neuropathy. If patients are being pre-exposed to a taxane then they have a higher likelihood of developing neuropathy when they were treated.

Ixempra (ixabepilone) and Eribulin have similar problems that they are also agents that target the microtubular system and therefore one of their side effects is a peripheral neuropathy. Both agents probably have somewhat different neuropathies than the taxanes, particular in the sense that they probably recover better than from neuropathy associated with taxanes.

Gemcitabine and Vinorelbine are very effective drugs, and I think that their biggest practical weakness is that they don't have an indication for use as a single agent for breast cancer. As a result they were never seriously marketed and are predominantly used off-label.

NKTR-102 in BREAST CANCER:

Marko Kozul: Moving on to Nektar's compound, the PEGylated Irinotecan candidate of NKTR-102, data was presented back in December at SABCS. What are your general thoughts about this compound and can you review your impressions of the data that were presented?

Consultant: So the simplest answer to your question is that I have no question that it's an effective active agent in metastatic breast cancer, and that's because the active agent is irinotecan, which is a drug that was evaluated in the '90s for breast cancer. It was an active drug but I assume that in part because of business decisions from whoever owned irinotecan back then, it wasn't developed further than breast cancer yet the drug works in breast cancer.

Now the next more challenging question is what the best way of strategizing an approval plan is. I think the data that have been presented are actually pretty good so I think it does support what we knew about the preclinical rationale of the drug. The rationale of Irinotecan is that is an active drug in breast cancer and that by formulating the drug with the PEGylated presentation you increase the half-life and you decrease big doses that translate to more activity and less toxicity.
The breast cancer trial that was conducted is basically the same design or similar in design to the ovarian cancer trial. It evaluated patients with metastatic breast cancer that had all received a taxane as part of their prior therapy. Patients were allowed only to have up to 2 prior regiments for metastatic breast cancer. Patients were randomized to receiving the same dose of NKTR-102, administered either every 2 or every 3 weeks. So one of the strengths of the trial is that it's a fairly

homogeneous group of patients and was a fairly pre-treated group of patients but still homogeneous. The majority of patients received an Antracycline, a Taxane, and Xeloda (capecitabine). Part of the aspect is that a large number of the patients had a Triple-Negative breast cancer which is still one of the biggest challenges that we have to treat. In all, the response rate that was reported is roughly ~30% with no big differences between the every 2 and every 3-week scale. I think in this group of patients there has been a relatively high response rate.

The sponsor (NKTR) then started looking into different subsets, such as patients who had received Anthracycline/Taxane (AT), Anthracycline/Taxane/Capecitabine (ATC), Triple-Negative patients, and patients with metastases to visceral organs such as the liver which are usually harder to treat. In all the subsets, the response rate remained in the 30% range which is very promising. Although, I think we have to remember that the overall trials including only 70 patients, so when you start looking into different subsets you end with different subsets of 15 to 20 patients where one or more response could completely change your numbers.

The toxicity that was observed was expected. There was some diarrhea, no neuropathy, not a lot of hair loss (alopecia), and not a lot of myelosuppression. As I mentioned earlier, most of the drugs we use in breast cancer share a common side effect which is a neuropathy that is a cumulative problem for patients. One or two does not have neuropathy as a side effect; so I think the NKTR-102 data appear promising.

REVIEW OF FIRST 70 PATIENTS in PHASE 2 TRIAL:

Marko Kozul: Thanks for reviewing the NKTR-102 data from December. In terms of any predictions you can make on how data might mature from here in terms of Progression Free Survival (PFS), Overall Survival (OS), or at least benchmarks that would suggest the drug is competitive?

Consultant: I think data from the Phase 2 trial are probably going to remain similar. I do not believe they are going to change. I don't recall, I do not believe NKTR has reported a lot in terms of PFS and OS, but I suspect they are probably going to have PFS of around 6 months or something like that, and median survival of around 8-10 months. I believe the data from the Phase 2 trial are going to hold and show it is clearly an active agent in this heavily pretreated group of patients. I think that's not going to change too much, and I think that the drug is an important, useful drug in that patient population. What I believe is more challenging is that for breast cancer I don't think this Phase 2 non-randomized trial has any chance of serving for approval on the face value.

NKTR-102 PHASE 3 TRIAL DESIGNS:

Marko Kozul: That leads to my next question which is, based on the data that's available, how would you advance NKTR-102 forward into pivotal Phase 3 trials?

Consultant: I believe there are 2 potential approaches: 1) looking into the overall population, meaning patients who have received a couple of therapies for metastatic breast cancer, and I think one has to conduct a randomized Phase 3 trial, and probably a reasonable design is looking into the Xeloda (capecitabine) +/- NKTR-102. At least what we know, where it is not taken as used conventionally but it is in colon cancer, and there are supposed to be some synergies between pro-drugs such as Xeloda (capecitabine) and irinotecan. So, I believe that would be one of the approaches. The second approach would be to look at the Triple Negative breast cancer patients where there is really no drug approval specifically with an indication for these patients. therefore, it is also an unmet need because we don't really have fairly active agents in this setting. I don't know if FDA would buy it this but to me a reasonable study would be something similar to the Eribulin trial in which your control arm is a physician's choice. Because I think as a physician we have to acknowledge that there's really no good drug for patients who have received one or two lengths of chemotherapy for Triple Negative breast cancer, we can treat them with many things but none of the are very active. For these reasons I believe a physician's choice control arm is reasonable and this would be the most reasonable design.

Marko Kozul: Maybe just to helm in a little more on each of those, at least an AT failures, ATC failures and Triple Negative breast cancer patients, can you list/refresh what the likely control arms would need to be or make sense for each of those settings?

Consultant: In the AT failure setting, I probably think it should be Xeloda (capecitabine) +/- NKTR-102. In the ATC failure setting, I think one would probably think that your control arm would have to be Ixempra (ixabepilone) because it is

actually approved in that indication. In Triple Negative breast cancer patients, I think the pure control could be a physician's choice. You would need to evaluate patients that have received at least one, if not two lines of prior therapy.

Marko Kozul: Maybe moving back to AT failure patients, what are some of the strengths and weaknesses, or pros and cons of Xeloda (capecitabine) as a control arm?

Consultant: There are 2 things: 1) the dose of capecitabine that is FDA approved is a dose that no one uses in daily practice because it is too toxic. Many trials have been conducted in the last few years, and my opinion is that use of capecitabine as the control arm at the approved dose is part of what the FDA would demand. However, because physicians feel comfortable, they prefer to use the lower dose which they believe is as effective but there is no hard-pressed proof that that is accurate. At the same time, I think companies developing new agents are very happy with using the FDA approved dose as their control arm because they know this control arm is going to be extremely toxic. So an investigational arm against capecitabine would always appear a little bit better, really in terms of toxicity.

The challenge is getting physicians to enroll patients into those studies, because they always are reluctant to give a dose of capecitabine that is much higher than what you would normally use. Most of those trials have very clear and aggressive guidelines for dose modifications so that patients do not run into lots of toxicity, but I still believe in the end that many centers would only enroll one or two patients, because no investigator is too enthusiastic about enrolling their patients to the single agent as a loader.

The other challenge is the design. I think we are in a time of fluctuation in terms of how the FDA looks at what would be the primary endpoint that would satisfy our regulatory agency. Personally, I think that if you had a clinically important improvement in progression-free survival (PFS) and response rate (ORR), even if there is no improvement in survival (OS), then that should be enough. We now know that this is not enough, based on the Avastin story. So now every time you have to improve survival this would require a larger trial, a more expensive, and you are also moving the bar up and making it a little more difficult.

Marko Kozul: Maybe just briefly, the same discussion for ATC failures possibly against the eribulin.

Consultant: For ATC failures I probably would use Ixabepilone, not Eribulin. I would use Ixabepilone but you could use Eribulin as well. If I were to design a trial, I don't know which of the two drugs is better but I do think that Ixabepilone is a lot more toxic. So, I think if you were to evaluate NKTR-102 against Eribulin, you would be evaluating it against the least toxic agent whereas you would actually want compare it against the most toxic drug.

But if we use the two designs, I think the advantages are that you can be very confident that NKTR-102 is going to be a winner in terms of less toxicity and by that I mean the neuropathy. The patients getting either Ixabepilone or Eribulin are going to encounter a fair amount of neuropathy simply because they have received Taxane treatment previously. I think that currently there is a push of saying that when you are looking into drugs in early metastatic breast cancer (mBC), it is difficult to demonstrate improvement in survival because patients live for a longer time. They are exposed to many other drugs that influence resulting overall survival (OS).

As you get patients treated further down the line, there are obviously less options that patients are going to receive as part of their treatment. The endpoint of interest is unfortunately also shorter and you can demonstrate improving the survival. So in AT failures, it may be somewhat difficult to demonstrate an improvement survival or at least the bar would be higher. For ATC failures it is probably a bit easier to show an improvement in survival.

Marko Kozul: Thanks, and to briefly ask the same questions regarding potential in Triple Negative breast cancer patients?

Consultant: In Triple Negative patients I believe the biggest/special challenge is that most drug developers are looking into evaluating drugs in this subset of patients. It is a relatively uncommon patient population, so it becomes harder to conduct trials if everybody is running a trial in that setting, and there are simply less available patients to enroll into the study. It is probably the hardest of the subsets to treat intrinsically as patients are resistant to chemotherapy. This is why we have no effective treatment options for these patients. At the same time because the control arm, either physician's choice or whatever, is unlikely to be a fairly effective because of its nature.
I think that if the data that NKTR-102 has demonstrated in Triple Negative cancer holds up, there would be a reasonable probability of being a positive trial.

Marko Kozul: Thank you. I heard you mentioned neuropathy a couple of times as one of the issues with some of the potential comparative arms. I wanted to ask you something now for balancing all these factors, what might be ideal or your favorite design for NKTR-102 moving forward?

Consultant: I probably would do the Triple Negative trial looking at patients who have received 1 or 2 course of therapy and rondomycin, with NKTR-102 against physicians' choice. I think the data in Triple Negative and all the other subsets, although it still looks very good, there's not a huge difference. If we look at the response rate of capecitabine which was approved many years ago, and the AT failures, maybe a response rate of around 20% and NKTR-102 has demonstrated response rates of ~30%, but the point is there's not such a huge difference.

In the recent BSI-201 studies for Triple Negative breast cancer, the control arm used 2 chemotherapy drugs, so you would expect a higher response rate. In the study, the response rate was 15-16%, so you would expect that with single agent the response rates might be 5-10%. If the response with NKTR-102 in Triple Negative stays in the mid-30s, I believe it is clearly the one where it seems to be a big difference compared to what's already available out there.

Marko Kozul: Would you incorporate neuropathy as a feature in the trial design?

Consultant: I probably wouldn't include it as our important endpoint but I would include it probably just as overall toxicity quality of life (QoL). This way I would have more thorough documentation of neuropathy than what's obtained from most clinical trials. I would not document it to the extreme that Eribulin did in a trial last year where they randomized patients to Eribulin or Ixabepilone, looking into neuropathy only and they were monitoring the specific evolution of neuropathy with little machines that actually quantified the neuropathy and this was very time consuming. I wouldn't go to that extreme, but I would incorporate it as part of the toxicities, and report them as separated category.

Marko Kozul: What percentage of the patients are Triple Negative?

Consultant: It fluctuates, but somewhere probably between 20% of patients.

Marko Kozul: Obviously in the news recently there have been various stories regarding Avastin in breast cancer and the BSI-201 compound. What are your general thoughts or any takeaways from these recent announcements?

Consultant: I think the Avastin story has unfortunately been taken out of context from both the media and how the FDA came to their conclusion. In my mind, nothing has changed with the Avastin data compared to the data which was available when it was approved in 2008. We knew that Avastin improved response rate and PFS and that it did not improve survival and that is also what we know today. Why the FDA decided to take away the indication, I don't think is related to new data becoming available that shows anything different. It is the same data but for whatever reason the FDA decided that it was not enough to maintain the indication of the drug. The media has taken it out of context as well suggesting there is a new discovery that Avastin is a bad drug for breast cancer patients. It is not a bad drug for breast cancer rather it is just not as good as the FDA wants it to be. For BSI-201, I was surprised because of Phase 2 trial looked so promising.

On the other hand, one of the issues about many drugs, such as Avastin and BSI-201, is that they are targeted agents. Ideally, when you're dealing with a targeted agent you have to identify your subset of patients that have the target present in order for the drug to be an effective treatment for those settings. Examples in breast cancer for the HER2+ tumors and receptive positive tumors, in which both Avastin and BSI-201 could potentially treat many patients, we hope that a small subset have the target, but we have not been able to identify them, so we treat the whole patient population. In the end, I think that is the explanation for why BSI-201 was not a positive trial, and there is hope that eventually one will find the target but we are still not there.

OVARIAN CANCER:

Marko Kozul: Maybe we can spend the next 5 minutes on ovarian cancer. Starting with the NKTR-102 data presented at ASCO 2010 in ovarian, what are some of your impressions, differentiating factors, pros and cons of the data.

Consultant: I think there are some big strengths and weaknesses. It is a study with the same design as breast cancer looking at patients that have platinum resistant ovarian cancer with 2 different doses of administering NKTR-102, every 2 or every 3 weeks. The definition in the trial was that you needed to be resistant to platinum, meaning patients experienced relapse within 6 months of their last platinum-based regimen. There was no limit in terms of the number of other chemotherapies so the patient population was much more heterogeneous than for the breast cancer trial population. I think this is a weakness because it is a very disparate group of patients.
We know that a significant number of patients received 2, 3 and up to 4 courses of prior platinum with a large number of patients receiving 3 median courses of prior chemotherapy. I don't know the range but, there were probably patients that had 4-6, prior lengths of therapy. We do know that if we look at the overall patient population, a response rate of 20% is good. If you don't look at the whole group of patients with platinum resistant ovarian cancer, I think there is really nothing too exciting about it. We have many drugs that in platinum resistant patient populations demonstrate response rates of ~20% and that is how Doxil was approved. That is also how Topotecan was approved, and drugs with other approvals such as Pemetrexed, Avastin.

NKTR-102 showed the same the thing by starting to look into different subsets of patients. The company looked at 2 groups of patients. In the first group, they looked at patients who experienced relapse or had progressed while they receiving platinum, which are called Platinum-Refractory, and which normally experience an incredibly low response rate. These patients have response rates of maybe 5-10%. The company also looked into patients who had also been previously treated with Doxil, and who were platinum resistant. Doxil failure patients generally demonstrate low response rates to other agents, in the high single digit, or low teens. In every subset they evaluated in the breast cancer population, the response rates of +20% hold up. So it started becoming a much more exciting and promising drug, either for the Platinum-Refractory patients, or for the Platinum and Doxil failures. Because Platinum-Refractory is actually a pretty uncommon scenario, the new study is focusing on the Platinum-Resistant and Doxil failures. In these patients, currently available drugs have response rates of 10%, so if NKTR-102 could demonstrate a response of 25% it would be a clear step forward.

Marko Kozul: So a quick question on that second stage of the study. Do you have any sense of how enrolments may be progressing?

Consultant: I think it's probably progressing fairly well, probably more or less at the rate they were expecting. Because it is a more homogeneous patient population, the accrual is slower than it was before. Previously, they really had no strict enrollment criteria for anyone as long as they were platinum resistant. Now you have to be platinum resistant and you have to have received your Doxil after the platinum. So that is when a patient who might have gotten the Doxil before they became platinum resistant, and so on. I think that has cut down the accrual, but that' is just expected. I think they are probably still going on the target they had planned.

Marko Kozul: If enrolment were to complete by the end of the quarter, or by the end of March, how long would you generally expect it would take to generate, objective tumor response rate (ORR) data, and maybe even PFS?

Consultant: I would expect that for response rate data, they would probably need 3-4 months. For PFS they probably would need closer to 6-8 months.

Marko Kozul: If the company were to generate some preliminary data towards the end of the year, maybe November or December, would you read into that as a positive sign?

Consultant: Yes, yes.

Marko Kozul: Maybe a general question, which of the 2 trials do you see as more promising, the breast or ovarian cancer, given the themes that we've just discussed?

Consultant: I see an easier target in ovarian cancer, yes.

ENDOCYTE (ECYT) EC-145:

Marko Kozul: Then just last, but not least, on the Endocyte compound, the EC-145. Can you provide us with some of your general thoughts on the compound and it's involvement on where we are so far?

Consultant: From the data presented at ASCO last year, a Phase 2 randomized a trial of Doxil with or without EC145, the data showed a higher response rate, a significant improvement in progression-free survival (PFS), and even a trend towards an improvement in overall survival (OS). However, I always become a little leery about Phase 2 randomized trials and I think BSI-201 supports this. The limitations I see with the EC-145 data are that as far as I know there's no data about the agent administered as monotherapy. The more time goes by, the more I suspect that when drugs are not active by themselves, when you combine them with chemotherapy, they are unlikely to really change or make a huge change. As scientists we like to talk about synergism and non-cross resistance, but I think that's very nice in the laboratory but in humans you need to have your 2 agents having activity as single drug.

That doesn't mean that EC-145 doesn't have it, I just haven't really seen a good Phase 2 study where they have some responders. A big strength that I see from the Phase 2 randomized trial is that normally I expect that when you combine 2 chemotherapy drugs, your combination arm increase in toxicity. The examples in ovarian cancer include Yondelis (Trabectedin) from a couple of year ago. This trial basically had the same design, Doxil with or without Trabectedin, which was a positive trial and it least improved with how the trial was designed. It improved the primary endpoint of progression free survival (PFS), it demonstrated high response rates, it did not demonstrate any improvement in survival, but that was not the design of the study. As expected, there was more toxicity with the combination arm when the 2 drugs were put together. With EC-145, although it is a chemotherapy drug, it is a targeted chemotherapy drug that is being delivered into the tumor, it does not seem to increase the toxicity. I think the main reason why Yondelis was not approved was because of the higher toxicity in combination. So they don't seem to have this limitation and the data look very promising if the data from that Phase 2 trial hold up.

Q&A SESSION:

Marko Kozul: Thank you for the thorough answers. Operator, why don't we check with the audience and see if there are any questions at this point?

Operator: At this time if you would like to ask a question, press star followed by the number one on your telephone keypad. We'll pause for just a moment to compile the Q&A roster. Your first question comes from client #1.

Investor #1: Thank you for taking my question.

Consultant: OK.

Investor #1: In the beginning you noted some of the drugs that were most interesting for breast and ovarian cancer, NKTR-102 was not one of them. I'm just curious, what would NKTR-102 need to show in order to make that list, or why was that not on the list?

Consultant: Well it was a mistake. I think it is a very promising drug in both tumors, just trying to get it approved it is cleaner in ovarian cancer. I think I probably didn't mention it because it was my understanding NKTR-102 was one of the drugs we were going to talk about so I expected that is one of the important drugs.

Investor #1: Got it, thank you.

Operator: Again, star-one to ask a question. And there are no further questions at this time.

Marko Kozul: I have another one, and then we will check again with the audience. If NKTR-102 were developed further in trials designed as you described, in Triple Negative breast cancer patients, and were to succeed in meeting the primary endpoint and garner approval, how do you think it would actually be used in the real world? Would it be used only in those patients, or might it find broader use? Also, what might determine that? Is the market somewhat crowded and could you speak to that?

Consultant: So I think all treating oncologists recognize and acknowledge that we do not have effective drugs for Triple Negative breast cancer and that's why the oncology community is extremely disappointed in the BSI-201 reshelf. Because we just don't have active drugs. I think if NKTR-102 or any drug is approved in that setting it would very fast

become the main player in that subset of patients. I think that relatively quickly patient and physicians would start using it off-label in other settings for metastatic breast cancer. A lot would depend on the specific indication of the drug and reimbursement. I believe it would be a problem if it were just not possible to obtain reimbursed for Non-Triple Negative breast cancer.

I think it would move much slower in the other settings, until people start becoming familiar and excited with their experience in Triple Negative breast cancers. In other breast cancer patients, as physicians, we think that we have lots of options albeit with none of them is wonderful. This is why patients get sick on 3rd, 4th, 5th line therapy because physicians believe they still have other options. I think it would be a little harder for people to use it off-label. Now at the same time, I think doctors are very driven by their own experiences so maybe you treat a couple of patients with Triple Negative disease where nothing was going to help the patients and they experience very good responses. It would not take long to say I am going try it in one of my other breast cancer patients. However, I think a major issue would be a reimbursement beyond the Non-Triple Negative patients.

Marko Kozul: Thank you for the answer. Operator, why don't we try one more time with the audience, otherwise I have one more question.

Operator: You do have a question from Investor #2.

Investor #2: Good morning, thank you very much for the call. I wanted to ask your opinion about 2 other compounds. The first is the (AEZS-108), it's a drug conjugate it to LHRH, they have Phase 2 data for both ovarian and endometrial cancer.

Consultant: When I saw their data in ovarian cancer maybe a year ago, it didn't seem a lot better than Doxil to me. That is the data a year ago, and I haven't really seen anything more recent. In principle, I think all of these drugs that are targeted chemotherapy drugs such as TDM-1, EC-145, and these sorts of drugs, should be very active and with very little toxicity. It is true that the toxicity for this agent was pretty low, but the activity to me didn't seem so impressive.

Investor #2: There are some who say that NKTR-102 has efficacy that is better than the chemo?

Consultant: I think probably, yes.

Investor #2: OK, thanks, also with regard to endometrial cancer, but I assume you're also involved in endometrial cancer.

Consultant: Yes.

Investor #2: They have some data on endometrial cancer, and I was wondering if you could talk about that in general, how they see the market for endometrial cancer?

Consultant: Good, so for endometrial cancer all the different mTOR Inhibitors have some trials and are looking into it. There is some data with Everolimos and all of them have shown some response rates and all have been evaluated in patients who received prior chemotherapy where normally the response rates are very low. However, I think the mTOR inhibitors in endometrial cancer have the same limitations that I mentioned earlier as they are only supposed to work on the subset of patients where the mTOR pathway is involved. The subset of patients in endometrial cancer that are driven by that pathway but there is another large subset of patients in endometrial cancer where that pathway doesn't really have a major role.

Investor #2: Sorry, which percentage would you say?

Consultant: I would say that the ones which have the pathway as an important growth factor might be 20%. So until we develop a good diagnostic test, I think all mTOR inhibitor trials are going to show response rates of 10-15% and that is not really going to lead to approval of any of them. As single agents, we have to find out a diagnostic to identify the subset of patients, or maybe in combination with some chemotherapy you could improve the outcome.

Operator: Your next question comes from Client #3.

Investor #3: I had a question back to breast, and Nexavar. What your thoughts on both the SALTY study, as well as the Paclitaxel combo study that were presented in 2009. What are your thoughts regarding the chances to show, not just a PFS advantage, but also an overall survival (OS) advantage and the RESILIENT study?

Consultant: Yes, I am probably biased against it because of what I mentioned earlier. I think that you have to have drugs that have activity as single agents to really make a big difference. I think that is what happened with Avastin in breast

cancer, it doesn't do anything by itself and in combination does very little. It really has no activity as a single agent in breast cancer. The trial was a Phase 2 randomized trial that looks very promising, but there's a big thing that I think is sometimes overlooked, the combination was very very toxic.

In the Phase 3 randomized trial they cut down the doses they used on their Phase 2 study. I don't know that if you cut down the doses that you are going to retain the same efficacy. In pretty much every drug there is a dose response. There's a moment at which if you go further you probably don't gain a lot but there is also a point if you drop the dose you do decrease efficacy.

So to me, that is one of the limitations, without really good and compelling data, they said we acknowledge this is too toxic so let's use a lower dose and it should work as well. I think that is a big if, so I am always hoping that Nexavar has to be positive for the benefit of my patients, but I'm actually not too optimistic about that study.

Investor #3: There were 2 studies, the SALTY study with capecitabine and the other study they ran with paclitaxel.

Consultant: OK, yes, yes.

Investor #3: It didn't show anything because of increased deaths in India?

Consultant: Correct. Or at least that was their justification. But at the end of the day, I don't think Nexavar is so different than Sunitinib or even Avastin. All the Sunitinib trials none of them were positive and in the Avastin trials it really looks as if it is the only trial that is really positive. All the others, although they might be positive numerically, the benefits are very small and probably the best example was the trial of Xeloda and Avastin conducted by Genentech probably 5 years ago which was a completely negative study looking again into previously-treated patients.

So I am not very enthusiastic that the VEGF Angiogenesis Inhibitors we have today are going to improve the outcome of metastatic breast cancer below frontline. So maybe it's frontline, but as long as you go below frontline, I think they're not going to work. So I am not enthusiastic about the Nexavar trials, I hope I'm wrong but I'm not convinced.

Operator: There are no further questions at this time.

Marko Kozul: OK, great. Well I'd like to thank the audience for the questions and our consultant for the last hour of discussion in Q&A, thank you very much, very helpful and a good day, to all. Thank you

NKTR-102 Breast Cancer (BC) Development Program:

Phase 2 NKTR-102 BC Data: In late 2008, NKTR initiated a 2 stage Phase 2a/2b NKTR-102 monotherapy trial in women with advanced metastatic BC that failed a previous taxane based regimen. Anthracyclins (A) with taxanes (T) and/or capecitabine (C) are a frequent combination utilized as a first course of therapy for mBC patients. Unfortunately, many patients treated with AT or ATC initially respond but later develop resistance to these regimens. As a result, many KOLs treating BC patients are seeking drugs with novel and differentiated MOAs to treat their relapsing or refractory patients. Given NKTR-102 is a topo-isomerase 1-inhibitor, it may provide an encouraging new mechanism to add to the BC therapy armamentarium should it continue to generate encouraging data in this patient population. Approximately, ~85% of patients in the Phase 2a/2b trial had received prior AT based therapies. Preliminary ORR data released from the study in June-10 were encouraging in these patients as a single agent mBC treatment candidate. Data presented at the San Antonio Breast Cancer Symposium (SABCS) on December 12 show a 29% overall ORR with 9% of patients experience 100% resolution of their primary tumor.

Exhibit 1: NKTR-102 Phase 2 metastatic Breast Cancer Trial Design:

Phase 2 mBC Trial (3rd-line or better with taxane given at some point):	
Purpose:	Evaluate safety/efficacy in metastatic/locally advanced Breast Cancer patients that failed prior taxane-based treatment Multicenter, open-label, 2-arm, 2-stage, trial, Patients 1:1 randomized to 1 of 2 treatment arms
# of Pts:	**N=70**
Design	Interventional, randomized, parallel assignment, open label, treatment
Trial Arms:	NKTR-102 administered at **145 mg/m2 in both arms** **Arm A:** NKTR-102 given on **q14d** schedule **Arm B:** NKTR-102 given on **q21d** schedule
Primary End Point:	**Objective Response Rate (ORR) determined by Response Evaluation Criteria in Solid Tumors (RECIST)** ▪ Time Frame: 12 Months
Start:	October 2008
End:	December 2009 (Final data collection date for primary outcome measure)
Status:	ongoing, but not recruiting (10.28.10)
Sponsors:	**NKTR**
Clin.Trials. Gov.ID:	NCT00806156 **08-PIR-04**

Source: ThinkEquity LLC research and company reports

Exhibit 2: SABCS NKTR-102 Phase 2 metastatic Breast Cancer Data (12.14.10):

Preliminary Phase 2 NKTR-102 single agent Data in mBC patients that failed previous taxane therapy	
General:	▪ **87% (61/70)** patients received prior anthracycline (A)/taxane (T) with or without capecitabine (C) ▪ **94% (66/70)** patients assessable for ORR evaluation (primary endpoint) ▪ **2 median lines of prior cytotoxic treatments** ▪ 73% (51/70) patients received neoadjuvant and/or adjuvant therapy ▪ 87% (61/70) patients had visceral disease
Safety:	▪ Adverse Events (AEs) generally manageable ▪ **DLT** (dose-limiting toxicity) - **17-23% Grade 3 diarrhea** - typically occurring after 3+ months of therapy ▪ **6-9% Neutropenia** ▪ 1% (1/70) **Grade 2 alopecia** ▪ **No Grade 3/4 neuropathy** ▪ Neuropathy/ Alopecia are significant AEs commonly associated with standard breast cancer therapies
Efficacy:	▪ **ORR Confirmed (CR+PR) for evaluable patients (as of Oct.26.10):** ▪ **32% (10/31) for q14d** ▪ **7% CR** ▪ **26% PR** ▪ 42% SD ▪ **26% (9/35) for q21d** ▪ 0% CR ▪ **26% PR** ▪ 48% SD ▪ **29% ORR** for all evaluable patients ▪ 33% previously treated with ATC ▪ 39% with metastatic triple-negative BC ▪ 29% with visceral disease ▪ **9% patients had 100% disappearance of all target lesions (2 CRs + 4 almost CRs)** ▪ **41% Clinical benefit rate** (CR+PR+SD greater than or equal to 6 months) ▪ **5 month (20 wk) preliminary PFS for all patients**

Source: ThinkEquity LLC research and company reports

NKTR Milestones:

Exhibit 3: Projected Future NKTR Milestones

Product:	Phase:	Indication:	Timing:	Milestone:
NKTR-102 (proprietary):	**Phase 2**	Ovarian Cancer (platinum resistant)	1H11	Phase 2 PFS + ORR for initial 71 patients
			4Q11	**Phase 2 extension trial data**
			2012	Phase 2 extension trial Overall Survival (OS) data
			2H12	**FDA Approval for Ovarian Cancer**
		CRC (2nd-line)	2012	Data from 2nd-line Phase 2 vs. Irinotecan head-to-head study (N=174)
			2013	Possible NDA Submission (not modeled for)
			2017	**FDA Approval for CRC**
		Breast Cancer (metastatic)	ASCO-11	Phase 2 PFS and possibly OS data
			2Q11	Finalize Phase 2 Study Design
			4Q11	Start Phase 3 Breast Cancer trial
			2015	Phase 3 BC data
			2016	**FDA Approval for BC**
	Phase 1	GI & Solid Tumors (5-FU combo)	2011	Phase 1 GI & Solid Tumor data
NKTR-105 (proprietary):	**Phase 1**	Solid Tumors	1Q11	Data from Phase 1
			2H11	Start Phase 2 expansion trial
NKTR-118 & 119 (AZN partner):	**Phase 3**	Opioid Induced Constipation	1H11	Start Phase 3 trials
			2015	**FDA Approval for Opioid Induced Constipation**
NKTR-181 (proprietary):	Preclinical	Moderate to Sever Pain	**1H11**	**Phase 1 trial start**
NKTR-171:	Preclinical	Neuropathic Pain	2012	Phase 1 trial start
NKTR-194:	Preclinical	Mild/Moderate	2012	Phase 1 trial start

Source: ThinkEquity LLC and company reports

New NKTR $11 PT and Hold Rating:

We are decreasing our price target to $11 (prev. $17) and moving to a Hold rating (prev. Buy). We foresee a number of potential positive drivers starting in late 2010 and would take advantage of weakness if shares drift below $8 during the interim. Overall, we believe NKTR-102 is worth roughly $4.50 per share, AZN partnered NKTR-118 is worth roughly $0.50 per share to which we add $3 per share in technology value (estimate $300M) and FY11E cash on near $3 per share.

EXHIBIT 4: Sum-of-the-parts Analysis

Product	Status	On Market	Year in Peak Sales	Peak revenue/ royalties ($ in MM)	5x Sales	Discount Rate	Fair Value ($ in MM)	Fair Value Per Share
NKTR-102 in Ovarian:	P2	2012	2016	**$250**	$1,250	**35%**	279	$ 1.97
NKTR-102 in CRC:	P2	2017	2021	**$650**	$3,250	**40%**	112	$ 0.85
NKTR-102 in BC:	P2	2016	2020	**$600**	$3,000	**35%**	201	$ 1.53
NKTR-118:	P3	2015	2019	**$200**	$1,000	**35%**	91	$ 0.69
Technology Value:								$ 3.00
Cash:							429	$ 3.04
					Total Value:		**1,112**	**~$11**

Source: ThinkEquity LLC research and company reports

Risks to Price Target:

Major risk factors include NKTR-102 and NKTR-118: 1) clinical failures or delays, 2) regulatory risk, 3) competitive risk, and 4) continued cash burn requiring potential additional financings before potentially achieving profitability. We believe this makes NKTR shares best suited for sophisticated investors with diversified portfolios and a high tolerance for risk.

Nektar Pharmaceuticals (NKTR)
Income Statement
($ in thousands except per-share data)

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	2009	1Q10	2Q10	3Q10	4Q10E	2010E	1Q11E	2Q11E	3Q11E	4Q11E	2011E	2012E	2013E
Revenues													
NKTR-102 Royalties													
NKTR-102 Milestones													
NKTR-118 Royalties													
Product Sales & Royalties	35,288	3,584	11,154	7,230	12,261	34,229	25,000	3,109	2,903	3,988	35,000	35,000	35,000
License Collaboration & Other	36,643	29,653	31,409	30,695	29,293	121,050	9,874	10,034	11,654	10,188	41,750	64,200	89,200
Total Revenue	**71,931**	**33,237**	**42,563**	**37,925**	**41,554**	**155,279**	**34,874**	**13,143**	**14,557**	**14,176**	**76,750**	**99,200**	**124,200**
Y/Y growth	*-20%*	*242%*	*228%*	*271%*	*7%*	*116%*	*5%*	*-69%*	*-62%*	*-66%*	*-51%*	*29%*	*25%*
Expenses													
COGS	**29,830**	**4,296**	**4,889**	**6,245**	**8,434**	**23,864**	**2,376**	**3,687**	**4,465**	**4,822**	**15,350**	**18,420**	**22,104**
Y/Y growth	*11%*	*-16%*	*-52%*	*10%*	*-4%*	*-20%*	*-45%*	*-25%*	*-29%*	*-43%*	*20%*	*20%*	*20%*
Gross margin	*59%*	*87%*	*89%*	*84%*	*80%*	*85%*	*93%*	*72%*	*69%*	*66%*	*80%*	*81%*	*82%*
R&D	**96,227**	**23,286**	**25,600**	**27,724**	**35,494**	**112,104**	**27,845**	**29,043**	**33,023**	**34,525**	**124,436**	**138,124**	**153,318**
Y/Y growth	*63%*	*-3%*	*6%*	*18%*	*44%*	*17%*	*20%*	*13%*	*19%*	*-3%*	*11%*	*11%*	*11%*
SG&A	**41,006**	**9,013**	**10,207**	**10,181**	**11,605**	**41,006**	**9,102**	**10,254**	**10,101**	**12,779**	**42,236**	**43,503**	**44,808**
Y/Y growth	*-4%*	*-18%*	*12%*	*3%*	*6%*	*0%*	*1%*	*0%*	*-1%*	*10%*	*3%*	*3%*	*3%*
Other													
Total operating expenses	**167,063**	**36,595**	**40,696**	**44,150**	**55,533**	**176,974**	**39,323**	**42,984**	**47,589**	**52,126**	**182,022**	**200,047**	**220,230**
Operating Income (EBIT)	**(95,132)**	**(3,358)**	**1,867**	**(6,225)**	**(13,979)**	**(21,695)**	**(4,449)**	**(29,841)**	**(33,032)**	**(37,950)**	**(105,272)**	**(100,847)**	**(96,030)**
Y/Y growth	*2%*	*-89%*	*-106%*	*-78%*	*154%*	*-77%*	*32%*	*-1698%*	*431%*	*171%*	*385%*	*-4%*	*-5%*
Operating margin	-132%	-10%	4%	-16%	-34%	-14%	-13%	-227%	-227%	-268%	-137%	-102%	-77%
Other Income and Expenses, net	(7,640)	(2,464)	(2,353)	(2,208)	(2,513)	(9,538)	(2,464)	(2,353)	(2,208)	(2,513)	(10,500)	(12,532)	(14,045)
Income Before Taxes	**(102,772)**	**(5,822)**	**(486)**	**(8,433)**	**(16,492)**	**(31,233)**	**(6,913)**	**(32,194)**	**(35,240)**	**(40,463)**	**(115,772)**	**(113,379)**	**(110,075)**
Provision for Taxes	(253)	308	31	278	345	962	308	31	278	345	602	555	542
Tax Rate													
Net income	**(102,519)**	**(6,130)**	**(517)**	**(8,711)**	**(16,837)**	**(32,195)**	**(7,221)**	**(32,225)**	**(35,518)**	**(40,808)**	**(116,374)**	**(113,934)**	**(110,617)**
EPS (LPS) Basic	**(1.11)**	**(0.07)**	**(0.01)**	**(0.09)**	**(0.18)**	**(0.34)**	**(0.06)**	**(0.34)**	**(0.38)**	**(0.35)**	**(1.12)**	**(0.94)**	**(0.90)**
EPS (LPS) Diluted													
Y/Y growth													
Basic Shares	**92,772**	**93,631**	**94,065**	**94,213**	**95,155**	**95,155**	**115,481**	**94,065**	**94,213**	**117,005**	**104,058**	**121,139**	**123,562**
Diluted Shares				109,213	110,155	110,155	130,481	109,065	109,213	132,005	119,058	136,139	138,562

Source: ThinkEquity LLC estimates and company reports

COMPANIES MENTIONED IN THIS REPORT:

Company	Exchange	Symbol	Price	Rating
Nektar Therapeutics	NASDAQ	NKTR	$11.23	Hold

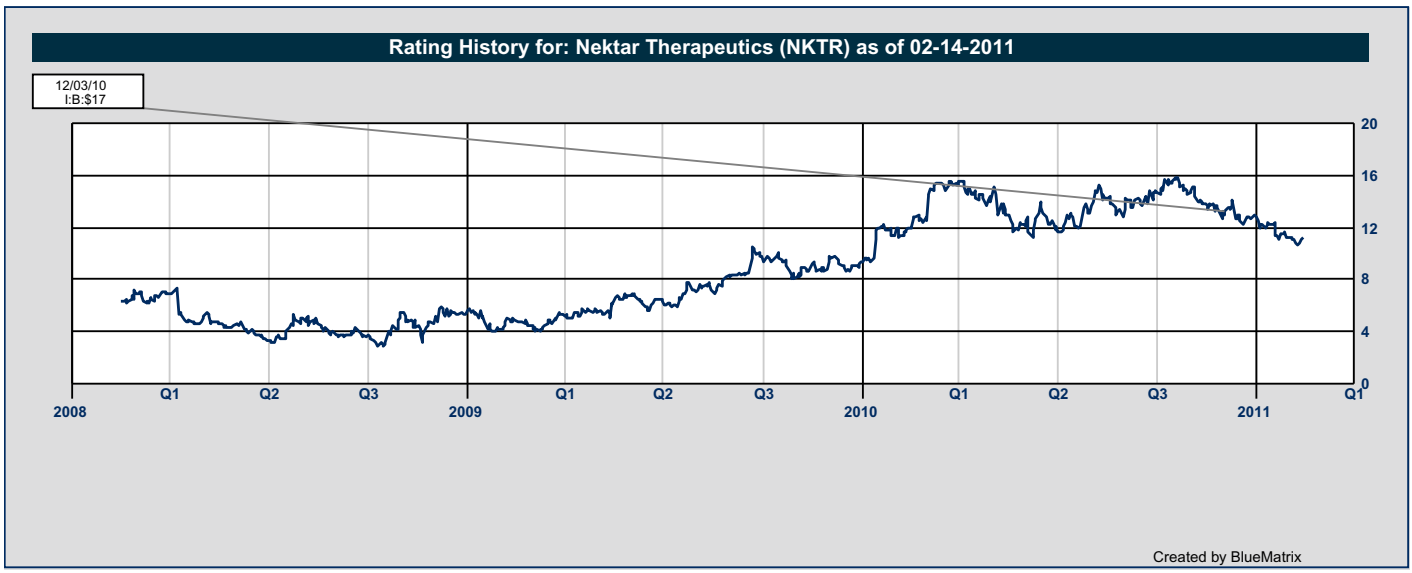
Important Disclosures

Analyst Certification

I, Marko Kozul, M.D., hereby certify that all of the views expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be directly or indirectly related to the specific recommendations or views expressed in this research report.

The analyst(s) responsible for preparing this report has/have received compensation based on various factors, including the firm's total revenues, a portion of which is generated by investment banking activities.

ThinkEquity LLC makes a market in Nektar Therapeutics securities; and/or associated persons may sell to or buy from customers on a principal basis.



Rating Definitions

Effective October 7, 2009, ThinkEquity LLC moved from a four-tier Buy/Accumulate/Source of Funds/Sell rating system to a three-tier Buy/Hold/Sell system. The new ratings appear in our Distribution of Ratings, Firmwide chart. To request historical information, including previously published reports or statistical information, please call: 866-288-8206, or write to: Director of Research, ThinkEquity LLC, 600 Montgomery Street, San Francisco, California, 94111.

Buy: ThinkEquity expects the stock to generate positive risk-adjusted returns of more than 10% over the next 12 months. ThinkEquity recommends initiating or increasing exposure to the stock.

Hold: ThinkEquity expects the stock to generate risk-adjusted returns of +/-10% over the next 12 months. ThinkEquity believes the stock is fairly valued.

Sell: ThinkEquity expects the stock to generate negative risk-adjusted returns of more than 10% during the next 12 months. ThinkEquity recommends decreasing exposure to the stock.

Distribution of Ratings, Firmwide

ThinkEquity LLC

Rating	Count	Percent	IB Serv./Past 12 Mos. Count	IB Serv./Past 12 Mos. Percent
BUY [B]	156	67.20	21	13.46
HOLD [H]	74	31.90	0	0.00
SELL [S]	2	0.90	0	0.00