**US Equity Research**
24 June 2015

**BUY**
unchanged

**PRICE TARGET**
unchanged

**Price (23-Jun)**
US$62.72

**Ticker**
KITE-NASDAQ

**52-Week Range (US$):**
21.00 - 89.21

**Avg Daily Vol (M):**
895.3

**Shares Out. (M):**
38.3

**Market Cap (US$M):**
2,404

**FYE Dec**

<table>
<thead>
<tr>
<th></th>
<th>2014A</th>
<th>2015E</th>
<th>2016E</th>
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<tr>
<td>Revenue (US$M)</td>
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<tr>
<td>EPS Adj &amp; Dil (US$)</td>
<td>(1.91)</td>
<td>(0.95)</td>
<td>(1.02)</td>
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**Quarterly Revenue**

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<tr>
<td>2015E</td>
<td>2.881.0</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>2016E</td>
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**Quarterly EPS Adj & Dil**

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<th>Q4</th>
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<td>(0.66)</td>
<td>(2.27)</td>
<td>(0.24)</td>
<td>(0.33)</td>
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<tr>
<td>2015E</td>
<td>(0.20)</td>
<td>(0.25)</td>
<td>(0.25)</td>
<td>(0.25)</td>
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<tr>
<td>2016E</td>
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**Company Update**

**TCRs center stage at R&D day, KRAS, HPV-16 E7 enter clinic in 2015**

**KRAS and HPV-16 E7 TCRs to enter clinic in 2015**

TCR constructs targeting HPV-16 E7 and KRAs will enter human testing during 2015, broadening KITE’s push into solid tumors. Mutated KRAS is present in colorectal, lung, and pancreatic cancer, three very large commercial markets. We note that prior investor disappointment with mesothelin studies is not necessarily indicative of other antigens. In addition, dose escalation for TCR constructs usually proceeds slowly, with early data not necessarily indicative of the final result at higher doses.

**Phase 1 pivotal DLBCL data expected at ASH, Dec 2015**

Kite gave details on its pivotal Phase 1/2 DLBLCL program, with pivotal Phase 1 data expected at ASH in December 2015. Importantly, patients will be treated in the hospital setting during Phase 1 and observed for toxicity. Assuming the rate of severe toxicity is acceptable, the trial will proceed to Phase 2. Interestingly, the conditioning regimen intensity has been established as a range of “low” to “high.” We look to understand additional detail regarding any potential differences in conditioning intensity versus the NCI Phase 1 pilot study going forward.

**Next-generation manufacturing and CAR fidelity interesting**

We suspect Kite will utilize act inhibitors in next-gen manufacturing of Chimeric Antigen Receptor constructs, which may mitigate terminal differentiation and preserve central memory phenotype, and result in enhanced T-cell persistence. Dr. Steven Rosenberg mentioned the act inhibition technique and has previously published on this topic, and the idea was mentioned at the R&D day. We also believe that Kite’s "CAR fidelity" research approach may mitigate off-target toxicity by adding a second inhibitory receptor towards targets on healthy cells but not tumor cells.

**TCR melanoma data previously established solid tumor viability**

As previously discussed, we firmly believe that TCR efficacy has been demonstrated in solid tumors based on previously published melanoma data. NCI data in melanoma targeting NY-ESO-1 (n=19) have previously shown a 53% ORR (32% PR, 21% CR). We believe that both the existing NCI study in melanoma and the upcoming TCR studies against KRAS and HPV will provide additional proof-of-concept data in solid tumors, holding meaningful upside.
Appendix: Important Disclosures

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Target Price / Valuation Methodology:
Kite Pharma - KITE
Our target price is $90, based on a probability adjusted NPV valuation.

Risks to achieving Target Price / Valuation:
Kite Pharma - KITE
Although NCI is conducting a phase 1/2a trial of anti-CD19 CAR T-cell therapy, KITE’s KTE-C19 trial has not begun. Any delays or significant negative results from NCI’s clinical trials could negatively affect Kite’s IND application and delay the timing to start their own phase 1-2 clinical trial. KITE is highly dependent on the third parties for R&D and early clinical testing of CAR and TCR product candidates. These collaborations related to the intellectual property licensed from the NIH relating to product candidates targeting the EGFRvIII antigen, the SSX2 antigen and the NY-ESO-1 antigen and from Cabaret for intellectual property relating to KTE-C19. The differences in manufacturing compared to NCI may render the product incomparable, particularly with respect to clinical trials, which could negatively affect our valuation. Although plans for manufacturing and processing is based on current approach undertaken by the NCI, the company cannot ensure that even minor changes in the product process will not result in significantly different T-cells that may not have similar efficacy or toxicity. KTE-C19 could fail in clinical studies, resulting in significant downside to our price target and shares of the stock. Kite faces significant competition from other biotechnology and pharmaceutical companies in the space of immunotherapy, including Novartis, Juno, Bluebird, Cellectis and Adaptennune, as well as companies developing novel targeted therapies for cancer.

Distribution of Ratings:
Global Stock Ratings (as of 06/24/15)

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<th>Rating</th>
<th>Coverage Universe</th>
<th>IB Clients</th>
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<td>Hold</td>
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HOLD: The stock is expected to generate risk-adjusted returns of 0-10% during the next 12 months.

SELL: The stock is expected to generate negative risk-adjusted returns during the next 12 months.

NOT RATED: Canaccord Genuity does not provide research coverage of the relevant issuer.

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**Kite Pharma Rating History as of 06/23/2015**

![Graph showing Kite Pharma Rating History from July 2012 to April 2015](attachment:image)

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Kite Pharma, Inc.

KITE – BUY – Investor Day 2015; Kite and Bluebird Soar Together into TCR's

June 24, 2015

- We attended the Kite Investor Day yesterday, June 23, 2015. KITE has grown significantly over the past year and a half since its IPO, growing from 8 employees at launch to over 100 employees today and raising over $400M to date to develop their programs, including 6 products in clinical development.

- KITE develops engineered T cells that redirect the patient's immune system to kill cancer cells. Such engineered T cells can eradicate cancer without harming normal tissue.

- KITE focused on several topics, including their collaborations (NCI, AMGN, NKI, UCLA, Tel Aviv, and now bluebird bio), product development (KTE-C19 being advanced to pivotal trials later this year), and building out the TCR franchise (recent agreement with bluebird on HPV-16 TCRs, AMGN collab, and other TCRs including NY-ESO and MAGE TCRs).

- KITE is also expanding manufacturing (Santa Monica facility opening in October, El Segundo facility in 2017, with existing PCT site in Mountain View and a CMO in EU) to support the over 300 patients who will be treated in KTE-C19 trials as well as further development of other candidates in the future.

- We await pivotal Ph. 1 data on KTE-C19 in aggressive NHL/DLBCL at ASH in December, while the remaining CAR and TCR pipeline is advancing rapidly with 3 additional pivotal studies in KTE-C19 (IND submission planned 2H16) as well as KRAS and HPV16 E7 TCRs initiating clinical trials in 2H15.
Birds of a feather fly together: KITE and bluebird bio collaborate on TCRs: KITE and bluebird bio (BLUE, NC, $174.31) announced a new collaboration to develop second generation TCR product candidates directed against human papillomavirus type 16 E6 (HPV-16 E6) oncoprotein. Bluebird bio has demonstrated expertise and substantial promise using their lentivirus/gene therapy technologies to treat Beta-thalassemia and sickle cell disease. The collaboration will likely primarily allow for both companies to share intellectual property and methodologies to develop the second generation TCR therapies to target HPV-16 E6. Expenses for development and profits will be split equally between the companies, and none of the existing KITE HPV programs will be affected by this standalone agreement.

The HPV-16 E6 oncoprotein is constitutively expressed on HPV-16+ cancer cells and is absent from healthy tissues, allowing HPV-16-directed T cells to target and kill only cancer cells. Primary HPV-associated cancers include cervical and oropharyngeal head and neck cancers, which combined can constitute up to a yearly incidence of 42,500 eligible patients. KITE is currently evaluating a first generation HPV-16 E6 TCR for diverse HPV-16+ cancers in a Phase 1/2 study with an estimated enrollment of up to 61 patients and expected completion in May 2019.

Getting KTE-C19 to market in DLBCL: One of the key focuses of the Investor Day was what steps are necessary to begin the KTE-C19 program and what trial designs will be used. KITE has already started the pivotal study in DLBCL, and they indicated they will begin the pivotal studies in MCL, ALL, and aggressive NHL later this year (table below provides an overview of pivotal trial design). Dr. Jeff Wezorek, VP of Clinical Development detailed an overview of the trial designs, mentioning that many of the same sites will be performing both Ph. 1 and 2 studies. Chemo-conditioned patients will be hospitalized around the infusion, which follows a 6-8 day manufacturing period (which KITE is still optimizing with automation steps and other measures) post-leukapheresis. Following the hospitalization, the follow up period begins with first tumor assessment on day 30. In aggressive NHL, KITE is targeting a BLA filing for KTE-C19 by YE 2016, with Ph. 1 data presented this December at ASH and Ph. 2 data to follow sometime next year. Over the life span of all KTE-C19 pivotal trials, over 300 patients will be treated.

<table>
<thead>
<tr>
<th>KITE KTE-C19 Pivotal Trial Designs 101-103 in NHL, MCL, and ALL</th>
<th>Key eligibility criteria</th>
<th>Endpoints</th>
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<tr>
<td><strong>KTE-C19 101</strong></td>
<td>Aggressive NHL</td>
<td><strong>Size of Ph. 2 [n]</strong></td>
</tr>
<tr>
<td>Cohort 1 in DLBCL: n=72</td>
<td>- Chemotherapy refractory disease - 5D or PD to last therapy or - Relapsed post transplant within 1 year</td>
<td>Adequate prior therapy - At minimum, anthracycline-containing regimen and anti-CD20 mAb</td>
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<tr>
<td>Cohort 2 in PMBCl/TFL (n=40)</td>
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<tr>
<td><strong>KTE-C19 102</strong></td>
<td>MCL</td>
<td>n=70</td>
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<tr>
<td></td>
<td>- Relapsed or refractory disease</td>
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<tr>
<td></td>
<td>- Adequate prior therapy - Anthracycline or bendamustine-chemo and - Anti-CD20 monoclonal antibody therapy and - ibrutinib</td>
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<tr>
<td></td>
<td>- ECOG 0 or 1</td>
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<tr>
<td></td>
<td>- Age &gt;18</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Adequate hepatic, renal, cardiac function</td>
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<tr>
<td><strong>KTE-C19 103</strong></td>
<td>ALL</td>
<td>n=50</td>
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*Source: KITE presentations*
Improving DLBCL/NHL therapy: KITE reiterated the emphasis of lymphodepletion and chemotherapy preconditioning as necessary for the CAR-T therapy process. At ASCO, KITE presented data demonstrating that chemo-conditioning with cyclophosphamide and fludarabine induced immune homeostatic cytokines (IL-15, IL-7), chemokines (MCP-1), and pro-inflammatory markers including CRP and PLGF. The method used for pre-conditioning the patient does therefore affect activation and trafficking of T cells. This will be key in clinical trials, and KITE intends to optimize this factor in CAR therapy. As presented at ASCO, KITE and Rosenberg mentioned that durable responses can occur without long lasting CAR-T cells in circulation, allowing for normal B cell recovery. Rosenberg commented that many robust responses have been achieved in several weeks post T-cell administration. KITE also emphasized CAR kinetics, in that the rapidity of achieving a CR as well as the ability to then sterilize the body of tumor cells is important. We note that this message differs slightly from JUNO’s, who highlighted at ASCO that it seeks to improve the LT plateau of the KM curve in DLBCL patients by first improving cell persistence. Initial JCAR017 data in DLBCL reads out sometime next year, and JUNO’s goal is to achieve a high CR rate as well as a durable tail.

DLBCL is KITE’s lead indication, with a market size of ~22,000 patients in the U.S. Wiezorek emphasized that DLBCL in particular poses a large unmet need (table below outlining non-CD19 CAR responses), while CD-19 directed CARs have demonstrated response rates north of 60%, with many durable responses as well.

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>ORR</th>
<th>CRR</th>
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<tr>
<td>Any (n=29)</td>
<td>76%</td>
<td>38%</td>
</tr>
<tr>
<td>DLBCL/PMBC (n=17)</td>
<td>65%</td>
<td>35%</td>
</tr>
<tr>
<td>CLL (n=7)</td>
<td>86%</td>
<td>57%</td>
</tr>
<tr>
<td>Indolent NHL (n=5)</td>
<td>100%</td>
<td>20%</td>
</tr>
</tbody>
</table>

*Source: ASCO 2015 data, Kochenderfer et al, Blood 2012 and JCO 2015 data

Ramping up manufacturing; commercial manufacturing ready for KTE-C19 launch in 2017: KITE will treat approximately 300 patients over the next year and a half, requiring a fairly extensive manufacturing build-out to support this development. In addition to relying on PCT in Mountain View, CA (used primarily for the DLBCL program) KITE has also built out a facility in Santa Monica that is anticipated to open in October. Along with KITE’s EU program, led by Dr. Ton N. M. Schumacher, KITE is also engaging facilities for CMO production in Europe. The company is also building a facility in El Segundo, CA near the LA airport with an expected launch in 2017. Dr. Marc Better, VP of Product Sciences, commented that they fully expect the Santa Monica facility to be able to support manufacturing for the KTE-C19 program by YE. KITE believes its engineering process, which is relatively shorter compared to competitors at 6-8 days, offers superiority in the young phenotype of the product (not too many rounds of expansion) as well as no bead selection.

Where KTE-C19 fits into the treatment paradigm of new immunotherapies: Dr. Ron Levy from Stanford School of Medicine said that KTE-C19 fills a unique niche in the emerging landscape of new immunotherapies. While Rituximab raised the cure rate for DLBCL from 30% to 50%, CD-19 CARs are achieving RR’s north of 60% that are durable, and Levy believes that CAR-T therapies such as KTE-C19 can eventually replace bone marrow transplants. In terms of comparing to other new immunotherapies such as ADC’s, BTK inhibitors, and PI3K-delta inhibitors, Levy mentioned that they do not work especially well with DLBCL, achieving short-duration RR’s of ~20-30%, as such therapies tend to work better in slower growing, low grade lymphomas such as follicular lymphoma. CAR-T therapies, in comparison, induce responses that are complete, durable and long lasting.

GUGGENHEIM SECURITIES, LLC
**TCR franchise buildout:** Dr. Ton Schumacher, CSO of KITE Europe and head of the KITE’s collaboration with the Netherlands Cancer Institute, presented an overview of KITE’s next-gen TCR programs. While CAR targets represent ~27% of the human proteome, TCR targets are more numerous due to TCR's ability to access intracellular targets, representing ~73% of the human proteome. KITE EU's proprietary TCR GENERator technology allows high-affinity of TCRs, though he emphasized the importance of an optimal affinity that is still within the natural range and binds tightly to the peptide MHC complex. KITE has active protocols at the NCI surgery branch, including HPV-16 E6 and HPV-18 E6 and E7 in cervical, head and neck cancers, mNY-ESO1 in pancreas and other cancers, Kras (G12D and G12V) in colorectal, and MAGE A3 in various tumors. The collaboration with bluebird expands this portfolio, and KITE commented that filing is 2-3 years out for 2nd gen TCRs, while it files in 1H16 in the first-generation HPV-16 E6 program.

**Future combos with checkpoint inhibitors:** During the later Q&A panel, Dr. Levy commented that he believes combining checkpoint blockade with CAR-T’s is the most exciting potential development in cancer immunotherapy. While checkpoint blocking antibodies have demonstrated tremendous efficacy, they only work on a certain subset of patients, so the question remains how to expand to a broader population. Some CAR-T players have already partnered on checkpoint inhibitors and CAR-T therapies: Juno (JUNO, NEUTRAL, $51.40) and AstraZeneca (AZN, NC, $67.59) announced their partnership on a PD-L1/CD19-CAR in NHL April 23. The study, which initiates later this year, assesses the impact that inhibiting PD-L1 with AZN’s MEDI4736 has on the safety and efficacy of Juno’s CAR-T construct. Inhibiting PD-1/PD-L1 would essentially prevent cancer cells from avoiding the host immune system, directly allowing increased exposure and efficacy of CAR-T engineered T cells. In addition, epitope spreading could be enhanced due to the immune response bolstered by the combo therapy further triggering an autoimmune response against proteins found on the surface of tumor cells.

**Upcoming catalysts:** 1) Pivotal Ph. 1 data at ASH in Dec. 2015 in aggressive NHL, 2) 3 additional pivotal trials in KTE-C19 initiating 2H15, 3) HPV-16 E6 TCR submitting IND in 1H16, 4) KRAS and HPV16 E7 TCRs initiating clinical trials under KITE-NCI CRADA in 2015, 5) KITE-AMGN CAR programs submitting IND’s in 2H16, and 6) Ph. 2 pivotal data in KTE-C19 aggressive NHL in 1H16 and BLA filing for KTE-C19 by YE 2016.

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**Chimeric Antigen Receptor (CAR)**

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**T Cell Receptor (TCR)**

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*Source: KITE presentations*
KITE Valuation: As data continue to emerge supporting the viability of KITE’s program/platform, we believe the risk could reduce and value could increase. Value should increase because the net present value of commercialization rises. We believe KITE may generate revenue by 2018. We estimate peak sales in second and third line NHL, assuming $200-250k per treatment, approach $1.5B by 2021. Medivation (MDVN, NC, $116.06) and Pharmacies (PCYC, NC, $261.25) are similar companies with early-stage product launches by partner companies and have market valuations approaching $9.7 billion and $19.7 billion, respectively. We estimate, at a current market cap of ~$2.2 billion, it is possible KITE could grow to 7-9 times its current size by 2022. We discount that valuation to today by 15% annually, which yields our price target of $73 (unchanged).

Key KITE Risks: KITE is an experimental stage company very early in development. Poor clinical readouts or inability to successfully commercialize its products is a risk. Risk of side effects of CAR-T therapies is also high, notably with cytokine release syndrome with even death in some patients, potentially limiting its use in earlier lines of therapy. There is also limited data outside of ALL, and establishing a durable response is critical to commercial success. Moreover, manufacturing and process development is not at commercial scale yet, and we note being able to deliver CAR-T to patients with affordable COGS is imperative. Further, given the number of companies currently in the CAR-T space, KITE’s lead and platform could be commoditized. We believe profitability is several years away. Therefore, the stock can and may be highly volatile.
SECTOR: BIOPHARMACEUTICALS

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Kite Pharma, Inc.

Investor Day—Under the Hood; No Near-Term Changes

Summary

We are reiterating our Buy rating and $90 PT following KITE's first Investor Day. While there were no clinical data updates or significant announcements, we gained 1) a deeper understanding of the platform and 2) a frank KOL discussion into the future of cancer immunotherapy. Industry collaborations and close academic ties put KITE in a strong position as therapy moves out of lymphoma. "Off-the-shelf" approaches were downplayed, as was the importance of defined-cell populations and long-term persistence, contrasting with some competitors. Catalysts remain 4Q data (ASH) and 2016 readouts.

Key Points

- Manufacturing techniques to keep cells less differentiated. KITE is focusing development on new processes and pharmacologic agents that block differentiation and keep a more youthful cell phenotype, which appears to be needed for efficacy. An overview of KITE's TCR GENERator platform technology was provided, which could give KITE a competitive advantage in TCR development. A new commercial manufacturing facility under construction will be ready for a commercial launch of KTE-C19 by 2017, and support 4,000-5,000 doses per year.

- Catalysts were broadly reiterated. Key upcoming catalysts are 1) KTE-C19 Phase I NHL data at ASH year-end, and Phase II pivotal data in 2016, 2) initiation of MCL, ALL and CLL pivotal trials in 2H15, and 3) HPV-16 E6 TCR IND submission in 1H16, followed by KTE-C19 BLA filing by YE 2016.

- Defined-cell populations and long-term persistence were downplayed. In contrast to competitors that have focused on defined-cell populations as an important aspect of manufacturing, KITE appears to be playing down the importance at this stage. Regarding persistence of CAR T-cells, panelists at the meeting thought that the current evidence points to needing the CAR to persist for only a couple of weeks to a month in order to produce effective treatment, which downplays the need to substantially improve persistence.

- Panel members see combo therapy as an eventuality. The panel expects that CAR and TCR will evolve into an integral part of combination therapy. Dr. Steven Rosenberg, Chief of Surgery at NCI and a key collaborator, had a substantial part of his talk and comments focused on increasing the personalization of CARs. The panel was negative on off-the-shelf approaches to CAR therapy, which would be a negative for companies like CLLS (Not Rated, $36.54) and ZIOP (Neutral-rated).

Please refer to page 10 of this report for important disclosure and analyst certification information.
Manufacturing Techniques to Keep Cell Products Less Differentiated, and TCR Development

CSO Margo Roberts, who received a patent on a second generation CAR in 1995, presented a look at KITE's design approach for CAR's, which can be as quick as 18 months from the initial design of the single chain variable fragment (scFv) that targets the CAR to the tumor, to IND filing. While using precisely defined cell populations were less of a concern for KITE, having a T cell population that was in general composed of less differentiated, more "youthful" T cells that drive proliferation (more stem cell memory and central memory cells) was important. KITE is focusing development on new processes and pharmacologic agents that block differentiation and keep a more youthful cell phenotype.

KITE's European CSO, Ton Schumacher, presented an overview of TCR development, which has been overshadowed by CAR development but could target 2x-3x more antigens. In particular was an overview of the TCR GENERator platform technology acquired with KITE's acquisition of T-Cell Factory B.V. in March. The platform, which could provide KITE with an advantage in TCR development, enables high-throughput generation of peptide-MHC (pMHC) complexes that are used to select the most promising TCRs for development.

Manufacturing and Scale Always a Concern

KITE is actively investing in developing both capacity and manufacturing protocols. KITE's new commercial manufacturing facility, under construction now, will be ready for a commercial launch of KTE-C19 in 2017, and support 4,000-5,000 doses per year.

Catalysts Broadly Reiterated

HPV-16 E6 TCR will be next product for IND submission, in 1H16, and the expanded NCI CRADA announced in March will include KRAS, a colorectal cancer target (93,000 new cases per year in the U.S.). Key upcoming catalysts are 1) lead program KTE-C19 Phase I NHL data at ASH year-end, and Phase II pivotal data in 2016, 2) initiation of MCL, ALL and CLL pivotal trials in 2H15, and 3) HPV-16 E6 TCR IND submission in 1H16, followed by KTE-C19 BLA filing and IND filings from the AMGN (Not Rated, $161.69) collaboration by YE 2016.

Importance of Defined-cell Populations and Long-term Persistence Downplayed

In contrast to competitors like JUNO (Not Rated, $51.40) that have focused on defined-cell populations as an important aspect of CAR and TCR manufacturing, KITE appears to be playing down its importance at this stage from both a clinical efficacy and manufacturing perspective (as was shown in ASCO data), though has not ruled it out entirely as a factor.
Regarding persistence of CAR T-cells, panelists at the meeting thought that the current evidence points to needing the CAR to persist for only a couple of weeks to a month in order to produce effective treatment, which downplays the need to substantially improve persistence. As far as CAR design, substantial, basic work still needs to be done across the industry- for instance, there has not been a robust study yet on the best co-stimulatory domain to use.

**Limited Insight into New bluebird bio Collaboration**

We know the BLUE (Not Rated, $174.31) collaboration will focus on a next-gen HPV-16 E6 TCR, which is likely 2-3 years away. The collaboration could also enable editing of T-cells to be more resilient in the tumor micro-environment, a key obstacle to overcome to improve solid tumor efficacy. The negative reaction to mesothelin solid-tumor data from UPenn appeared to be largely anticipated by the experts, who had a history of working with the target and didn't believe it would be among the promising targets.

**Panel Members See Combo therapy as an Eventuality**

The panel expects that CAR and TCR will evolve into an integral part of combination therapy, such as combining with checkpoint inhibitors, or developing effective sequencing of different therapies which will include CARs. Dr. Steven Rosenberg, Chief of Surgery at NCI and a key collaborator, had a substantial part of his talk and comments focused on increasing the personalization of treatment, with the use of tumor neoantigens especially prominent- for instance, exomic sequencing of the tumor and identification of integral antigens, followed by development of a personalized CAR, all within the span of a couple of weeks. The panel was negative on off-the-shelf approaches to CAR therapy, which would be a negative for companies like CLLS (Not Rated, $36.54) and ZIOP (Neutral-rated) that are making allogenic, off-the-shelf development more of a focus.
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Source: Company reports and Mizuho Securities USA, Inc.
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<td>KTE-C19 Product revenue</td>
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<tr>
<td>Collaboration revenue</td>
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<tr>
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<td><strong>Cost of Sales</strong></td>
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<td><strong>Gross Profit</strong></td>
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<td>Gross Margin</td>
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<tr>
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<td>SG&amp;A</td>
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<tr>
<td>Extra. &amp; Amortization</td>
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<tr>
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<tr>
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<tr>
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<td>Diluted Shares Outstanding</td>
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Source: Company Reports and Mizuho Securities USA Inc. estimates
### Kite Pharma, Inc.

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<tr>
<td>Kite-C19 Product Revenue</td>
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<tr>
<td>Kite-C19 Royalty revenue</td>
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<td>Collaboration revenue</td>
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<td><strong>Total Revenue</strong></td>
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<td>$ 0.0</td>
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<td><strong>Cost of Sales</strong></td>
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<tr>
<td><strong>Gross Margin</strong></td>
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<td><strong>Operating Expenses</strong></td>
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<tr>
<td>Research and Development</td>
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<td>SG&amp;A</td>
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<td>$ 1.4</td>
<td>$ 1.5</td>
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<tr>
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<td>$ (1.4)</td>
<td>$ (1.5)</td>
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<tr>
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<td>$ (1.5)</td>
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<td><strong>Income Tax Expense</strong></td>
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<td>0.0%</td>
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<tr>
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<td>$ (1.1)</td>
<td>$ (1.4)</td>
<td>$ (1.5)</td>
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<tr>
<td><strong>Extra &amp; Amortization</strong></td>
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<td>$ (0.1)</td>
<td>$ (0.1)</td>
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<td>($0.25)</td>
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Source: Company Reports and Mizuho Securities USA Inc. estimates
## Kite Pharma

### Annual Cash Flow Statement

($) in millions, except per share data

<table>
<thead>
<tr>
<th></th>
<th></th>
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<td><strong>Operating Activities</strong></td>
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<tr>
<td>Net Income</td>
<td>$ (2.6)</td>
<td>$ (7.8)</td>
<td>$ (36.5)</td>
<td>$ (95.1)</td>
<td>$ (115.8)</td>
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<td>(0.4)</td>
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<td>(8.5)</td>
<td>60.0</td>
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<td>0.0</td>
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<td><strong>Net Cash from Operations</strong></td>
<td>$ (2.8)</td>
<td>$ (5.6)</td>
<td>$ (41.3)</td>
<td>$ (33.5)</td>
<td>$ (121.9)</td>
<td>$ (56.3)</td>
<td>$ 76.4</td>
</tr>
</tbody>
</table>

| **Investing Activities** |      |      |      |       |       |       |       |
| Acquisitions, net       | $ 0.0 | $ 0.0 | $ 0.0 | $ (20.0) | $ 0.0 | $ 0.0 | $ 0.0 |
| Capital Expenditures    | (0.0) | (0.3) | (2.0) | (20.0) | (20.0) | (10.0) | (10.0) |
| Other                    | 0.0 | 0.0 | (116.5) | 0.0 | 0.0 | 150.0 | 0.0 |
| **Net Cash from Investing** | $ (0.0) | $ (0.3) | $ (118.5) | $ (40.0) | $ (20.0) | $ 140.0 | $ (10.0) |

| **Financing Activities** |      |      |      |       |       |       |       |
| Issuance / Reduction of Debt | $ 0.0 | $ 0.0 | $ 0.0 | $ 0.0 | $ 0.0 | $ 0.0 | $ 0.0 |
| Issuance of Common Stock | 0.0 | 19.6 | 379.6 | 16.0 | 0.0 | 10.0 | 10.0 |
| Dividends                | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Other                    | 0.3 | 0.0 | (32.8) | 0.0 | 0.0 | 0.0 | 0.0 |
| **Net Cash from Financing** | $ 0.3 | $ 19.6 | $ 346.8 | $ 16.0 | $ - | $ 10.0 | $ 10.0 |

| Net Exchange Rate Effect | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |

| **Net Change in Cash** | $ (2.5) | $ 13.7 | $ 187.0 | $ (57.5) | $ (141.9) | $ 93.7 | $ 76.4 |
| Cash from Prior Period | 11.2 | 8.7 | 22.3 | 209.3 | 151.8 | 9.8 | 103.6 |
| **Net Cash**            | $ 8.7 | $ 22.3 | $ 209.3 | $ 151.8 | $ 9.8 | $ 103.6 | $ 180.0 |

| **Cash Flow** |      |      |      |       |       |       |       |
| Cash Flow       | $ (2.6) | $ (6.3) | $ (36.2) | $ (93.1) | $ (111.8) | $ (44.3) | $ 90.6 |
| Cash Flow Per Share | ($0.07) | ($1.16) | ($1.59) | ($2.12) | ($2.43) | ($5.92) | $1.80 |

| **EBITDA** |      |      |      |       |       |       |       |
| EBITDA       | $ (2.6) | $ (6.4) | $ (36.4) | $ (95.0) | $ (112.8) | $ (45.3) | $ 134.1 |
| EBITDA Per Share | ($0.07) | ($1.17) | ($1.60) | ($2.16) | ($2.45) | ($5.94) | $2.67 |

| **Free Cash Flow** |      |      |      |       |       |       |       |
| Free Cash Flow    | $ (2.8) | $ (6.0) | $ (34.8) | $ (113.5) | $ (141.9) | $ (66.3) | $ 66.4 |
| Free Cash Per Share | ($0.07) | ($1.10) | ($1.53) | ($2.58) | ($3.09) | ($1.38) | $1.32 |

Source: Company Reports and Mizuho Securities USA Inc. estimates
Kite Pharma
Annual Balance Sheet

(\$ in millions, except per share data)

<table>
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<td>$299.9</td>
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Kite Pharma
Ratio Analysis

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<td>$4.08</td>
<td>$16.08</td>
<td>$7.89</td>
<td>$4.46</td>
<td>$3.09</td>
<td>$4.48</td>
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<td>0.0%</td>
<td>0.0%</td>
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<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

Source: Company Reports and Mizuho Securities USA Inc. estimates
Price Target Calculation and Key Risks

We derive our price target by applying both a discounted cash flow analysis and discounted P/E analysis to yield a price target of $90. Risks to our price target outside of clinical failure relate to 1) platform risk, 2) competitive risk and 3) commercialization risk.
Companies Mentioned (prices as of 6/23)
Amgen Inc (AMGN- Not Rated)
ZIOPHARM Oncology, Inc. (ZIOP- Neutral $11.79)

IMPORTANT DISCLOSURES
The disclosures for the subject companies of this report as well as the disclosures for Mizuho Securities USA Inc. entire coverage universe can be found at https://msusa.bluematrix.com/sellsid/Disclosures.action or obtained by contacting EQSupervisoryAnalystUS@us.mizuho-sc.com or via postal mail at Equity Research Editorial Department, Mizuho Securities USA Inc., 320 Park Avenue, 12th Floor, New York NY, 10022.

Ownership Disclosures and Material Conflicts of Interest or Position as Officer or Director
None

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As of October 3, 2011
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Buy:
Stocks for which the anticipated share price appreciation exceeds 10%.
Neutral:
Stocks for which the anticipated share price appreciation is within 10% of the share price.
Underperform:
Stocks for which the anticipated share price falls by 10% or more.
RS:
Rating Suspended - rating and price objective temporarily suspended.
NR:
No Rating - not covered, and therefore not assigned a rating.

Prior to October 3, 2011
Buy:
Estimated stock price appreciation of 20% or more.
Outperform:
Outperform the stock market averages by 12% or more.
Neutral:
Perform in line with the stock market averages (Hold).
Underperform:
Underperform the stock market averages by 12% or more.
Sell:
Estimated stock price decline of 20% or more.

Rating Distribution
(As of 6/23)
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<th>% of coverage</th>
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<td>Hold (Neutral)</td>
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<tr>
<td>Sell (Underperform)</td>
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For disclosure purposes only (NYSE and FINRA ratings distribution requirements), our Buy, Neutral and Underperform ratings are displayed as Buy, Hold and Sell, respectively. However, our Buy, Neutral and Underperform ratings are determined on a relative basis (please refer to definitions above).
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Kite Investor Day Update and Bluebird Bio Collaboration

This afternoon we attended Kite Pharma’s Investor Day where management provided a corporate overview and the company’s key collaborator at the NCI (Steven Rosenberg) gave an overview of the field that hinted at some potentially earthshaking data to come (see below). Kite’s recent collaboration with Bluebird was reviewed and looks like a high-level hand-holding exercise as both companies look to enter new areas without wasting time. As expected, the next IND will involve TCRs targeting HPV proteins which are increasingly being viewed as the best TCR target outside of neoantigens.

Rosenberg’s Next Miracle? Steven Rosenberg delivered principally an overview of the field but also showed a slide of some patients where his group at the NCI has isolated both neoantigens and their recognizing TCRs from tumors other than melanoma — specifically gastrointestinal cancers. As a result, we expect he has treated these patients with TCR therapeutics and early data can’t be far away (SR has been mentioning this program since ASH). We believe these data are compelling and CRs are seen for neoantigen-based TCR therapeutics it will be viewed as a major proof-of-concept for Kite’s focus on the neoantigen approach in solid tumors. As we have said in previous notes — the operational hurdles for this approach to treating solid tumors are non-trivial — but the approach puts cure on the table for as many as 50% of patients with solid tumors.

The Bluebird Collaboration. The two companies yesterday announced a collaboration agreement to co-develop second generation TCR products, specifically product candidates directed against the HPV-16 E6 oncoprotein. With Bluebird being a gene-editing focused company and Kite specializing in T-Cell therapeutics, the two will leverage each other’s strengths to design next-generation T-Cell therapeutics. Kite is almost certainly looking to modify TCR therapeutics to combat the immunosuppressive tumor environment. As a result, we expect they are knocking out some of the receptors found on T-Cells that tumors use to put tumor-hunting TCRs to sleep. As reported at ASCO 2015, KTE019 T-Cells begin to express PD-1 after introduction into patients and tumor cells are expected to express PD-L1 and the resultant interaction potentially reduces efficacy. As a result, knocking out PD-1 in TCR (and CAR-T) therapeutics seems like an obvious things to try. The subsequent list of candidate genes to delete to stimulate TCR therapeutics is very long — probably spurring Kite’s urge to find an expert partner.

Next IND – HPV. As was probably expected, Kite’s second IND submission will be a TCR therapeutic targeting Human papillomavirus (HPV, a first generation

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<td>Rating</td>
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<tr>
<td>Target Price</td>
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<tr>
<td>FY15E EPS</td>
<td>—</td>
<td>$(1.49)</td>
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<tr>
<td>FY16E EPS</td>
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<td>$0.02</td>
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Price (06/23/15): $62.72
52-Week Range: $80 – $21
Market Cap.(mm): 2,665.6
Shr.O/S-Diluted (mm): 42.5
Avg Daily Vol (3 Mo): 1,268,003
Net Cash/Share: $5.31
Cash (mm): $203
Debt (mm): $0.0
Dividend($ / %) $0.00 / 0.0%
S&P Index 2,124.20

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<th>2016E</th>
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<td>Q3</td>
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<td>(0.38)</td>
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<td>Q4</td>
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<td>FY Dec</td>
<td>$(1.91)A</td>
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Quarterly EPS do not sum to annual due to the issuance of shares.

Thomas Shrader, PhD, CFA  
shradert@stifel.com 
Stifel Equity Trading Desk  
(212) 271-3577 
(800) 424-8870

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approach outside the Bluebird deal). This is a large market opportunity as HPV is the most common viral infection of the reproduction tract, with two viral strains, type 16 & type 18, believed to cause 70% of cervical cancers and a significant percentage of head and neck cancers. In addition, HPV antigens are expected to be very clan as normal cells are not expected to express this target — by definition. Furthermore, HPV antigens are considered excellent targets due to their expression on “essentially every cell” of a tumor. All in all — we view this program very favorably and view it as a second example of our theme that Kite is very close to showing the world definitively that T-Cell therapeutics will treat a lot more than pediatric leukemias.
Target Price Methodology/Risks
We use a multiple of future earnings to derive our $83 target price for KITE. Specifically, to generate our valuation for development-stage biotech companies, we use a 30x multiple of future earnings, which represents a discount to the 20-year average earnings multiple for profitable biotech companies of 37x. Kite’s valuation is driven primarily by KTE-C19, currently in Phase I/IIa testing. We apply a 25% discount rate, which we feel reflects the degree of uncertainty surrounding KTE-C19. With a multiple of 30x, we calculate a $83 target price based on our 2022 diluted EPS estimate of $15.92, discounted back 7.5 years.

Development risk for KTE-C19 - If Kite is not able to successfully develop the experimental CAR-T technology, we would have to lower our revenue estimates.

Competitive risk for KTE-C19 - If a competitor proves more effective or tolerable in the treatment of DLBCL, or their drugs are easier to produce, our estimates could prove optimistic.

Regulatory risk for KTE-C19 - The FDA has never approved a CAR-T-based therapy before and there exists no precedent for the approval of a genetically engineered autologous cell product. If KTE-C19 is not approved on the timeline that we envision, we would have to reduce our estimates.

Company Description
Kite Pharma, Inc. is a clinical-stage biopharmaceutical company focused on the development and commercialization of novel cancer immunotherapy products designed to harness the power of a patient's own immune system to eradicate cancer cells. To achieve this, Kite is developing a pipeline of product candidates for the treatment of advanced solid and hematological malignancies using the engineered autologous cell therapy system, in which a patient's own immune system is engineered to recognize and destroy their cancer. Kite’s products use engineered chimeric antigen receptor T-cells (CAR-T) or T-cell receptors (TCRs). Kite’s technology has been developed through a collaboration agreement with the NCI-Surgery Branch. Kite’s most advanced product is KTE-C19, a CAR-T therapy that recognized CD19 and will be developed for diffuse large B-cell lymphoma.
### Kite Pharma (KITE)

#### Income Statement

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<td>114.2</td>
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<td>312.2</td>
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<td>107.9</td>
<td>334.4</td>
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<td>(36.7)</td>
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<td>(201.3)</td>
<td>(312.2)</td>
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<td>(42.6)</td>
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<td>(16.0)</td>
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<td>(63.8)</td>
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<td>(2.6)</td>
<td>(6.4)</td>
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<td>(312.2)</td>
<td>(401.6)</td>
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<td>Stick Dividend (Series A)</td>
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<tr>
<td>EPS (basic)</td>
<td>(0.48)</td>
<td>(1.16)</td>
<td>(1.91)</td>
<td>(0.36)</td>
<td>(0.35)</td>
<td>(0.38)</td>
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<td>(7.81)</td>
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<td>EPS (diluted)</td>
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<td>(1.16)</td>
<td>(1.91)</td>
<td>(0.36)</td>
<td>(0.35)</td>
<td>(0.38)</td>
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#### Long-term debt

- **Margin Analysis**
  - COGS (% of sales) NM
  - R&D (% of total revenue) NM
  - SG&A (% of total revenue) NM
  - Effective Tax Rate NM
  - Gross Margin NM
  - Operating Margin NM
  - Profit Margin NM
  - Net Margin NM

#### Annual Percentage Change

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<th>KITE-C19 WW Sales</th>
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<th>282%</th>
<th>79%</th>
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</tr>
<tr>
<td>KITE-C19 ex-US sales</td>
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<td>Total revenue</td>
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<td>76%</td>
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<tr>
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<td>50%</td>
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<tr>
<td>EPS</td>
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(a) Assumes full revenues from US sales; no revenues from ex-US, instead receiving partnership royalties
(b) Assumes 17-21% ex-US royalty
(c) As of March 31st, 2014, Kite had 5,568,632 options outstanding at an average exercise price of $1.00

Source: Company reports and Stifel estimates
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Prior to August 18, 2014, a different Stifel research analyst provided research coverage of Kite Pharma, Inc. and its securities. Kite Pharma, Inc.’s price chart for the period prior to August 18, 2014 reflects the rating and price target history of the former Stifel research analyst for such issuer and its securities.

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Hi Steve,

Please take a look at the NY ESO 1 Nature Med paper,

Arie


Via Yahoo Finance.

Arie Beldegrun, MD FACS
President and CEO, Chairman
Kite Pharma

www.kitepharma.com
See below

Arie Belldegrun, MD FACS
President and CEO, Chairman
Kite Pharma

www.kitepharma.com

Begin forwarded message:

From: Lisa Burns <L.Burns@burnsmc.com>
Date: July 24, 2015 at 12:21:08 GMT+2
To: Arie <arie@kitepharma.com>, C Butitta <cbutitta@kitepharma.com>, "David Chang M.D. D. Ph. D. (dchang@kitepharma.com)" <dchang@kitepharma.com>, "Helen Kim (Kite Pharma)" <hkim@kitepharma.com>
Cc: "Catherine Bechtold (kbechtold@kitepharma.com)" <kbechtold@kitepharma.com>, "Linda Barnes (lbarnes@kitepharma.com)" <lbarnes@kitepharma.com>, Kite Team <Kite.Team@burnsmc.com>
Subject: ADAP - Executing Toward Major Milestones - Cowen and Company

From: Eric Schmidt, Ph.D. [mailto:eric.schmidt@cowen.com]
Sent: Friday, July 24, 2015 4:01 AM
To: Lisa Burns
Subject: QUICK TAKE - ADAP - Executing Toward Major Milestones - Cowen and Company
The Cowen Insight

We hosted meetings with Adaptimmune’s CEO James Noble, COO Helen Tayton-Martin, CFO Adrian Rawcliffe, VP of IR Will Roberts. Adaptimmune is focused on leveraging its antigen/peptide identification and TCR engineering platforms to develop engineered T cell therapies for multiple tumor types. H2:15 will see the initiation of multiple new cohorts/trials, and lay the groundwork for a data-rich 2016.

Remind Me What Adaptimmune Does Again?

Adaptimmune is developing engineered T cell therapies for oncology. Adaptimmune has a fully integrated R&D platform that (1) identifies novel antigen targets expressed within tumors; (2) engineers high affinity T cell receptors (TCR) specific to these targets, and (3) deploys these TCR constructs in engineered T cell therapies. Adaptimmune’s most advanced product, NY-ESO-1, is partnered with GSK and has generated positive early data in synovial sarcoma and multiple myeloma. Adaptimmune’s lead wholly-owned candidate, MAGE A10, is set to enter the clinic this year. With a preclinical pipeline of at least 30 targets, we expect multiple additional candidates to begin clinical development in the coming years and Adaptimmune to emerge as a leader in TCR-based cell therapies for cancer.

NY-ESO-1 Generates Durable Responses In Sarcoma; Much Data In 2016

NY-ESO-1 is a cancer testes antigen that is expressed during embryonic development, but is generally not expressed in healthy adult tissues. Its expression is reactivated in many cancer cells including those found in esophageal, melanoma, NSCLC, ovarian, multiple myeloma, and synovial sarcoma tumors. Adaptimmune has already presented multicenter Phase I/II data indicating an ORR of 60% (including 1 CR) in synovial sarcoma and a nCR/CR rate of 59% in post-transplant multiple myeloma. While early, these datasets compare favorably to existing standards of care. In terms of durability of effect, management reports that long-term persistence of NY-ESO-1 TCR cells along with responses continue beyond two years in the multiple myeloma study and one year in the synovial sarcoma cohort (with the aid of surgical resection). The primary reason for increased durability in myeloma is that this study predates the synovial study by >1 year. During 2016, management intends to release updated data from these trials as well as begin trials in esophageal, lung, ovarian, melanoma, and salvage setting multiple myeloma.

MAGE-A10 IND Active, Dose Escalation To Begin In H2

MAGE A10 is another cancer testes antigen. Data from Adaptimmune and other collaborators indicates that MAGE A10’s expression is turned on in many bladder, breast, GI, head and neck, lung, melanoma, and ovarian cancers. Adaptimmune has identified an HLA-A2 presented peptide specific to MAGE A10 and engineered a high affinity TCR specific for this MHC:peptide complex. At the time of its IPO, Adaptimmune MAGE A10 TCR construct had completed its NIH RAC review. Last week, Adaptimmune announced that its IND had been cleared by the FDA. In meetings with investors, Adaptimmune outlined the initial steps in MAGE A10’s clinical development. During H2:15 (likely Q4), Adaptimmune will initiate a Phase I dose escalation trial for MAGE A10 in NSCLC. This trial will treat patients with 100K, 1 or 5B transduced T cells. Management believes at least 1B cells are required to see any signs of efficacy. Data from this trial is expected to be presented in H2:1. If management observes T cell expansion without any major toxicity signals (e.g. significant off-tumor responses) it will expand the MAGE A10 program beyond NSCLC to bladder, breast, head and neck, and GI cancers. Management has not decided if it will begin this expansion as a "basket trial" enrolling any HLA-A2+, MAGE A10+ cancer patient or with separate tumor specific trials. This trial(s) is expected to begin in 2016.

AFP To Enter The Clinic In 2016

Alpha fetoprotein (AFP) is primarily expressed within hepatocellular carcinoma cells. Adaptimmune has nominated AFP as the next target to enter the clinic. Management highlighted preclinical data from this program demonstrating the
power of its TCR engineering platform. This data demonstrates that a wild-type AFP specific TCR had a $K_D$ of 754uM and showed minimal ability to generate a cell response to AFP$^+$ cell lines. After engineering the TCR to possess a $K_D$ of 20uM (38X increase in affinity) the TCR was able to efficiently generate T cell responses against some AFP$^+$ cell lines but not others. TCRs with a $K_D$ of $\sim$10uM (1X further increase in affinity) were able to recognize additional AFP$^+$ cell lines. However, TCRs with a $K_D$ of <5uM demonstrated significant cross-reactivity with AFP$^+$ cell lines. This demonstrates the high level of sensitivity TCRs have for changes in affinity and reaffirms our belief that Adaptimmune’s TCR engineering platform could be critical for the successful development of cell therapies against many cancer antigens.

**Two INDs Per Year Beginning In 2017**

Management reports that its antigen discovery platform has identified cancer specific MHC presented peptides from 30+ antigens (including NY-ESO-1, MAG A10 and AFP). Adaptimmune reports that of these 30 antigens only 9 are the previously described cancer testes antigens. In addition, 12 of the 30+ targets are under active development. Within these 12 active R&D programs, GSK only has rights to NY-ESO and one additional unnamed target. Therefore, Adaptimmune has retained the vast majority of the economics on its lead programs. Management believes its pipeline of cancer specific targets can supply an average of two INDs per year from 2017 onwards. In order to provide manufacturing capacity for this level of clinical activity, Adaptimmune plans to build a pilot cell production facility. This facility will be located in Philadelphia and be capable of supplying cells for "several hundred" patients per year. Management hopes to sign a property lease soon and have the plant active in 2017.

Please see addendum of this report for important disclosures.

www.cowen.com
Hi Steve,

Proprietary Information, Redacted Per Agreement

All the best,

Arie Belldegrun, M.D., FACS
President and CEO
Chairman of the Board; Founder
Kite Pharma Inc.

2225 Colorado Ave
Santa Monica, CA 90404

310 824-9999 x102
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Kite Pharma Provides Update on KTE-C19 Clinical Trial

Kite KTE-C19 Trial on Track to Advance to Pivotal Phase 2

Kite to Host Conference Call and Webcast on August 17, 2015 at 9:00am Eastern Time

SANTA MONICA, Calif., August 17, 2015 (GLOBE NEWSWIRE) -- Kite Pharma, Inc. (Kite) (Nasdaq:KITE) today provided an update from the Company's ongoing Phase 1/2 clinical trial of KTE-C19 in patients with refractory aggressive non-Hodgkin's lymphoma (NHL) who have failed prior chemotherapy treatments and have a poor prognosis. KTE-C19 is an investigational therapy in which a patient's T cells are genetically modified to express a Chimeric Antigen Receptor (CAR) designed to target the antigen CD19, a protein expressed on the cell surface of B-cell lymphomas and leukemias.

In May, Kite announced that the first patient was treated with KTE-C19 in the Phase 1 portion of the trial and we have since treated multiple patients. Complete responses have been observed by investigators. The responses happened shortly after treatment was administered and Kite is monitoring these patients to determine durability of treatment. To date, toxicities associated with treatment have been similar to those observed in the National Cancer Institute's study of anti-CD19 CAR T cell therapy. There was one patient death early in the study, which was determined to be unrelated to KTE-C19 by the study investigator. After appropriate discussions with the U.S. Food and Drug Administration (FDA), Kite continued to enroll and treat patients in its study and the study was never placed on clinical hold. Kite has submitted an abstract and plans to present topline data from the Phase 1 portion of the trial at the upcoming 2015 American Society of Hematology (ASH) Annual Meeting, to take place in Orlando, FL, December 5-8, 2015.

"We are encouraged by the progress of the KTE-C19 clinical trial and excited by the responses we have seen so far. We believe the KTE-C19 clinical findings are in line with previous results demonstrating the potential of this promising therapeutic approach," said Arie Belldegrun, M.D., FACS, Chairman, President and Chief Executive Officer of Kite. "In agreement with ASH, we have taken this exceptional step of providing an update on the trial in order to address recent misinformation in the market related to our clinical program. We are on track to transition to the Phase 2 portion of the trial and plan to present Phase 1 data at ASH later this year."

Kite's Phase 1/2 clinical trial of KTE-C19 is a single arm, open-label, multi-center study, designed to determine the safety and efficacy of KTE-C19 in patients with refractory diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), or transformed follicular lymphoma (TFL). Upon completion of the Phase 1 portion of the study, Kite expects to proceed with the Phase 2 portion that will include a total of approximately 112 patients. Additional information about Kite's Phase 1/2 study may be found at ClinicalTrials.gov, using Identifier NCT: 02348216.

Conference Call and Webcast Details

Kite will host a live conference call and webcast on Monday, August 17, 2015, at 9:00am Eastern Time to provide a corporate update. The live webcast and subsequent replay may be accessed by visiting the Company's website at ir.kitepharma.com. Please connect to the Company's website at least 5-10 minutes prior to the live webcast to ensure adequate time for any necessary software download. Alternatively, please call (844) 856-8656 (U.S.) or (443) 877-4062 (international) to listen to the live conference call. The conference ID number for the live call is 15633524. Please dial
in approximately 10 minutes prior to the call. The webcast will be available on the Company's website for two weeks following the call.

About Kite Pharma, Inc.

Kite Pharma, Inc., is a clinical-stage biopharmaceutical company engaged in the development of novel cancer immunotherapy products, with a primary focus on engineered autologous T-cell (eACT™) designed to restore the immune system's ability to recognize and eradicate tumors. Kite is based in Santa Monica, CA.

Kite Pharma, Inc. Forward-Looking Statements

This press release contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. The press release may, in some cases, use terms such as "predicts," "believes," "potential," "proposed," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements include statements regarding intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things: the success and timing of the Phase 1/2 KTE-C19 clinical trial and the ability of Kite to present at ASH. Various factors may cause differences between Kite's expectations and actual results as discussed in greater detail in Kite's filings with the Securities and Exchange Commission, including without limitation in its Form 10-Q for the quarter ended June 30, 2015. Any forward-looking statements that are made in this press release speak only as of the date of this press release. Kite assumes no obligation to update the forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

# # #

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Kite Pharma Conference Call Script For August 17, 2015

Kite Pharma Participants:
Arie Belldegrun, MD, FACS, Chairman, President, and Chief Executive Officer
David D. Chang, MD, PhD, Executive Vice President, Research & Development, and Chief Medical Officer
Kate Bechtold, Investor Relations

Operator

Good morning, ladies and gentlemen. Thank you for standing by, and welcome to Kite Pharma’s Conference Call. At this time, all participants are in listen-only mode. Later, we will conduct a question-and-answer session, and instructions will follow at that time. Please be aware that today’s conference call is being recorded. I would now like to turn the conference over to your host Kate Bechtold of Kite’s Investor Relations. Please go ahead.

Kate Bechtold: Welcome & Forward-looking Statement

Thank you, Operator. Good morning and thank you for joining us for today’s conference call. In addition, today’s call is being webcast live on our website and will be available for replay.

Joining me on the call today are Dr. Arie Belldegrun, our Chairman, President, and Chief Executive Officer, and Dr. David Chang, Kite’s Executive Vice President of Research & Development, and Chief Medical Officer.

As a reminder, during today’s call, we will be making certain forward-looking statements. These statements may include statements regarding the success, results, and timing of our ongoing and planned clinical trials, among other things. These forward-looking statements are based on current information, assumptions, and expectations that are subject to change and involve a
number of risks and uncertainties that may cause actual results to differ materially from those contained in the forward-looking statements. These and other risks are described in our periodic filings made with the Securities and Exchange Commission, including our form 10Q for the quarter ending June 30th, 2015, as filed with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, and the Company disclaims any obligation to update such statements.

I will now turn the call over to Dr. Arie Belldegrun.

Dr. Arie Belldegrun

Thank you, Kate. Good morning, everyone. As some of you are aware, we believe there has been a high level of noise and misinformation recently in the market concerning Kite's ongoing Phase 1/2 clinical trial of KTE-C19 in patients with refractory aggressive Non-Hodgkin Lymphoma (NHL). While it is not our desire or practice to disclose information regarding ongoing clinical studies, and we are under no obligation to do so, we have decided to take the exceptional step of holding this call to address the misinformation relating to our clinical trial.

Let me start off this morning by addressing misinformation that has been brought to our attention and make something perfectly clear – Kite’s groundbreaking Phase 1/2 clinical trial of KTE-C19 in patients with refractory aggressive NHL has treated multiple patients, continues to advance and it is not now, nor has it ever been on any type of clinical hold by the FDA or any other regulatory body. As we said on our quarterly report call last week, we believe that we will move into the Phase II portion of this trial as well as commencing additional Phase II trials in other indications later this year. We not only remain on track, but are excited about the impressive clinical responses we have seen to date. More on that a bit later.

Please keep in mind that there is a very important reason for not publicizing clinical information in an ongoing trial. It is not about stock price or competitive advantages. It is about the health,
safety and welfare of subjects in the study, our patients and their families, and their treating physicians who are considering potentially life-altering treatment options offered by our clinical trial. Also it is important not to introduce any bias based on partial information that may compromise the scientific integrity of study. Decisions should not be made based upon anecdotes or selective information leaked into the market. I have dedicated my entire professional life to the care and treatment of patients and have personally conducted countless clinical trials in an academic setting. At Kite, I am far from the exception. We have assembled a stunning array of talented men and women similarly dedicating their lives to others. Collectively, the clinical development team at Kite and the amazing investigators assembled for this groundbreaking study, have decades of experience of treating very sick and dying patients. We know that information about our ongoing trial would never be disclosed by any of the professionals at Kite, and we remain committed to protecting patient information, complying with our regulatory obligations, and preserving scientific integrity.

For those following Kite, you know that 2015 has been an amazing year of “firsts” for the company, which I hope have not gotten lost in the market noise of the last few days. Perhaps most importantly, in May, we announced that we treated our first patient with KTE-C19. We are very pleased to report that we have successfully treated a small but growing number of patients in a multi-center setting using a centralized and proprietary cell manufacturing process. Toxicities associated with the treatment were similar to those observed in the NCI study and complete responses have been observed by investigators.

Our clinical trial was designed to treat patients with aggressive refractory NHL. For many listening to this call, you immediately understand what this means. To others, let me explain: Patients who enroll in this study MUST have disease that has progressed through or early after the use of known and accepted treatments. We expect that patients in our trial will have failed on average between 4 to 5 prior rounds of often debilitating chemo- and immune- therapy and, despite this treatment, the prognosis for all of the patients in our study by definition and design is very poor. We took on the risk of moving forward with KTE-C19 in this extremely challenging
patient population with our eyes open — Why? Because we are committed to helping patients who have no other alternatives.

Months ago and very early in our study, a patient with advanced disease died. This was a sad and unfortunate situation for all those involved. A clinical investigator of the study conducted an in-depth review of the death and concluded that this death was unrelated to our product candidate, KTE-C19. This conclusion was not made or influenced in any way by anyone at Kite. As the sponsor, even before the death, we notified the FDA that the patient’s health had worsened, and following the patient’s death, we submitted all required and necessary information to the FDA as well as to the institutional IRBs that oversee the well-being and interest of clinical trial participants.

With all of the relevant information before us and after proper consultation and discourse with the FDA, we continued enrolling and treating patients. While I will not be reporting detailed data here today, we are extremely pleased and excited about the results we have seen in the ongoing KTE-C19 clinical trial from both before and after the one patient’s death. We have seen tumors melting away in weeks and complete responses in a very sick and desperate group of patients with one of the worst types of aggressive cancers. Obviously, longer follow-up is necessary to determine how long these impressive responses last and the durability of this treatment. Nonetheless, these early clinical responses are extremely gratifying and we continue to believe that engineered CD-19 T cell therapy offers the best possible hope for patients with no other viable alternatives.

In addition to the exciting initial results, we have been able to demonstrate that KTE-C19 can be successfully manufactured and delivered to patients across multiple centers throughout the United States, which is a strong validation of the potential for immuno-oncology to be a viable treatment option for patients. Kite is fully committed to bring KTE-C19 and other future engineered T cell products to patients across the country and beyond, so that patients can receive CAR therapy at a treatment facility near their home or convenient to their family.
While we are encouraged by what we have seen in the elimination of tumors, it is still too early in the study to provide additional details, including with respect to durability. Accordingly, we are enthusiastic to discuss the detailed clinical results, including the most updated follow up, from the first portion of our historic trial at a scientific meeting, and we have submitted an abstract detailing the study results to the upcoming 57th American Society of Hematology (or ASH) Annual Meeting, which will take place in Orlando, Florida, in early December.

In addition, we are affirming our current intention to transition to the Phase II portion of our trial and begin additional studies of KTE-C19 in other indications this year. We expect that this will be a registration trial leading to the filing of our BLA by the end of 2016.

I would also like to take this opportunity to quickly refer to our recent filing of a petition with the US Patent Office for an Inter Partes Review (or IPR) of a patent issued to Memorial Sloan Kettering Cancer Center, subsequently licensed to Juno Therapeutics. I want to reiterate that based upon the conclusions of the top intellectual property attorneys in this country, we at Kite believe that with our ownership of the seminal and broad patent portfolio from Professor Zelig Eshhar we have freedom to operate in our space. We look forward to the resolution of our petition by the Patent Office. Again, we do not believe there are any valid, issued patents that would impact our freedom to operate on KTE-C19.

In closing, I want to once again underscore that we are proud to have initiated the first company-sponsored multi-center clinical trial in patients with aggressive refractory NHL and to have observed KTE-C19 delivering initial complete responses, very much in line with what has been reported from the NCI trial. This therapy is active and, in my professional opinion as a cancer doctor, the early results are impressive. Despite challenges, we believe that, based on the information we have today, we are advancing the most effective therapy for patients with aggressive refractory NHL, allowing us to give hope to terminally ill patients who have no other options. And, we remain on track to potentially commercialize KTE-C19 in 2017.

With that, Operator, could you please open the line for questions?
Closing Statement from Dr. Arie Beldegrun

Thank you, all, for your time today. We are excited by the progress we have made and look forward to reporting additional data from our KTE-C19 study later this year. As always, we want to thank all the patients, their caregivers, the members of the medical community who have participated in our clinical trials, and, of course, all our employees and shareholders for their continued support. We believe we are closer than ever to delivering potentially curative therapies to patients.

Thank you for your participation on our call, and, Operator, you may now disconnect.

#   #   #
Sweeney, Timothy (NIH/NCI) [E]

From: David Chang <DChang@KitePharma.com>
Sent: Monday, August 17, 2015 10:11 AM
To: Rosenberg, Steven A. (NIH/NCI) [E]
Cc: Arie Belidegrun; Jeff Wiezorek
Subject: FW: kite call.

Steve,

Proprietary Information, Redacted Per Agreement

Thanks,
David

From: Shrader, Thomas [mailto:shradert@stifel.com]
Sent: Monday, August 17, 2015 6:32 AM
To: Arie Belidegrun <Arie@kitepharma.com>; David Chang <DChang@KitePharma.com>
Subject: FW: kite call.

Link to my question. I was asked to ask – but thank you for the answer and the call.


Suspected Unexpected Serious Adverse Reaction: serious adverse reactions in subjects given a drug, that may or may not be dose related, but are unexpected, as they are not consistent with current information. A SUSAR may occur during clinical trials or clinical care. Reporting is mandatory for clinical investigators in the EU. In the USA, reporting of adverse events during clinical trials is mandatory, but during clinical care, it is voluntary
Hi Steve,

Just FYI.

Shana Tova!

Arie Beldegrun, MD, FACS
Chairman, CEO, Founder
Kite Pharma
Santa Monica, CA 90404

Begin forwarded message:

From: "Kite Pharma, Inc." <jjackson@burnsmc.com>
Date: September 14, 2015 at 14:07:52 GMT+2
To: <Arie@kitepharma.com>
Subject: Kite Pharma Expands Collaboration With Netherlands Cancer Institute (NKI)

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Kite Pharma Expands Collaboration With Netherlands Cancer Institute (NKI)

Kite and NKI Sign Master Services Agreement and Kite Obtains From NKI Exclusive Option to License T Cell Receptor (TCR) Cancer Immunotherapy Product Candidates

SANTA MONICA, Calif., Sept. 14, 2015 (GLOBE NEWSWIRE) -- Kite Pharma, Inc. (Kite) (Nasdaq:KITE) today announced that it has expanded its
entered into an agreement under which Kite will receive from the NKI the exclusive option to license multiple T cell receptor (TCR) gene sequences for the development and commercialization of cancer immunotherapy candidates targeting solid tumors. Kite has also expanded its access to additional resources and research facilities through a master services agreement with the NKI.

"We are excited with the progress of the TCR research programs with Kite and look forward to further advancements of the programs and our collaboration," said Professor René Medema, Director of NKI. "NKI believes that TCR technologies hold great potential for cancer care, and we are committed to making these new therapies a reality for patients."

Kite Pharma EU, based in Amsterdam, will be conducting preclinical research related to candidates under the agreement with NKI. Kite Pharma EU is comprised of a leading team of immuno-oncology researchers and collaborators, including Professor Dr. Ton N. M. Schumacher, who serves as Chief Scientific Officer of Kite Pharma EU. Professor Dr. Schumacher, a pioneer in T cell biology and gene therapy, is a developer of Kite's proprietary TCR-GENERator™ discovery platform, an industry-leading R&D engine for rapid, high-throughput identification of TCR-based product candidates.

"With Kite Pharma EU, we have established a central hub of cancer immunotherapy efforts in Europe, attracting leading scientific experts, researchers and collaborators in this field," said Arie Beldegrun, M.D., FACS, Chairman, President and Chief Executive Officer of Kite. "Kite's relationship with the NKI, an internationally renowned cancer research and clinical institution, provides an important operational platform, as we advance TCR-based immuno-oncology product candidates."

About Kite Pharma, Inc.

Kite Pharma, Inc., is a clinical-stage biopharmaceutical company engaged in the development of novel cancer immunotherapy products, with a primary focus on engineered autologous cell therapy (eACT™) designed to restore the immune system's ability to recognize and eradicate tumors. Kite is based in Santa Monica, CA. For more information on Kite Pharma, please visit www.kitepharma.com.

Kite Pharma, Inc. Forward-Looking Statements

This press release contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. The press release may, in some cases, use terms such as "predicts," "believes," "potential," "proposed," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements include statements regarding intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things: the ability to advance, and the success of, TCR-based product
and actual results as discussed in greater detail in Kite's filings with the Securities and Exchange Commission, including without limitation in its Form 10-Q for the quarter ended June 30, 2015. Any forward-looking statements that are made in this press release speak only as of the date of this press release. Kite assumes no obligation to update the forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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CRISPR-Cas9 delivery to hard-to-transfect cells via membrane deformation

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The CRISPR (clustered regularly interspaced short palindromic repeats)-Cas (CRISPR-associated) nuclease system represents an efficient tool for genome editing and gene function analysis. It consists of two components: single-guide RNA (sgRNA) and the enzyme Cas9. Typical sgRNA and Cas9 intracellular delivery techniques are limited by their reliance on cell type and exogenous materials as well as their toxic effects on cells (for example, electroporation). We introduce and optimize a microfluidic membrane deformation method to deliver sgRNA and Cas9 into different cell types and achieve successful genome editing. This approach uses rapid cell mechanical deformation to generate transient membrane holes to enable delivery of biomaterials in the medium. We achieved high delivery efficiency of different macromolecules into different cell types, including hard-to-transfect lymphoma cells and embryonic stem cells, while maintaining high cell viability. With the advantages of broad applicability across different cell types, particularly hard-to-transfect cells, and flexibility of application, this method could potentially enable new avenues of biomedical research and gene targeting therapy such as mutation correction of disease genes through combination of the CRISPR-Cas9-mediated knock-in system.

INTRODUCTION

The CRISPR (clustered regularly interspaced short palindromic repeats)-Cas (CRISPR-associated) nuclease system is an easy-to-use, highly specific, efficient, and multiplexable genome editing tool that has been used in various organisms, including human and mouse cell lines (2–3). In the two-component system, a single-guide RNA (sgRNA) directs Cas9 nuclease to introduce sequence-specific targeted loss-of-function mutations into the genome (3, 4). Cas9 can be easily programmed to induce DNA double-strand breaks through RNA guides, which can generate insertions and deletions (indels) and stimulate genome editing at specific target genomic loci (5, 6). The ability to perturb the genome in a precise and targeted manner is crucial to understanding genetic contributions to biology and disease (3, 7).

Successful delivery of sgRNA and Cas9 into cells guarantees efficient genome editing. Typical intracellular delivery techniques use liposomes or polymeric nanoparticles to induce cell membrane poration or endocytosis (8–11), and recently, cell-penetrating peptide-mediated delivery of sgRNA and Cas9 has been used for gene disruption (12). In these methods, delivery efficiency is often dependent on cell type and the structure of the target molecule. Electroporation is an attractive alternative for many applications and allows highly efficient RNA-guided genome editing via delivery of purified Cas9 ribonuclease protein (13–15). However, this method can cause cell damage and generate a high cell death rate. Moreover, commonly used virus (adeno-associated virus, retrovirus, or lentivirus)-mediated delivery of sgRNA and Cas9 is often associated with uncontrolled chromosomal integration (16, 17), limiting its clinical potential.

Rapid mechanical deformation of cells can produce transient membrane disruptions that facilitate passive diffusion of material into the cytosol. Using physical constriction to deform and shear cells for delivery has achieved high efficiency with low cell death rate. This method has the advantage of high-throughput delivery of almost any macromolecule into almost any cell type (18). Membrane deformation–based microfluidic devices have been used in the delivery of a range of materials such as carbon nanotubes, proteins, and short interfering RNAs (siRNAs). They have been used for delivering transcription factors for cell reprogramming (18). Microfluidic membrane deformation has the potential to serve as a broad-based universal delivery platform and boasts the advantages of precise control over treatment conditions at the single-cell level, with macroscale throughput. Here, we optimized the physical constriction in a microfluidic setup, considering both delivery efficiency and cell viability. Through this, we successfully delivered single-stranded DNA (ssDNA), siRNAs, and large-sized plasmids into different cell types, including adherent and non-adherent cells, hard-to-transfect lymphoma, and embryonic stem cells. Size analysis, together with biochemical and functional analyses, demonstrated highly efficient genome editing and successful gene generation of gene-knockout cell lines, using our delivery device in different cell types. To the best of our knowledge, this is the first demonstration of membrane deformation for CRISPR/Cas9 gene editing. Thus, we expect that our new microfluidic delivery method will facilitate RNA-guided genome editing and gene loss-of-function analysis across different cell types, especially difficult-to-transfect cells. Achievement of high genome editing efficiency in non-adherent lymphoma cells suggests that the approach also has potential for clinical use.

RESULTS

Delivery principle and chip design

When a cell passes through a constriction smaller than the cell diameter, it undergoes rapid mechanical deformation, causing transient membrane
disruption or holes. The shear and compressive forces imposed on the cell during passage through the constriction determine the degree of disruption and the size and frequency of the holes. Macromolecules small enough to pass through the holes can diffuse into the cytosol from the surrounding medium and may remain and function in the cell after the membrane recovers from the deformation (Fig. 1A and B). To apply this principle, we designed a family of microfluidic devices with a series of constrictions of different dimensions formed by structures of different shapes (fig. S1A).

Devices were fabricated with standard polydimethylsiloxane (PDMS) microfluidics technology. Each chip consists of 14 identical cell-scattering and deformation zones, and each zone contains 10 arrays of structures forming microconstrictions (Fig. 1C). The scatter zone is designed to prevent device collapse and also disperse or “scatter” the cell suspension. The deformation zone is where cells pass through microconstrictions, becoming deformed and generating transient membrane holes that ensure delivery of the macromolecule(s) of interest. Interconnected channels enable high throughput of treated cells by preventing clogging. To optimize the microconstriction design, we first prepared constrictions using structures of several different shapes, including circle, ellipse, and diamond (fig. S1A). Suspended cells were applied to the chip through a Tygon tube connected to the inlet, and fluid flow was controlled by a syringe pump. To optimize the design, we did a series of test deliveries of fluorescein isothiocyanate (FITC)-labeled ssDNA into human embryonic kidney 293T (HEK293T) cells. The smallest constriction width of the three designs, 4 μm, was chosen for further experiments. Of the three designs, the diamond pattern showed nearly identical delivery efficiency at a range of flow rates from 50 to 250 μl/min, with much higher cell viability than the circle or ellipse pattern (fig. S1B and C), and so this pattern was chosen for further experiments. To maximize the functional area, we minimized the length of the diamond edge to 10 μm (Fig. 1C). The parallel chip design (fig. S1D) was generated by arranging multiple devices side by side to demonstrate that delivery can be multiplexed. The cell recovery rate after delivery for both HEK293T and SUM159 cell lines was close to 100% (fig. S1E). Movie S1 shows cells passing through microconstrictions formed by the diamond pattern at a flow rate of 30 μl/min. Cell stress simulation (Fig. 1D and fig. S2) and flow velocity simulation (fig. S3) were applied to the diamond pattern design at the time point when a cell began to penetrate the microconstriction. Movie S2 shows the flow velocity simulation. With this chip design, we expect to successfully deliver plasmids encoding different sgRNAs and Cas9 into different types of cells and achieve precise genome editing and perform specific gene loss-of-function analysis, as depicted in Fig. 1B.

![Image](https://example.com/image.png)

**Fig. 1. Delivery mechanism and device design.** (A) Illustration of the delivery process wherein cells pass through the microconstriction and experience deformability. Plasmids encoding sgRNA and Cas9 protein are mixed with the cells to flow through the chip. (B) Illustration of the delivery mechanism whereby transient membrane holes are generated when cells pass through the microconstriction and specific genome editing is conducted after plasmids encoding sgRNA and Cas9 protein are delivered into the cell. Cell deformation was shown by microscopy when cells passed through the microconstriction. Scale bar, 15 μm. n.t., nucleotide. (C) Microscopy of the whole device structure. Scale bar, 0.5 mm. Scanning electron microscopy (SEM) of scattered and deformable zones in the device is also shown. Scale bar, 15 μm. One diamonded microconstriction of 15-μm depth and 4-μm width is indicated by the red arrow. The length of the diamond edge is 10 μm. (D) Cell stress simulation was applied on the diamonded microconstriction design with 15-μm depth and 4-μm width when a cell began to penetrate the constriction. A graphical representation of the cell stress gradient that forms across the membrane is shown.
Optimization of the delivery chip specifications
To optimize the delivery performance of the chip, we took into consideration constriction dimensions, fluid flow rates, and duration of cell passage through the chip as three key parameters. In the diamond design, the constriction depth was 15 μm, and the width varied from 4 to 5 μm (Fig. 1C). In pursuit of high delivery efficiency coupled with high cell viability, we did a series of testing deliveries of FITC-labeled ssDNA into HEK293T cells (Fig. 2A). Our data showed that delivery efficiency increased with increasing flow rate across design patterns (Fig. 2B). The 4-μm constriction width presented higher delivery efficiency than the 5-μm width at all flow rates, with minimal effect on cell viability. Increasing the number of operational cycles with the same chip allowed multiple cell passaging times, which would also enhance the delivery efficiency; however, the operation clearly decreased cell viability (Fig. 2, B and C). The data for the 0 μl/min flow rate represents a control whereby the cells were treated exactly as the other samples but were not applied with the membrane deformation, thus ruling out the possibility that cell FITC positivity was the result of any endocytotic or surface binding events.

Broad applicability
To investigate the adaptability of this technique, we first tried siRNA delivery for gene knockdown. Considering both delivery efficiency and cell viability, we chose a microconstriction width of 4 μm, a fluid flow rate of 250 μl/min, and single passage of the cells through the chip for all subsequent experiments. When we delivered three siRNAs specific for Akt1 into PC-3 cells, all of the oligos achieved >70% knockdown efficiency in 48 hours after delivery (Fig. 2D). Moreover, depletion of Akt1 by all three siRNAs suppressed cell growth, which is consistent with previous research (Fig. 2E), indicating that our technique is reliable for cell phenotype analysis and gene function study (19).

To further assess the delivery ability of the chip across different cell types, we used plasmids encoding green fluorescent protein (GFP) to measure the delivery efficiency. We successfully delivered plasmids encoding GFP with high efficiency into HEK293T cells, human luminal-like MCF7 and basal-like SUM159 breast cancer cells, human SU-DHL-1 anaplastic large cell lymphoma cells, and mouse AB2.2 embryonic stem cells (Fig. 2F), all with minimal cell death. Using our method, we achieved nearly the same percentage of GFP-expressing cells as

Fig. 2. Governing parameters and broad applicability. (A) Microscopy of HEK293T cells into which FITC-labeled ssDNA was delivered through our chip. Results shown are from two independent chips. Control indicated all the same treatments for the cells except passing through the chip. Scale bar, 50 μm. BF, bright field. (B and C) Delivery efficiency (B) and cell viability (C) 16 hours after treatment were calculated for (A) as a function of fluid speed at different parameter designs; 4 or 5 μm indicates the constriction width, and 4 μm x3 indicates cells passing through the same device three times. Error bars indicate SEM (n = 3). (D) Western blotting of PC-3 cells 48 hours after delivery with three different siRNA oligos targeting Akt1. Actin is shown as a loading control. (E) Cells from (D) were seeded in complete medium and, after 6 days, were recovered and trypsinized to count the numbers with a Countess II FL Automated Cell Counter (Life Technologies). Error bars indicate SEM (n = 3). *P < 0.005 determined by Student’s t test. (F) Delivery efficiency in different cell lines, HEK293T cells, human luminal-like MCF7 and basal-like SUM159 breast cancer cells, human SU-DHL-1 anaplastic large cell lymphoma cells, and mouse AB2.2 embryonic stem cells were delivered with plasmids encoding GFP. Untreated serves as a negative control and FuGENE HD serves as a positive control. Error bars indicate SEM (n = 3). *P < 0.005 determined by Student’s t test.
obtained with traditional FuGENE HD transfection (Fig. 2F and fig. S4, A to E). Our delivery method achieved even higher efficiency than FuGENE HD transfection in human anaplastic large cell lymphoma cells and mouse embryonic stem cells without inducing stem cell differentiation (Fig. 2F and fig. S4F), suggesting potential application in difficult-to-transfect cells. Device designs have not been optimized for different cell types, indicating that we can expect further improvement in delivery efficiency, with the goal of cell-specific delivery protocols, in future applications.

**EGFP knockout via chip**

We used cells stably expressing enhanced GFP (EGFP) to illustrate the potential application of this method in CRISPR-Cas9–mediated genome editing. EGFP was introduced into cells with lentivirus, and the EGFP encoding sequences were integrated into chromosomal DNA. Plasmids encoding Cas9 only or sgRNAs targeting EGFP (sgEGFP-1 and sgEGFP-2) and Cas9 were delivered into adherent MDA-MB-231 cells and non-adherent SU-DHL-1 lymphoma cells. To enhance delivery efficiency, cells were passed through the same chip three times. After delivery, cells were allowed to recover in culture for 7 days. Bright-field and fluorescence microscopic (Fig. 3A) and flow cytometric analyses (Fig. 3B and fig. S5A) showed that plasmid delivery was efficient and genome editing was successful in MDA-MB-231 cells, achieving >90% EGFP knockout efficiency with both sgRNAs targeting different EGFP coding sequences. In SU-DHL-1 lymphoma cells, bright-field and fluorescence microscopic analyses (Fig. 3C) and flow cytometric analyses (Fig. 3D and fig. S5B) showed >70% EGFP knockout efficiency, which was satisfactory for this difficult-to-transfect lymphoma cell line and could not be achieved by current transfection methods. As expected, EGFP expression was not affected in the negative control cells, which were delivered with plasmids encoding Cas9 only.

To analyze the indels at the EGFP locus generated by CRISPR-Cas9–mediated genome editing, we amplified the specific sgEGFP-1 target regions by polymerase chain reaction (PCR) and conducted TA cloning of the products in SU-DHL-1 lymphoma cells (fig. S5C). The results of sequence analysis showed that delivery of plasmids encoding sgRNA targeting EGFP and Cas9 via our chip caused different types of mutations in the EGFP locus (Fig. 3E). These data indicate that we successfully delivered plasmids encoding sgRNAs and Cas9 into different human cell lines using our chip and achieved highly efficient genome editing.

**Gene disruption platform**

To determine whether our delivery platform could be used for gene disruption and function analysis, we carried out further delivery of plasmids encoding Cas9 and sgRNAs targeting different genes in different types of cell lines. Plasmids encoding sgRNA targeting the endogenous AAVS1 locus and Cas9 were delivered into MCF7 cells. The cells were allowed to recover in culture for 7 days, followed by PCR amplification of the specific sgRNA target region. The results of TA cloning and sequence analysis showed that the delivery of plasmids encoding Cas9 and sgRNA targeting AAVS1 resulted in mutations, including indels, at the specific genomic loci (Fig. 4A). Surveyor mutation detection assay revealed substantial cleavage at the AAVS1 locus, with indels occurring at a frequency of about 18 to 46% when optimization was performed by passage of the cells through the chip three times (Fig. 4B).

We designed an sgRNA targeting the first exon of the NUAK2 gene and cloned it into a vector for coexpression with sgRNA and Cas9 (Fig. 4C). Plasmids encoding Cas9 and sgRNA targeting NUAK2 were delivered into HeLa cells via our membrane deformation method, and the cells were allowed to recover in culture for 7 days. PCR amplification of the sgRNA target region followed by TA cloning and sequence analysis showed deletion mutations at the specific genomic loci (Fig. 4D). Mutation detection assay revealed substantial cleavage at the NUAK2 gene locus, with indels occurring at a frequency of about 30% (Fig. 4E). The indel mutation frequencies could be optimized in a few ways such as passaging cells multiple times through the deformation chip, increasing the concentration of the plasmids, and using a selective drug to kill the nontransfected cells.
Next, we explored gene function and cell phenotype via our delivery chip. Plasmids encoding Cas9 and sgRNA targeting phosphatase and tensin homolog (Pten) (fig. S6A) were delivered into MCF7 cells, followed by culture for 48 hours and puromycin selection. More than 80% of the cells survived the selection process, indicating the high delivery efficiency of our method. Cells were allowed to recover for 7 days and then analyzed by Western blotting. The results of Western blotting analysis showed that endogenous Pten expression was abolished compared with expression in control cells transfected only with plasmid encoding Cas9. Moreover, the level of Akt phosphorylation increased with Pten depletion, consistent with activation of Akt by loss of Pten (Fig. S5A). Cells were immunostained to further confirm successful knockout of Pten and Akt activation (fig. S6B). Cell proliferation was also increased in MCF7 cells after Pten knockout (fig. S5B), which is consistent with a previous study (20).

Tumor suppressor p53 binding protein 1 (53BP1) is required for DNA damage response and tumor suppression (21–23). We designed an sgRNA targeting a 53BP1 gene locus and delivered plasmids encoding both sg53BP1 and Cas9 via our chip into HeLa cells (fig. S6C). Cells were cultured for 48 hours and then selected with puromycin. Similar to Pten knockout, more than 80% of 53BP1 knockout cells survived the selection process. Western blotting analysis showed the clear absence of 53BP1 expression compared with control cells (fig. S6D). Camptothecin (CPT) causes DNA strand breaks mediated by transcription and induces clear 53BP1 foci in the nuclei. Here, we showed that CPT treatment resulted in clear 53BP1 foci formation in the nuclei of control cells, but not in the cells treated with plasmids encoding both sg53BP1 and Cas9 (Fig. 5C). Consistent with this, cell survival was also greatly decreased in the cells delivered with plasmids encoding both sg53BP1 and Cas9 after CPT treatment (Fig. 5D). Together, these data show that our chip-mediated delivery is a rapid, efficient, and high-throughput method for CRISPR-Cas9–mediated genome editing and gene knockout analysis and may provide a multiplexable and integrated platform for gene phenotype and functional analysis.

**DISCUSSION**

Our delivery method uses the mechanical deformability of cells to generate transient holes in the cell membrane, permitting diffusion of biomaterials in the extracellular milieu into the cytoplasm. We achieved high delivery efficiency and high cell viability with delivery of siRNAs and plasmids. On the basis of the delivery principle, this method also has the potential to deliver other materials, such as proteins and nanoparticles. Moreover, the delivery method can be applied across different...
types of cells, including hard-to-transfect cells, such as immune cells and stem cells, to address clinical needs. In the future, with a better understanding of the nature of the deformation experienced by cells passing through a microconstriction and optimization of device parameters, one can expect to achieve better performance in a range of cell types and applications.

The mechanical deformability–based principle provides a new solution for delivery and has advantages over some existing methods. To our knowledge, this is the first application of this microfluidic deformation method to the delivery of the CRISPR-Cas9 system to achieve genome editing and gene disruption. Similar to microinjection, the method does not rely on cell type or the structure of the target molecule (24, 25); however, it is easier to use with higher throughput than microinjection. Electroporation has been successfully applied to CRISPR-Cas9 delivery and allows highly efficient RNA-guided genome editing. However, unlike our microfluidic method of delivery, electroporation damages cells and often affects cell viability. The high delivery efficiency and associated high cell viability of our method guarantee efficient genome editing and precise gene functional analysis. To increase genome editing activity, the cells may apply the cells multiple times through the deformation chip times, increase the concentration of the plasmids, and/or use a selective drug to kill the nontransfected cells. Using stable Cas9-expressing cells for sgRNA delivery or Cas9 protein/sRNA co-complexes may also be helpful to increase the indel frequencies. Given our achieved capability of the deformation-based CRISPR/Cas9 gene editing, we expect to expand the work to many other cells and model systems.

Microfluidics as a basic research tool has the advantage that it is capable of integration and incorporation into a larger system including multiple posttreatment modules. This enables potential integration of our CRISPR-Cas9 system delivery and gene loss-of-function or mutation correlation analysis. For example, the device could be integrated with the single-cell protrusion microfluidic chip developed in our laboratory for screening genes potentially involved in cell protrusion mechanics (26). Use of our device would generate large quantities of CRISPR–Cas9–mediated knockout or knockin cells for high-throughput cell phenotypic screening.

CRISPR-Cas9–mediated delivery for gene therapy has been reported recently for correction of some mutations associated with disease (7, 27–30). Our technique enables novel approaches to this type of gene therapy. We have achieved high delivery efficiency compared with traditional liposome–mediated delivery in SU-DHL-1 lymphoma cells, and successful application in anaplastic large cell lymphoma cells provides the possibility of delivery in primary patient cells. For example, a patient's target cells could be isolated from blood or other tissue, treated with the device to deliver the CRISPR–Cas9 knockin system with wild-type template to correct the disease gene mutation, and then reintroduced into the patient. The enhanced delivery efficiency of our method would increase the likelihood of correcting disease mutation genes by gene targeting therapy.

MATERIALS AND METHODS

Materials and reagents

SPR 220-7 provirus was purchased from Rohn and Haas Electronic Materials. PDMS (GE 615 RTV) was purchased from Fisher Scientific. Tygon tubing was purchased from Saint-Gobain. Flat steel pins were purchased from New England Small Tube. Fetal bovine serum (FBS), trypsin, and penicillin-streptomycin were purchased from Fisher Scientific. Dulbecco's modified Eagle's medium (DMEM), Ham's F-12 medium, RPMI 1640 and F-12K medium, insulin, hydrocortisone, and phosphate-buffered saline (PBS) were purchased from Life Technologies. FITC-labeled ssDNA DNA was purchased from Integrated DNA Technologies. siRNAs targeting Akt1 (siAkt1-1 SASI_Hs01_00105952, siAkt1-2 SASI_Hs01_00105953, and siAkt1-3 SASI_Hs01_00105954) were used previously and purchased from Sigma-Aldrich (31). Plasmids encoding sgRNA and Cas9 were purchased from Addgene, and specific sgRNA target sequences were cloned into the CRISPR_v2 vector (Addgene plasmid #52961). The 20-bp target sequences of sgRNAs targeting EGF, AAVS1, and Pten were used previously (4–6). The 20-bp target sequences of the indicated sgRNAs were as follows: sgEGFP-1, GGGCAGGAGCGTCGTCACC; sgEGFP-2, GAGCTGAGCGCGACGTAAA; sgAAVS1, GGGGACTAGGGACAGGAT; sgNUAK2, TTGATCGGCGCTTGCACAG; sgPten, AGATCGTATAAGAAACAA; sg53BP1, CATATTTTCTACCTACGTC. The primers used for PCR amplification of sgRNA target regions were as follows: EGFP-FF, ATGGTGAGGACGGGGAGGA; EGFP-RR, TTACCTTGACAGCCGTCGCA; AAVS1-FF, CCCCTTCTCGTTGTTTCC; AAVS1-RR, ATCTCTCTGGTCCGATCTCGT; NUAK2-FF, GCTTTACTGCGCGCTTGTACTG; NUAK2-RR, CAGCGGCGCCGAGCTTCC.

Chip design and fabrication

The microchip pattern was designed with AutoCAD (Autodesk). Each chip consists of 14 identical cell-scattering and deformation zones, and each zone contains 10 arrays of constriction. The constriction depth is 15 μm, and the width varies from 4 to 5 μm. The parallel chip design was generated by arranging multiple devices side by side. The microfluidic chip was fabricated using standard photolithography and soft lithography procedures. The negative photoresist SU8-3025 (MicroChem) was used to fabricate patterns on a silicon wafer. The silicon wafer was then siliconized using trimethylchlorosilane (Thermo Scientific) for 30 min to facilitate PDMS mold release. PDMS prepolymer (10A:1B, Sylgard 184 silicone elastomer kit, Dow Corning) was poured onto the silicon wafer and cured at 80°C for 1 hour. Holes were then punched in the PDMS for the inlets and outlets, and oxygen plasma treatment was used to chemically bond the PDMS mold to a glass slide.

Finite element method

The flow velocity distribution, cell trajectory, and stress on the cell were simulated using the finite element method. To perform the temporal simulation, the fluidic dynamics equation (incompressible Navier-Stokes equations) and solid mechanics equation (Newton's second law of motion) were coupled and implemented by fluid-solid interactions. This combined the spatial frame interface for fluid flow and the material frame for the cell. The mesh geometry was continuously moved and deformed by applying the arbitrary Lagrangian-Eulerian method. The dimensions of model geometries and mechanical properties were identical to the actual experiment. The stress on the cell was computed as the von Mises stress, which is a scalar value determined from the stress tensor of a particle under the pressure in fluid flow.

Cell culture

HEK293T, MCF7, MDA-MB-231, and HeLa cells were grown in DMEM supplemented with 10% FBS and 1% penicillin-streptomycin.
in a humidified atmosphere of 5% CO₂/95% air at 37°C. PC-3 cells were grown in F-12K medium supplemented with 10% FBS and 1% penicillin-streptomycin. SUM159 cells were grown in Ham’s F-12 medium supplemented with 5% FBS, 1% penicillin-streptomycin, insulin (5 μg/ml), and hydrocortisone (1 μg/ml). Human SU-DHL-1 anaplastic large cell lymphoma cells were cultured in RPMI 1640 supplemented with 10% FBS and 1% penicillin-streptomycin. Mouse AB2.2 embryonic stem cells were maintained on a 0.1% gelatin (Sigma-Aldrich)—coated tissue culture dish in high-glucose DMEM, supplemented with 15% FBS, 55 μM β-mercaptoethanol (Life Technologies), and 0.01% mouse leukemia inhibitory factor (Millipore) under feeder-free conditions.

**Delivery procedure and puromycin selection**

The channels in the device were wetted with PBS and blocked with 1% bovine serum albumin in PBS for 10 min. Cells were first suspended in the desired volume of Opti-MEM medium (Life Technologies) and then mixed with the desired amount of delivery material (ssDNA, siRNA, or plasmid) and loaded into plastic Tygon tubing with a 5-ml syringe. The tubing was then connected to the device inlet reservoir by a flat steel pin. During the flow experiments, a syringe pump controlled the fluid flow through the device. Treated cells were incubated in a 37°C incubator for 20 min to recover before further treatment.

Plasmids encoding both Cas9 and sgRNA targeting Pten or 53BP1 were delivered into MCP7 or HeLa cells, respectively, via our chip. After 48 hours of culture, the cells were grown in DMEM supplemented with 10% FBS, 1% penicillin-streptomycin, and puromycin (2 μg/ml, Sigma) for 2 to 3 days to kill the undelivered cells.

**Immunostaining, Western blotting, and flow cytometry**

Cells grown overnight on coverslips were fixed in 4% paraformaldehyde and then permeabilized with 0.5% Triton X-100 plus 300 mM sucrose. Cells were then immunostained and visualized under an Olympus FV1000 confocal microscope. The primary antibodies used were anti-53BP1 (NB100-304, Novus Biologicals), anti-Oct4 (ab18976, Abcam), anti-Pten (ab130224, Abcam), and anti–phospho-akt (Ser 473) (ab1283, Abcam). The secondary antibodies used were Alexa Fluor 488–conjugated goat anti-mouse (A-11001, Life Technologies) and Texas red–conjugated goat anti-rabbit (T-2767, Life Technologies).

For Western blotting after siRNA-mediated knockdown or sgRNA-Cas9–mediated knockdown, cells were allowed to recover in culture for 2 or 7 days, respectively. The primary antibodies used were anti-Akt1 (ab32505, Abcam), anti-53BP1 (ab21083, Abcam), and anti-actin (A3853, Sigma-Aldrich). For flow cytometric analysis after sgEFGP-mediated knockdown, cells were allowed to recover in culture for 7 days followed by analysis of EFGP fluorescence with a BD LSRFortessa cell analyser.

**Mutation detection assay, TA cloning, and sequencing**

Genomic DNA was extracted using the PureLink Genomic DNA Mini Kit (K1820-00, Life Technologies) according to the manufacturer’s instructions. PCR ampiclons of nuclease target sites were generated and analyzed for the presence of mismatch mutations using the Transgenic Surveyor Mutation Detection Kit (Integrated DNA Technologies) according to the manufacturer’s instructions. Briefly, PCR ampiclons of sgRNA target regions were denatured by heating for 10 min at 95°C, annealed to form heteroduplex DNA using a thermocycler from 95°C to 25°C at −0.3°C/s, digested with Surveyor Nuclease S for 2 hours at 42°C, and separated by 1% agarose gel electrophoresis. For sequence analysis, PCR products corresponding to genomic modifications were cloned into pCR4-TOPO vector using the TOPO TA Cloning Kit (Life Technologies). Clone products were sequenced using the M13 primer.

**Cell proliferation assay, CPT treatment, and sensitivity assay**

After chip-mediated delivery and recovery in culture for siRNA knockdown or sgRNA-Cas9–mediated knockout, cells (5 × 10⁵) were seeded in 60-mm dishes in complete medium and cultured for 7 days. Cells were harvested by trypsinization daily and counted in a Countess FL Automated Cell Counter (Life Technologies).

To assess CPT sensitivity, cells were treated with 1 μM CPT for 2 hours and immunostained with anti-53BP1 or treated with 10, 20, 30, or 40 nM CPT for sensitivity assay. CPT sensitivity was assessed by colony survival assay. Briefly, CPT-treated cells (500 to 1000) were plated in 60-mm dishes in complete medium and incubated for 2 to 3 weeks to form clones. Clones were stained with Coomasie blue, and survival rate was calculated.

**SUPPLEMENTARY MATERIALS**

Supplementary material for this article is available at http://advances.sciencemag.org/cgi/content/full/11/7/e1500454/DC1

**Fig. S1.** Performance of chip with different designs.
**Fig. S2.** Cell stress simulation.
**Fig. S3.** Flow velocity simulation.
**Fig. S4.** Comparison of FuGENE HD transfection and delivery via chip.
**Fig. S5.** Flow cytometric analysis of EGFK knockout cells.
**Fig. S6.** Pten and 53BP1 knockout mediated by delivery via chip.
**Movie S1.** Cells passing through the diamond microconstriction chip.
**Movie S2.** Flow velocity simulation in the diamond microconstriction chip.

**REFERENCES AND NOTES**


Funding: We acknowledge funding support from the Cancer Prevention and Research Institute of Texas (CPRIT-R1007), NIH-CA180083, NIH-US4CA143837, and Golfers Against Cancer Foundation. Author contributions: X.H. and L.Q. designed the experiments and developed the method. X.H. and Z.L. performed the experiments; M.C.J. assisted with flow velocity simulation; K.Z. and Y.L. assisted with device optimization; N.L. assisted with the CPT sensitivity assay; Z.Z. and Y.Z. provided SU-DHL-1 lymphoma cells and helpful suggestions for improved user-friendliness. X.H. and L.Q. wrote the paper. All co-authors reviewed and approved the manuscript. Competing interests: The authors declare that they have no competing interests.

Submitted 9 April 2015 Accepted 29 June 2015 Published 14 August 2015 10.1126/sciadv.1500454

Sweeney, Timothy (NIH/NCI) [E]

From: Arie Belldegrun <Arie@kitepharma.com>
Sent: Monday, October 05, 2015 9:04 PM
To: Patty Lettner; Kite Pharma US; Bianca Weissbrich; Bo Schrikkema; Carsten Linnemann; Gavin Bendle; Georg Dossinger; Laura Bies; Manon Freriks; Markwin Velders; Ton Schumacher
Cc: HR Support; Owen Witte (owenwitte@mednet.ucla.edu); Barbara Anderson [Asst: Owen Witte] (baanderson@mednet.ucla.edu); jeconomou@mednet.ucla.edu; Professor Zelig Eshhar (zelig.eshhar@weizmann.ac.il); Ron Levy; Allan Pantuck (apantuck@mednet.ucla.edu); Antoni Ribas MD PhD (aribas@mednet.ucla.edu); Inder verma; Beth Coyne [Asst: Inder Verma, Kite SAB Member] (coyne@salk.edu); Kohn, Donald; Rosenberg, Steven A. (NIH/NCI) [E]; Shell, Linda (NIH/NCI) [E]; Cary Freeny (cfreeny@mednet.ucla.edu); bmueller@mednet.ucla.edu; JoAnn Palaganas (jpalaganas@mednet.ucla.edu); Mary Jo Spaulding (mspaulding@conet.ucla.edu); vamaya82@stanford.edu
Subject: RE: Organizational Announcement - Jeff S Wiezorek, MD

Jeff,

We are all indebted to you. Your leadership in building the best clinical team in the industry and spearheading the most innovative trials is not only transforming Kite but also the lives of many desperate patients and revolutionizes the practice of oncology.

Thank you,

Arie Belldegrun, M.D., FACS
President and CEO
Chairman, Board of Directors; Founder
Kite Pharma Inc.

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Santa Monica, CA 90404
Tel: 310-622-9093
arie@kitepharma.com
www.kitepharma.com

From: Patty Lettner
Sent: Monday, October 5, 2015 11:38 AM
To: Kite Pharma US <Kite-US@kitepharma.com>; Bianca Weissbrich <BWeissbrich@kitepharma.com>; Bo Schrikkema <BSchrikkema@kitepharma.com>; Carsten Linnemann <C1innemann@KitePharma.com>; Gavin Bendle <GBendle@kitepharma.com>; Georg Dossinger <GDossinger@kitepharma.com>; Laura Bies <LBies@kitepharma.com>; Manon Freriks <mfreriks@kitepharma.com>; Markwin Velders <mvelders@kitepharma.com>; Ton Schumacher <tschumacher@kitepharma.com>
Cc: HR Support <HRSupport@kitepharma.com>; Owen Witte (owenwitte@mednet.ucla.edu) <owenwitte@mednet.ucla.edu>; Barbara Anderson [Asst: Owen Witte] (baanderson@mednet.ucla.edu) <baanderson@mednet.ucla.edu>; jeconomou@mednet.ucla.edu; Professor Zelig Eshhar (zelig.eshhar@weizmann.ac.il)
Message from David Chang:

I am delighted to announce that Jeff has been promoted to Senior Vice President, Clinical Development.

Jeff joined Kite in April, 2014 as Vice President, Clinical Development, Jeff has made several significant contributions, including building the clinical development organization and advancing KTE-C19 and other eACT programs. Under his leadership, the clinical development organization has made key hires in Jeff Aycoc, Will Go, Lynn Navale, Rajul Jain, and Zack Robert, and achieved key milestones including the successful submission of Kite's first IND and the initiation of KTE-C19 Phase 1/2 study in refractory aggressive non-Hodgkins lymphoma. Jeff will continue to report to me.

Prior to joining Kite Pharma, Dr. Wiezorek held roles of increasing responsibility over 9 years at Amgen. In his most recent position as Executive Medical Director, Global Development, he had global oversight of the clinical strategy for the immunotherapy, angiogenesis, and denosumab oncology product areas. He received his B.A. degree in biophysics from the University of Pennsylvania and his M.D. degree from Columbia University. Dr. Wiezorek trained in internal medicine at Stanford University and also completed a fellowship in oncology at UCLA. Prior to joining Amgen, he investigated the role of nuclear factor-kappaB in cellular proliferation and cancer pathogenesis in the laboratory of Dr. David Baltimore at the California Institute of Technology.

Please join me in congratulating Jeff on his promotion.
Dear Steve,


Thanks,  
David

Thanks for your time today David.


Thanks again for the intros.

Sincerely,
From: Arie Beldegrun <Arie@kitepharma.com>
Sent: Wednesday, October 07, 2015 10:55 AM
To: Rosenberg, Steven A. (NIH/NCI) [E]
Subject: FW: Kite Pharma Commends Steven A. Rosenberg, M.D., Ph.D., on the Prestigious Medal of Honor Award From the American Cancer Society

Congratulations!!

Arie Beldegrun, M.D., FACS
President and CEO
Chairman of the Board; Founder
Kite Pharma Inc.

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Santa Monica, CA 90404

310 824-9999 x102
arie@kitepharma.com

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From: Kite Pharma, Inc. [mailto:jjackson@burnsmc.com]
Sent: Wednesday, October 07, 2015 5:04 AM
To: Arie Beldegrun <Arie@kitepharma.com>
Subject: Kite Pharma Commends Steven A. Rosenberg, M.D., Ph.D., on the Prestigious Medal of Honor Award From the American Cancer Society

Kite Pharma Commends Steven A. Rosenberg, M.D., Ph.D., on the Prestigious Medal of Honor Award From the American Cancer Society

-- In addition, Dr. Rosenberg Recently Received the Service to America Medal for Career Achievement and the Betty Ford Lifetime Achievement Award

SANTA MONICA, Calif., Oct. 7, 2015 (GLOBE NEWSWIRE) -- Kite Pharma, Inc. (Kite) (Nasdaq:KITE) today announced that Steven A. Rosenberg, M.D., Ph.D., Chief of Surgery at the National Cancer Institute (NCI) and a special advisor to Kite, has received three significant awards for his achievements and career dedicated to advancing cancer research. The American Cancer Society (ACS), the largest voluntary health
Rosenberg its Medal of Honor for his pioneering leadership in cancer immunotherapy. The Medal of Honor is the ACS’ highest honor and was presented to Dr. Rosenberg at a ceremony held in Washington, DC, on September 30, 2015. Additional recent awards include:

- Dr. Rosenberg has been awarded the Samuel J. Heyman Service to America Medal for career achievement by the Partnership for Public Service. The "Sammies" are bestowed upon individuals to highlight excellence in the federal workforce and inspire other talented and dedicated individuals to go into public service. Dr. Rosenberg will receive his award during a gala and ceremony that is taking place tonight, October 7, in Washington, DC.
- Susan G. Komen, the world’s largest breast cancer organization, awarded Dr. Rosenberg the Betty Ford Lifetime Achievement Award for his four decades of work in fighting cancer at the NCI. This award recognizes individuals who have committed their lives to engaging the public in the fight against breast cancer, advocating for meaningful change, and educating communities to support women and men facing the disease. Dr. Rosenberg was recognized during the Honoring the Promise gala, which took place in Washington, DC, on September 24, 2015.

In 2012, Kite partnered with Dr. Rosenberg and the NCI under a Cooperative Research and Development Agreement (CRADA) to further the research and development of multiple chimeric antigen receptor (CAR) and T cell receptor (TCR) based product candidates for the treatment of advanced solid and hematological malignancies. Many of these product candidates are now being assessed in clinical trials and Kite has since exclusively licensed intellectual property related to certain of these product candidates.

"We have always appreciated the great honor of being able to advance cancer therapies with Steve and are thrilled that three of the most prominent awards in medicine and public service have been made in recognition of the pivotal role Steve has played in cancer care and research on the national stage," said Arie Belldegrun, M.D., FACS, Chairman, President and Chief Executive Officer of Kite. "During his long and successful career, Steve’s insights, time and again have had an astounding impact on the direction of cancer research. His contributions, including to the exciting field of cancer immunotherapy, have been immense, and we are elated for Steve to receive these awards."

About Kite Pharma, Inc.

Kite Pharma, Inc., is a clinical-stage biopharmaceutical company engaged in the development of novel cancer immunotherapy products, with a primary focus on engineered autologous cell therapy (eACT™) designed to restore the immune system’s ability to recognize and
more information on Kite Pharma, please visit www.kitepharma.com.

CONTACT: Kite Pharma:
Cynthia M. Butitta, Chief
Financial Officer and Chief Operating Officer
310-824-9999

For Media: Justin Jackson
For Investor Inquiries: Lisa Burns
Burns McClellan
212-213-0006
jjackson@burnsmc.com
lburns@burnsmc.com

Source: Kite Pharma, Inc.
From: David Chang <DChang@KitePharma.com>
Sent: Thursday, October 22, 2015 3:21 PM
To: Rosenberg, Steven A. (NIH/NCI) [E]
Cc: Arie Belldegrun
Subject: 
Attachments: Proprietary Information, Redacted Per Agreement

Dear Steve,

Proprietary Information, Redacted Per Agreement

David

David Chang, MD, PhD
office: (310) 622-9094

www.kitepharma.com

Sent from my iPad

Begin forwarded message:

All,

Proprietary Information, Redacted Per Agreement

Thanks,

Edmund

Edmund Kim, Ph.D.
Senior Director, Business Development
Kite Pharma, Inc.
2225 Colorado Avenue
Santa Monica, CA 90404
Office: 310.742.2842
Email: ekim@kitepharma.com
FYI, hot from the ASH abstracts. Will send more...

Arie Beldegrun, MD FACS
President and CEO, Chairman
Kite Pharma

www.kitepharma.com

Begin forwarded message:

From: Craig Gordon <craig.gordon@capitalglobal.com>
Date: November 5, 2015 at 08:21:20 EST
To: Arie Beldegrun <Arie@kitepharma.com>, "Helen Kim (HKim@kitepharma.com)"
<HKim@kitepharma.com>
Subject: FW: Adaptimmune announces data from clinical study of NY-ESO affinity enhanced T-cell therapy in synovial sarcoma

From: FactSet_Aletrats@factset.com [mailto:FactSet_Aletrats@factset.com]
Sent: Thursday, November 05, 2015 5:21 AM
To: Craig Gordon (CRDG)
Subject: Adaptimmune announces data from clinical study of NY-ESO affinity enhanced T-cell therapy in synovial sarcoma

5 Nov '15 8:20 AM  ADAP-US  StreetAccount

Adaptimmune announces data from clinical study of NY-ESO affinity enhanced T-cell therapy in synovial sarcoma
Thursday, November 05, 2015 01:20:30 PM (GMT)

- The data presented are the following:
  - In the primary efficacy analysis, 50% of synovial sarcoma patients receiving Adaptimmune’s affinity enhanced T-cell therapy targeting NY-ESO responded, and 75% remain alive and on long term-follow up. Sixty (60) percent of patients receiving the target dose responded, and 90% remain alive and on long term-follow up;
  - gAdaptimmune’s affinity enhanced T-cell therapy targeting NY-ESO in multiple myeloma generated responses that were better than expected for autologous stem cell transplant (ASCT) alone, despite the patients having advanced stage disease with 60% of patients having tumor chromosomal abnormalities; and
Adaptimmune's platform technology enables the generation of multiple TCRs to a large number of cancer targets. Once affinity engineered, these TCRs are subjected to an extensive preclinical safety and efficacy package.

- In the synovial sarcoma poster presentation the company is providing an update on Adaptimmune's NY-ESO-1 synovial sarcoma study, including all patients in the original cohort (n=12), and longer follow-up and time-to-event, as well as updated correlative and safety data, and characterization of the product pre- and post-infusion. All patients enrolled in the study had metastatic or relapse inoperable synovial sarcoma, and failed prior ifosfamide and/or doxorubicin therapy. The authors of the poster conclude:
  
  - Adaptimmune's affinity enhanced T-cell therapy targeting NY-ESO demonstrated robust clinical responses in synovial sarcoma, including a 50% (6/12) overall response rate (ORR) in patients receiving T-cells, and a 60% (6/10) response rate in a subset of patients who received the target dose of one to six billion total engineered T-cells. Two patients received below the target dose, and neither responded. This compares favorably to a historical partial response rate of approximately four percent observed with pazopanib, which is the only approved drug in this patient population.
  
  - Seventy-five (75) percent (9/12) of all subjects who received any dose of NY-ESO-1 T cells - and 90% (9/10) of subjects who received the minimum intended cell dose - are alive and on long term follow-up. Forty-two (42) percent (5/12) of patients who received any dose have survival data beyond one year.
  
  - NY-ESO-1 T-cells durably persist and maintain function without accumulation of exhaustion markers; persistence detected at up to 21 months in those receiving the minimum intended cell dose. Poor persistence was observed in subjects receiving less than 1B NY-ESO-1 T-cells, with no detectable cells beyond day 25.
  
  - The encouraging anti-tumor activity considered in the context of a generally manageable safety profile is supportive of a favorable benefit:risk for NY-ESO-1 T-cells in this patient population. Most treatment related adverse events resolve within 30 days of treatment. The most common adverse events include: nausea, anemia, pyrexia, lymphopenia, and neutropenia. There were no treatment related deaths. Cytokine release syndrome was seen in 4 subjects; Grade 3 cytokine release syndrome was observed in 2/4 subjects, no grade 4 events were observed.
  
  - The evidence of relapse seen in some patients provides rationale for testing of combination approaches or second generation T-cells designed to overcome the immune suppressive environment of selected tumors.

- See attached press release for additional poster presentation information:

**FactSet News Alert for: Craig Gordon MD**

*Industries: Biotechnology & Drugs*

**Primary Identifiers:** ADAP-US

**Related Identifiers:** ADAP-US

**Reference Links:**

- Adaptimmune Announces Data From Clinical Study of NY-ESO Affinity Enhanced T-Cell Therapy in Synovial Sarcoma at the 2015 Annual Meeting of the Society of Immunotherapy for Cancer (SITC)

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From: Arie Beldegrun <Arie@kitepharma.com>
Sent: Monday, December 07, 2015 7:27 AM
To: Rosenberg, Steven A. (NIH/NCI) [E]
Subject: Fwd: Kite Pharma Receives FDA Breakthrough Therapy Designation for KTE-C19 for the Treatment of Refractory, Aggressive Non Hodgkin Lymphoma (NHL)

Arie Beldegrun, MD, FACS
Chairman, CEO, Founder
Kite Pharma
Santa Monica, CA 90404

Begin forwarded message:

From: "Kite Pharma, Inc." <jjackson@burns.com>
Date: December 7, 2015 at 06:31:49 EST
To: <Arie@kitepharma.com>
Subject: Kite Pharma Receives FDA Breakthrough Therapy Designation for KTE–C19 for the Treatment of Refractory, Aggressive Non Hodgkin Lymphoma (NHL)

Kite Pharma Receives FDA Breakthrough Therapy Designation for KTE–C19 for the Treatment of Refractory, Aggressive Non Hodgkin Lymphoma (NHL)

SANTA MONICA, Calif., Dec. 7, 2015 (GLOBE NEWSWIRE) — Kite Pharma, Inc. (Nasdaq:KITE) today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy
C19, for the treatment of patients with refractory diffuse large B cell lymphoma (DLBCL), primary mediastinal B cell lymphoma (PMBCL), and transformed follicular lymphoma (TFL). KTE-C19 is an investigational therapy in which a patient's T cells are genetically modified to express a chimeric antigen receptor designed to target the antigen CD19, a protein expressed on the cell surface of B cell lymphomas and leukemias.

"The FDA’s designation of KTE-C19 as a breakthrough therapy recognizes the potential for KTE-C19 to address the unmet need for patients with refractory DLBCL, PMBCL, and TFL," noted Arie Belldegrun, M.D., FACS, Chairman, President, and Chief Executive Officer. "We are pleased to receive this designation and look forward to working more closely with the FDA as we continue to advance our program for KTE-C19."

Breakthrough Therapy Designation is granted by the FDA to expedite the development and review of new therapies to treat serious or life-threatening conditions. The criteria for Breakthrough Therapy Designation require preliminary clinical evidence that demonstrates the therapy may have substantial improvement on at least one clinically significant endpoint over available therapy. This designation conveys all fast track program features, as well as more intensive FDA guidance on an efficient drug development program and eligibility for rolling review and priority review.

About Kite’s ZUMA Clinical Programs

<table>
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<th>Study</th>
<th>Phase</th>
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<td>Phase 2</td>
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<tr>
<td>ZUMA-3</td>
<td>Phase 1/2</td>
<td>Relapsed/refractory Adult ALL</td>
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<td>NCT02614066 (N=75)</td>
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<td>ZUMA-4</td>
<td></td>
<td>Relapsed/refractory Adult ALL</td>
<td>Phase 1/2</td>
</tr>
</tbody>
</table>
DLBCL = diffuse large B cell lymphoma
PMBCL = primary mediastinal B cell lymphoma
TFL = transformed follicular lymphoma
MCL = mantle cell lymphoma
ALL = acute lymphoblastic leukemia

About Kite Pharma

Kite Pharma, Inc., is a clinical-stage biopharmaceutical company engaged in the development of novel cancer immunotherapy products, with a primary focus on engineered autologous cell therapy (eACT™) designed to restore the immune system's ability to recognize and eradicate tumors. Kite is based in Santa Monica, CA. For more information on Kite Pharma, please visit www.kitepharma.com. Sign up to follow @KitePharma on Twitter at www.twitter.com/kitepharma.

Cautionary Note on Forward-Looking Statements

This press release contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. We may, in some cases, use terms such as "predicts," "believes," "potential," "proposed," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things: the ability to advance multiple clinical trials of KTE-C19 and to obtain regulatory approval based on the studies of KTE-C19. Various factors may cause differences between Kite's expectations and actual results as discussed in greater detail in Kite's filings with the Securities and Exchange Commission, including without limitation in its Form 10-Q for the quarter ended September 30, 2015. Any forward-looking statements that we make in this press release speak only as of the date of this press release. We assume no obligation to update our forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.
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Chief Financial Officer and Chief Operating Officer
310-824-9999

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Source: Kite Pharma, Inc.