Company: NewLink Genetics Corp; NASDAQ: NLNK

Financials

Market Cap: ~$235 M
Cash: ~$108M (as of 2Q17)
Burn: ~$27M/Q (as of 2Q17)

Near-term Binary Events:

- Presentation of updated data from Phase 2 study of indoximod plus gemcitabine/nab-paclitaxel in metastatic pancreatic cancer in Q4 2017 or Q1 2018

Investment Thesis:
NewLink Genetics has faced many setbacks, including most recently disappointing data in its Phase 2 metastatic breast cancer trial with its indirect IDO inhibitor indoximod and Genentech pulling out of the co-development of the direct IDO inhibitor GDC-0919. However, the company has recently refocused its pipeline around indoximod, which has shown good results at least in melanoma, and with a valuation near its all-time low, AMP Biotech Research is cautiously optimistic about the current investment opportunity in NewLink. Indoximod is currently in several Phase 1 and Phase 2 trials for various cancer indications with plans to launch a key Phase 3 trial in metastatic melanoma in the fall of 2017. With a distinct mechanism of action from competitors, indoximod has also shown comparable efficacy to Incyte's IDO inhibitor epacadostat in metastatic melanoma. Even though they likely will be second to market, NewLink still has the opportunity to gain a significant market share in the melanoma market, and to find a niche for particular indications such as prostate cancer. Furthermore, it could represent a potential acquisition target for larger companies hoping to use IDO inhibitors in combination with their own therapeutic agents. Recently, NewLink announced a reformulation of indoximod (NLG802) that could potentially increase efficacy. As we wait for upcoming data on current trials and its plans for its Phase 3 metastatic melanoma trial, we are holding our small position in NewLink in our hypothetical fund with a watchful eye on possible driver events as we gradually increase our position.

Company Overview:
NewLink Genetics seeks to enhance current cancer therapies through the inhibition of the indoleamine 2,3-dioxygenase (IDO) pathway, which has pleiotropic effects on immune cells such as antigen-presenting dendritic cells and T cells. Its stock currently trades around $8/share, even with a double-digit bounce on August 31, 2017, still at or near all-time lows, after Roche/Genentech returned the rights to GDC-0919 (navoximod) when early results with advanced solid tumors were disappointing and after a failed Phase 2 trial of indoximod in metastatic breast cancer. Last year NLNK suffered another major setback when its pancreatic cancer vaccine failed a Phase 3 trial, which hit NLNK's stock price/valuation hard.

Pipeline:
Indoximod
NewLink recently announced in its Q2 earnings call that it is restructuring all future efforts around indoximod with the company reducing employees by 50% and cutting outside spending for non-indoximod programs. Indoximod (*D*-1MT) is distinct from other IDO inhibitors in that it acts as a tryptophan mimetic instead of a direct inhibitor of the IDO1 enzyme. Although the mechanism of action is not fully understood, indoximod has been reported to affect multiple IDO-related enzymatic pathways and effectively restore the activity of killer T cells, which are known to be deactivated by tumor cells. It has been suggested that the less specific activity of indoximod might actually be

clinically beneficial over more specific IDO1 inhibitors and tolerability, which might be an issue with a more general inhibitor, has not been an issue. NewLink's primary near-term goal is to start its indoximod + anti-PD-1 Phase 3 trial in advanced metastatic melanoma. The justification for this trial is based on its phase 2 melanoma trial results showing an overall response rate (ORR) of 59% and disease control rate (DCR) of 80% in 51 non-ocular melanoma patients (See Figure 1), results that interestingly are virtually identical to the updated results recently reported by Incyte with similar patient numbers, and apparently superior to the 42% ORR achieved by the anti-PD-1 inhibitor Keytruda® alone in its pivotal Phase 3 trial. Details about the NLNK Phase 3 melanoma trial design will be announced in the fall, and enrollment for the trial is expected to be completed in 2018. NDA submission is planned for 2020, with a potential launch in 2021. NewLink also hopes to submit in the EU in 2020-2021.

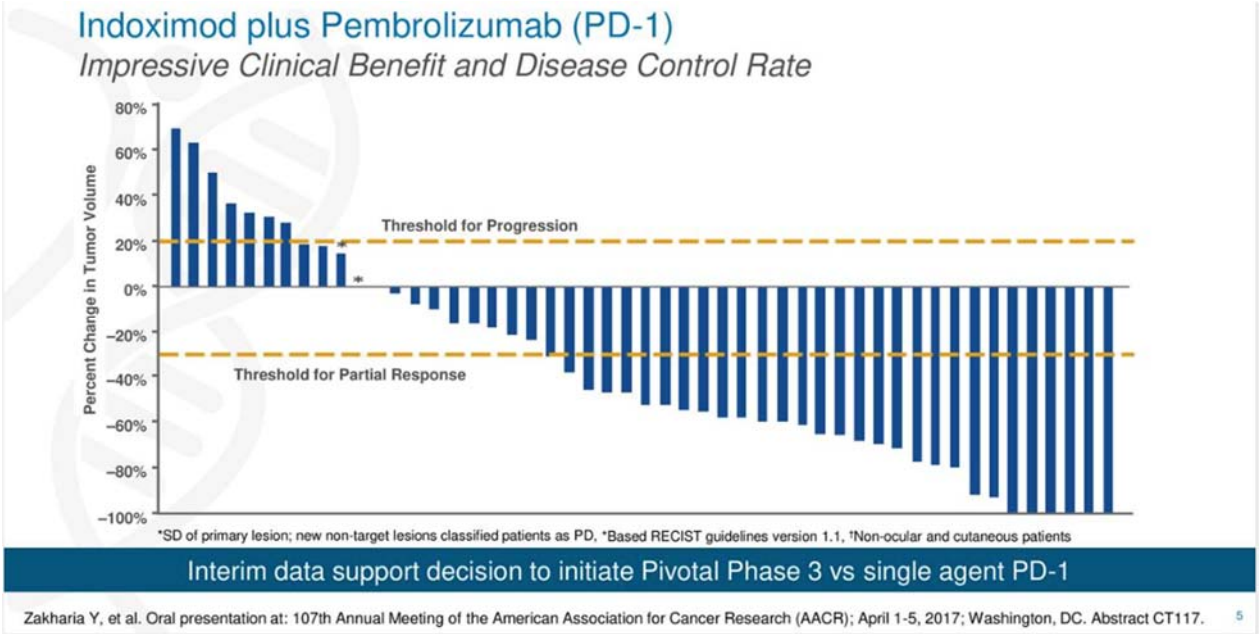

Figure 1. Metastatic Melanoma Data for Indoximod + anti-PD1 Treatment

Indoximod is also being explored for use in other indications, including metastatic pancreatic cancer, metastatic castrate resistant prostate cancer (mCRPC), newly diagnosed acute myeloid leukemia (AML), malignant brain tumors, and advanced non-small cell lung cancer (NSCLC). Moving forward, NewLink is seeking partnerships to further these specific programs as it focuses on melanoma.

Newlink's Phase 1/2 metastatic pancreatic cancer trial, a promising near-term catalyst, is looking at the dosing and regimen limiting toxicity at 10 months and overall survival out to 22 months for patients given indoximod in combination with chemotherapy (gemcitabine and nab-paclitaxel). Early interim analysis presented in 2016 with under a third of target enrollment patients evaluable for response showed 45% overall response rate (ORR), a secondary endpoint (See Figure 2). This response rate compares favorably to treatment with gemcitabine and nab-paclitaxel (standard of care), which showed a response rate of 23% in a 2013 published trial and 36.6% in a 2016 published trial. However, it is important to note that the current NLNK indoximod trial does not contain a control arm, so comparisons to standard of care cannot be determined from this study alone. For example, the general functional status of patients enrolled in the prior standard of care trials and the current NLNK trial has some differences, with less than 1% of patients in the 2013 study having a Karnofsky Performance Status (KPS) of less than 70% (able to care for self but unable to carry on normal activitity or do active work), 22% of patients in the 2016 study having a KPS of 60%-70% (requires

occasional assistance, but able to care for most of their needs) and no patients in the current NLNK trial having a KPS less than 70%. The NLNK study design without a control arm makes us less confident about how strongly the market will respond to trial data. However, if the ORR continues to be at or above 45% and/or if the overall survival at 22 months is at or above 25% in the NLNK trial, for example, those would seem to be very positive results, despite the lack of a control arm, with the 2013 and 2016 standard of care studies showing about 10% to 15% overall survival at 22 months, Full analysis of the NLNK trial with a target enrollment of 98 patients is expected in Q4 2017 or Q1 2018.

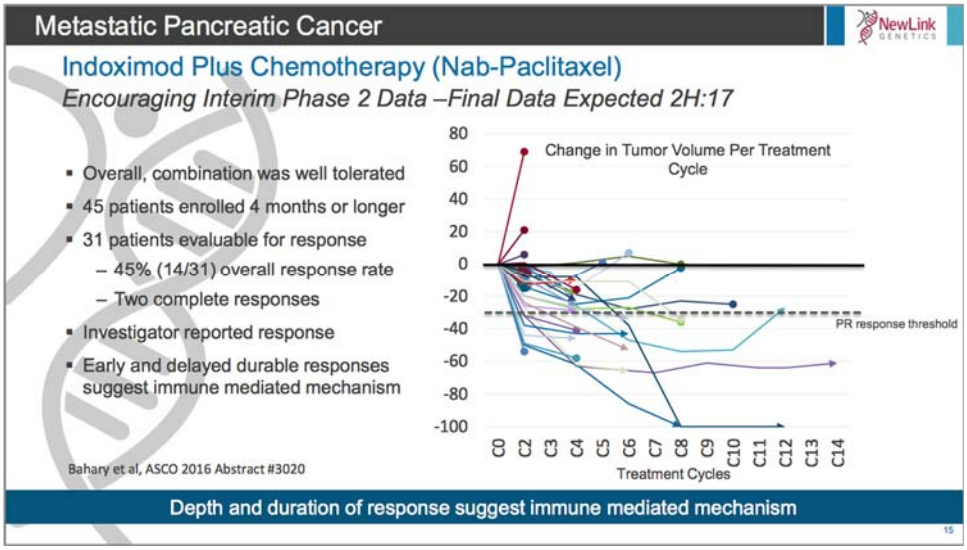

Figure 2. Metastatic Pancreatic Cancer Data for Indoximod + Gemcitabine/Nab-Paclitaxel

Furthermore, indoximod has shown promising data in combination with the PROVENGE vaccine (Sipuleucel-T) in the treatment of prostate cancer. These two treatments could be synergistic mechanistically since the vaccine primes dendritic cells for antigen presentation while indoximod inhibits the tolerogenic pathways in dendritic cells. The combination extended progression-free survival (PFS) to 10.3 months compared to 4.1 months with placebo (p=0.011). This indication represents an area of lower competition in relation to the IDO inhibitor market currently, providing a niche market that NewLink could capture, although NewLink's future plans for this combination and indication are unclear to us.

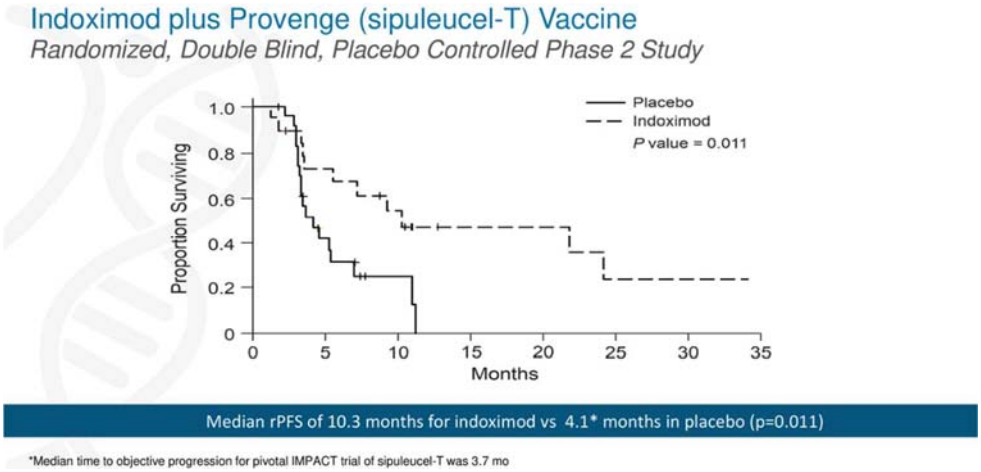

Figure 3. Metastatic Castrate Resistant Prostate Cancer (mCRPC) Trial Data for Indoximod + PROVENGE Vaccine

NLG802
The intellectual property of NewLink was strengthened recently when the company announced a new salt/pro-drug formulation of indoximod (NLG802). NLG802 increases the bioavailability of indoximod by 30-50%, which could enhance drug efficacy in future clinical trials. A Phase 1 trial in advanced solid tumors is expected to begin in 2017.

Competition:

The main competitor for NewLink in the IDO inhibitor space is Incyte (INCY), especially in the metastatic melanoma indication. Incyte has a direct IDO inhibitor (epacadostat) and has a clinical partnership with Merck to test its drug in combination with KEYTRUDA (pembrolizumab, anti-PD1 antibody) in melanoma. Incyte announced in March 2017 that this clinical partnership would extend beyond the current Phase 3 trial in metastatic melanoma to two Phase 3 trials in first-line NSCLC, two Phase 3 bladder cancer trials, one Phase 3 trial in first-line renal cell carcinoma, and one Phase 3 in squamous cell carcinoma of the head and neck. Incyte has the first-mover advantage in metastatic melanoma since it initiated its ECHO-301 clinical trial in June 2016 with estimated primary completion date in May 2018 and study completion date in April 2019. Incyte also has various Phase 1/2 studies looking at safety in combination with other treatments for various advanced or metastatic solid tumors, although there is no indication of a prostate cancer or pancreatic cancer trial.

While Incyte is generally favored by the market, the efficacy of its drug in metastatic melanoma is comparable to NewLink. Furthermore, although NewLink's stock dipped in light of its trial failure in metastatic breast cancer, this problem is not unique to NewLink. At ASCO 2017, Incyte also presented data showing that treatment of triple-negative breast cancer with epacadostat only led to a 10% objective response rate, which was disappointing.

Bristol-Myers Squib (BMS) also acquired the IDO inhibitor F001287 from Flexus to expand its immune-oncology program. Under the new name BMS-986205, BMS has a Phase 1 and Phase 1/2 clinical trial currently underway in advanced cancers such as melanoma and non-small cell lung cancer (NSCLC), but there is only limited data announced in April 2017 showing promising results, including potentially more potency in inhibiting IDO1 activity compared to Incyte's IDO1 inhibitor.

Market Evaluation:

Overall, the indications NewLink is aiming to treat represent large market opportunities that combined well exceed its market cap. Melanoma treatment overall is a very large market, although metastatic melanoma is only a portion of that, with melanoma yielding $864 million in pharmaceutical sales in the US and $1.34 billion globally as of 2013. These numbers were predicted to grow to $3.21 billion domestically and $5.64 billion globally by 2023. Other indications are also promising – in metastatic pancreatic cancer, Celgene's chemotherapy drug Abraxane specific for metastatic pancreatic cancer generated close to $1 billion in US revenue in 2015. AML represented a global market of $342.7 million in 2014 and projected to $932.6 million by 2024. In 2013, the overall prostate cancer market was $1.6 billion based on sales of commonly prescribed drugs in the US, with projected market sales to $3.7 billion in 2023. In summary, the potential markets for indoximod are large, and even if NewLink can only get a small portion of several of these indications, the current NewLink valuation looks attractive.

Summary:
NewLink has faced many hardships recently in light of clinical trial failures for its IDO program, and it is behind competition in Phase 3 clinical progression for its lead asset. However, NewLink's indoximod has shown very similar efficacy as Incyte's epacadostat in treatment of metastatic melanoma, and the new NLG802 pro-drug formulation has the potential to increase the efficacy of the inhibitor. Also, the failure in treating breast cancer is not unique to NewLink's IDO inhibitor, suggesting that NewLink's general IDO inhibitor is not necessarily inherently worse than Incyte's more specific IDO1 inhibitor. The market has been harsh to NewLink, which has created an opportunity. Although the pancreatic cancer trial, the only other NLNK IDO inhibitor trial to possibly report out this year, does not have a direct control arm, positive results could drive the price upward after its recent dip. Lastly, as combination therapies in immuno-oncology continue to become more popular and promising, it is possible that NewLink will be an acquisition target by a larger company hoping to also enter the IDO inhibitor market.

As the PD-1 and PARP inhibitor markets have shown, there is room for more than one type of inhibitor as the targeted oncology pharma market continues to expand. Based on these factors, we are optimistic about the future of NewLink and indoximod. We will continue to hold our position and will look to increase our position as we get closer to future drivers.