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INmune Bio, Inc. (INMB-NASDAQ)

INMB: Positive Preliminary Phase 1 Data for INB03…

Based on our probability adjusted DCF model that takes into account potential future revenues of INB03, XPro1595, and INKmune, INMB is valued at $19/share. This model is highly dependent upon continued clinical success of those compounds and will be adjusted accordingly based upon future clinical results.

Current Price (08/21/19)	$5.94
Valuation	**$19.00**

OUTLOOK

On August 5, 2019, INmune Bio, Inc. (INMB) announced positive preliminary data from an ongoing Phase 1 clinical trial of INB03 in patients with advanced solid tumors. INB03 is an engineered protein designed to interrupt tumor necrosis factor (TNF) signaling, which can decrease tumor cell killing by the immune system. INB03 was safe, well tolerated, and exhibited early signs of biological activity. Dosing is continuing and we anticipate a full report on the Phase 1 trial later in 2019 along with details regarding the Phase 2 trial. We also anticipate the initiation of clinical trials for XPro1595 in Alzheimer's patients and INKmune in patients with ovarian cancer during the second half of 2019.

SUMMARY DATA

52-Week High	**$11.00**
52-Week Low	**$5.32**
One-Year Return (%)	**N/A**
Beta	**N/A**
Average Daily Volume (sh)	**40,857**
Shares Outstanding (mil)	**11**
Market Capitalization ($mil)	**$64**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**0**
Insider Ownership (%)	**68**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2018 Estimate	**N/A**
P/E using 2019 Estimate	**N/A**

Risk Level	**High**
Type of Stock	**Small-Blend**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	0 A	0 A	0 A	0 A	0 A
2019	0 A	0 A	0 E	0 E	0 E
2020					0 E
2021					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	0 A	0 A	0 A	0 A	-$1.43 A
2019	-$0.20 A	-$0.04 A	-$0.18 E	-$0.18 E	-$0.61 E
2020					-$0.75 E
2021					-$0.63 E

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WHAT'S NEW

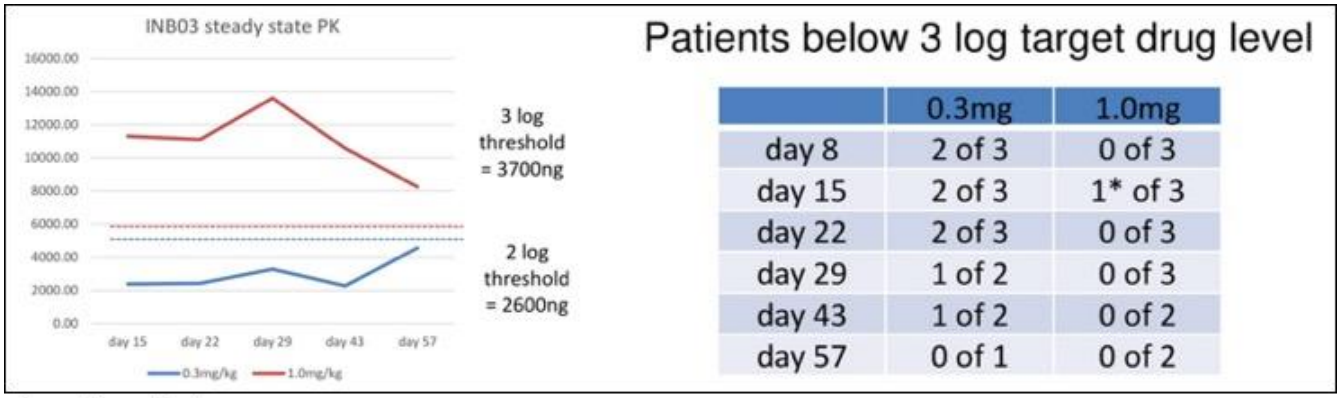
Business Update

Positive Preliminary Data from INB03 Phase 1 Clinical Trial

On August 5, 2019, INmune Bio, Inc. (INMB) announced positive preliminary data from the ongoing Phase 1 clinical trial of INB03, which is an open label, dose escalation trial in patients with advanced solid tumors. The goals of the trial are to determine the safety of INB03, the dose of INB03 to utilize in a Phase 2 trial, and to look for evidence of biological activity. Thus far, 11 of 12 patients have been enrolled in one of three dosing cohorts (0.3, 1.0, 3.0 mg/kg). The patients had a range of solid tumors and had all progressed following multiple lines of therapy.

Data from the first two cohorts included two males and four females who were suffering from prostate cancer, ovarian cancer, colon cancer (2), cholangiocarcinoma, or lung cancer. INB03 was administered once weekly for an average of 74 days (range of 12-119 days). Importantly, there were no reports of serious adverse events and INB03 was well tolerated. Discontinuation of INB03 in all patients was due to tumor progression. IL-6, a biomarker of tumor necrosis factor (TNF) function, decreased by >50% in half of the patients, which is indicative of a biological effect.

The dose for the Phase 2 portion of the study has been set at 1 mg/kg based on a goal of having the trough blood concentration of INB03 be at least two logs greater than the concentration of TNF. The following graph shows that the 1.0 mg/kg dose keeps the concentration of INB03 at least 3-log's above the TNF blood concentration and that only 1 patient in the 1.0 mg/kg cohort experienced one time point below the 3-log level.



Patients below 3 log target drug level

	0.3mg	1.0mg
day 8	2 of 3	0 of 3
day 15	2 of 3	1* of 3
day 22	2 of 3	0 of 3
day 29	1 of 2	0 of 3
day 43	1 of 2	0 of 2
day 57	0 of 1	0 of 2

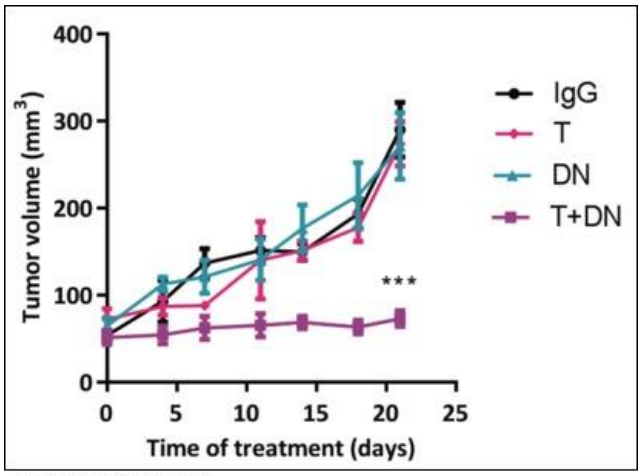
Source: INmune Bio, Inc.

We anticipate a final report on the Phase 1 trial later this year, at which time we anticipate learning additional details about the Phase 2 trial, including what cancer type(s) the company will be targeting. We expect the trial will examine INB03 treatment in combination with checkpoint inhibitor therapy or other immuno-oncology treatments and could be targeted for first line and/or second line therapy.

INB03 Potential in Breast Cancer

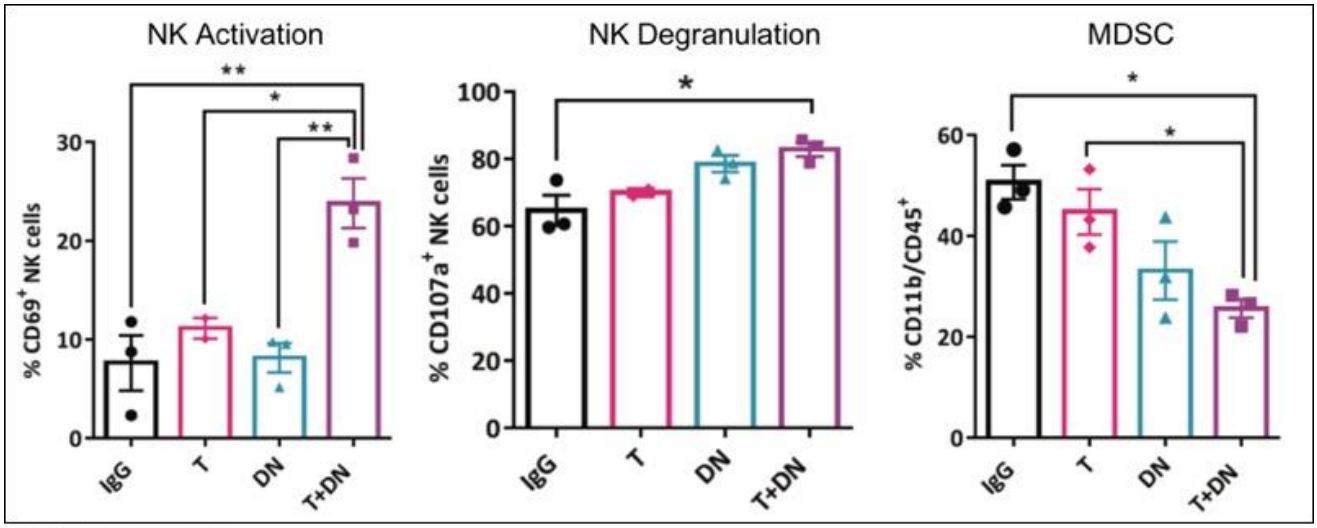
A poster presented at the 2018 San Antonio Breast Cancer Symposium investigated whether INB03 treatment could cause trastuzumab-resistant breast cancer cells to become trastuzumab-sensitive (Schillaci *et al*., 2018). This was a follow-up study to one that showed TNF overexpression resulted in trastuzumab-sensitive breast cancer cells becoming trastuzumab-resistant (Mercogliano *et al*., 2017). Trastuzumab resistance is driven by TNF-induced mucin 4 (MUC4) overexpression and MUC4 expression in HER2-positive breast cancer patients is associated with reduced disease-free survival and is an independent predictor of poor outcome in patients treated with trastuzumab.

The following figure shows that combined treatment with trastuzumab (T) and INB03 (DN) in mice injected with JIMT-1 cells (trastuzumab-resistant) resulted in significantly decreased tumor growth compared to mice treated with control IgG, only trastuzumab, or only INB03.



Source: Schillaci *et al.*, 2018

The anti-cancer effect shown by combined treatment with trastuzumab and INB03 appears to be the result of both an improvement in the innate immune response along with a less immunosuppressive tumor microenvironment. The following graphs show that combination treatment with trastuzumab and INB03 results in a significant increase in the percentage of activated and degranulated natural killer (NK) cells in the spleen (denoted through an increase in CD69- and CD107a-positive cells, respectively) and a significant decrease in the percentage of myeloid-derived suppressor cells (MDSC) in the tumor microenvironment.

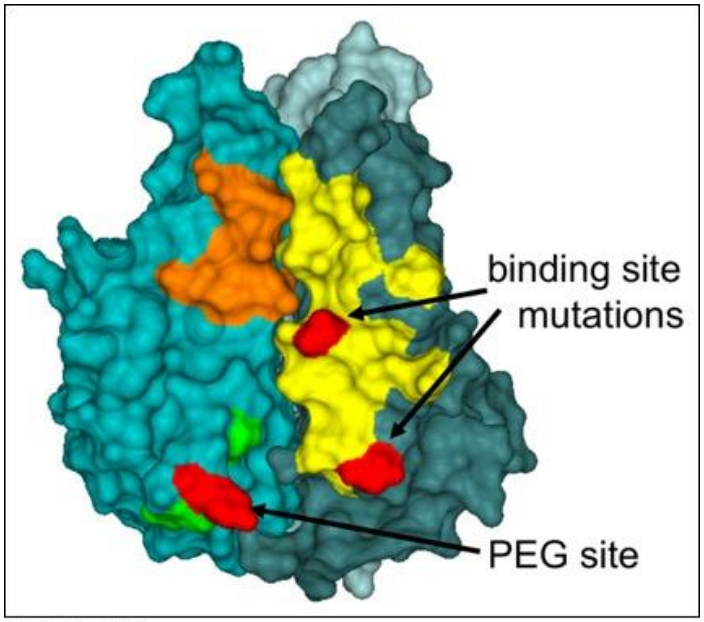


Source: Schillaci *et al.*, 2018

The results from these studies show that there is ample evidence to potentially treat HER2-positive breast cancer patients with INB03 to either prevent or overcome trastuzumab resistance, and while INmune has not decided on which cancer indication(s) to target in the upcoming Phase 2 study of INB03 we believe that breast cancer is a possibility based on the above results.

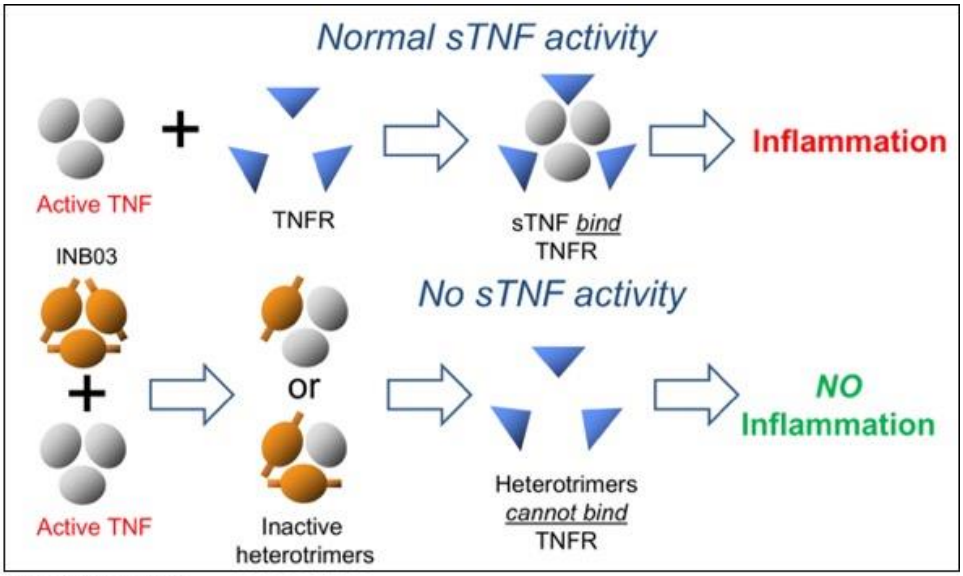
INB03 Overview

INB03 is designed to inhibit soluble TNF (sTNF) signaling while not impacting transmembrane TNF (tmTNF) signaling. It is an engineered protein that is nearly identical to sTNF except for six point mutations in the coding sequence and the addition of polyethylene glycol (PEG) to increase its half-life in circulation (Steed *et al.*, 2003). The following figure shows the crystal structure of INB03, the location of the altered amino acids in the binding site, and the PEG site.



Source: INmune Bio, Inc.

The mechanism of action for INB03 is predicated on the fact that sTNF forms homotrimers in order to bind to its receptors. INB03 is capable of forming heterotrimers with sTNF (a combination of 1 sTNF + 2 INB03 or 2 sTNF + 1 INB03), and the heterotrimers that form are incapable of binding to the receptor molecules TNFR1 or TNFR2. This is depicted in the cartoon below. The end result is that sTNF is sequestered and prevented from binding to TNFR, thus decreasing pro-inflammatory signals.



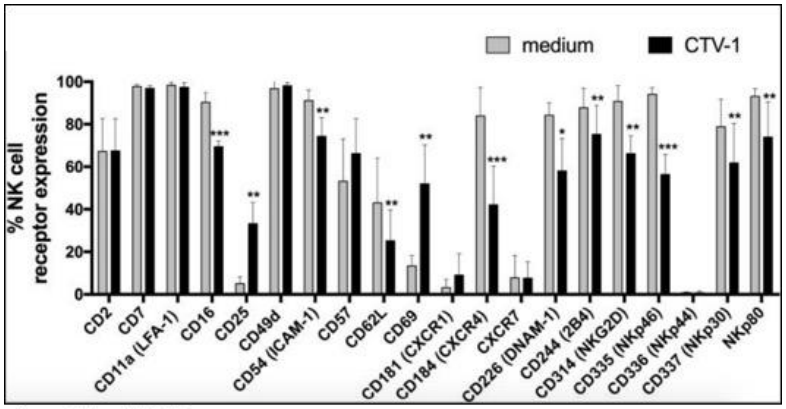
Source: INmune Bio, Inc.

Publication on INKmune Primed NK Cells

On June 27, 2019, INmune Bio announced the publication of an article titled “Tumor- and cytokine-primed human natural killer cells exhibit distinct phenotypic and transcriptional signatures” in the peer-reviewed journal *PLoS One*. The paper, co-authored by INmune’s Chief Scientific Officer Dr. Mark Lowdell, reports on experiments conducted to elucidate tumor-specific NK cell responses, including a unique signature that is discernable following binding to CTV-1 tumor cells, which are the parent clone of INmune’s INB16 cells (INKmune). The study examined differences between priming with K562 cells (which are lysed by NK cells and lead to NK cell anergy) and CTV-1 cells (which prime NK cells for subsequent killing of other targets) (Sabry *et al*., 2011).

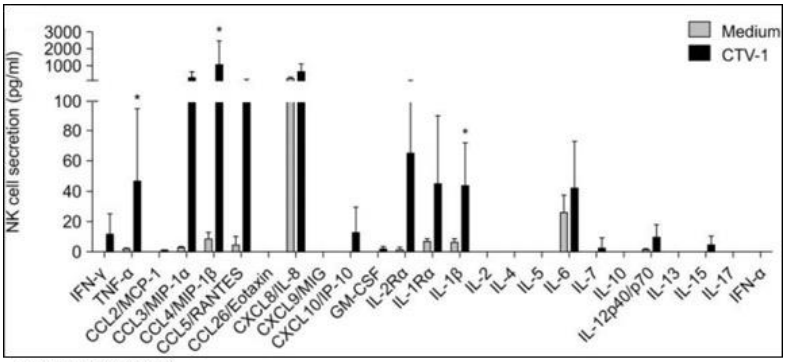
While the response of NK cells to exogenous cytokines (e.g., IL-2) is well characterized, the response to tumor cell exposure is less well studied. The following figure shows the change in surface expression of 20 different NK cell

activation receptors following overnight incubation of freshly isolated NK cells from healthy donors with CTV-1 tumor cells. Results showed an increase in the percentage of cells expressing CD25 (IL-2α receptor) and CD69.



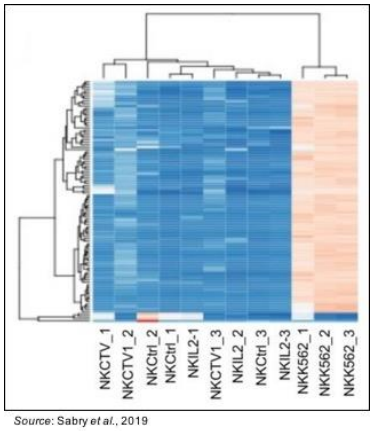
Source: Sabry *et al.*, 2019

The NK cell antigen profile induced by CTV-1 (previous figure) is similar to that of NK cells stimulated with K562 cells. However, while the cytokine profile of NK cells stimulated with K562 cancer cells is well characterized, there have been no prior studies examining the cytokine profile of CTV-1 induced NK cells. The following figure shows the concentration of 25 different soluble factors following incubation of resting NK cells with CTV-1 cells for six hours. Low to moderate levels of various chemokines and cytokines were detected, with most factors at a greater concentration after incubation with CTV-1 cells.



Source: Sabry *et al.*, 2019

The genomic expression profile of NK cells is altered upon activation (Wang *et al.*, 2015). To investigate the influence of exposure to different tumor targets on NK cell transcription, resting NK cells were incubated with medium alone, K562 cells, CTV-1 cells, or IL-2 after which RNA was extracted and analyzed using RNA-Seq. While stimulation with K562 or CTV-1 cells resulted in the expression of several common genes, there was also a specific tumor-induced gene expression signature that could differentiate between K562 and CTV-1 stimulation, as shown in the following figure. Blue represents genes that are downregulated and red represents genes that are upregulated, with CTV-1-activated NK cells clustering separately from K562-activated NK cells.



Source: Sabry *et al.*, 2019

While incubation of NK cells with CTV-1 or IL-2 resulted in similar gene expression profiles, further analysis revealed that tumor-priming with CTV-1 cells preferentially induced overexpression of genes related to cell death and survival, in contrast to IL-2 priming, which preferentially induced overexpression of genes involved in cell-to-cell signaling, as shown in the following table.

NK cell gene expression exclusively affected by CTV1- or IL-2-priming.

NK cell stimulus	Genes affected (vs medium)	Top biological functions
CTV-1	Upregulated: *BIRC5, CCNB2, CD70, CXCL10, DUSP2, DUSP6, EEF1A1, EGR2, EGR3, FGFR1, FLT1, GPR183, HIST2H2AA3, IL4I1, INSIG1, MAP2K3, MARCKSL1, NDC80, NR4A2, RHOC, RHOG, SERPINE1, STAT5A, TNFAIP3, TNFSF9, TOP2A, TTK* and *VEGFA*. Downregulated: *CCR1, FCGR2A, NCF2, RAB3D, SERPINB2* and *THB*.	Cell death and survival, cellular function and maintenance, cellular movement, cellular development, cellular growth and proliferation
IL-2	Upregulated: *ACTB, ADAMTS1, ADORA2A, AGK, ARF6, BATF, CALR, CASP7, CCL1, CCL20, CCL22, CCR7, CD274, CD38, CD40, CD40LG, CEBPB, CEBPG, CSF1, CXCL1, CXCL2, CXCL3, CXCL5, CXCL8, CYTIP, DPP4, ELOVL6, FURIN, G6PD, GCH1, GZMA, HAVCR1, HIF1A, ID2, IL27RA, IL3RA, IL6, IRF, ISG15, ITGB7, JAK3, LAG3, LAMP3, LDLR, LTB, MAFF, MSC, MX1, MX2, PDE4A, PSMB9, PSME2, PTGER2, RIPK2, SERPINB2, STAT1, STAT3, TAP1, TAP2, TAPBP, TNFRSF1B, TNFSF4, TRAF2, TRAFD1, TREX1* and *VASP*. Downregulated: *AIF1, AOAH, C3AR1, CD27, CD84, CEBPA, CLEC7A, CXCR2, CXCR4, FCGR2B, HDAC5, HLA-DMA, JAML, LAPTM5, MRC1, OLR1, PTGDR, RASAL1, S1PR1, SMARCD3, SPTBN1, TLR1* and *TYROBP*.	Cell-to-cell signaling and interaction, cellular movement, cellular function and maintenance, cellular growth and proliferation, cellular development

Source: Sabry *et al.*, 2019

The key finding from this study is that there is a specific tumor-induced signature in NK cell responses and this signature could potentially be utilized to identify key signaling molecules that play a role in tumor target recognition in NK cells primed by tumor cells, including CTV-1 cells. This could ultimately lead to more targeted therapeutic options to optimize NK cell therapy for the treatment of cancer.

Financial Update

On August 12, 2019, INmune Bio announced financial results for the second quarter of 2019. As expected, the company did not report any revenues. The company reported a net loss of $0.4 million in the second quarter of 2019, which included a non-cash waiver of common stock issuable of $1.5 million. R&D expenses in the second quarter of 2019 were approximately $0.3 million compared to approximately $0.3 million in the second quarter of 2018. During the second quarter of 2019, the company had $0.6 million of R&D expenses that were partially offset by $0.3 million of grants from the Alzheimer's Association, which was recorded as an offset to R&D expenses. G&A expenses in the second quarter of 2019 were $1.7 million compared to $5.9 million in the second quarter of 2018. The decrease was primarily due to lower non-cash stock-based compensation partially offset by higher investor relations and payroll expenses.

INmune Bio exited the second quarter of 2019 with approximately $9.4 million in cash and cash equivalents. This was due in part to a private placement that closed in May 2019 in which the company raised approximately $4.7 million through the sale of 522,212 shares of its common stock, with both the CEO and CFO participating in the raise. We estimate the company has sufficient capital to fund operations into the second quarter of 2020.

As of August 9, 2019, INmune had approximately 10.8 million shares of common stock outstanding and when factoring in stock options and warrants a fully diluted share count of approximately 13.9 million.

Conclusion

We are glad to see positive early data from the Phase 1 trial of INB03 and look forward to additional data later this year along with an update on the Phase 2 trial plan, including which cancer type(s) the company will be targeting. In the second half of 2019 we also anticipate the initiation of patient enrollment in a Phase 1 study of XPro1595 in patients with Alzheimer's disease and the initiation of a clinical trial for INKmune. Our current valuation is $19.

PROJECTED FINANCIALS

INmune Bio, Inc.
Income Statement

INMune Bio, Inc.	2018 A	Q1 A	Q2 A	Q3 E	Q4 E	2019 E	2020 E	2021 E
INB03	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
INKmune	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Other Income	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$1.1	$0.1	$0.3	$0.3	$0.3	$1.0	$2.0	$2.5
General & Administrative	$11.3	$1.8	$1.7	$1.6	$1.6	$6.7	$7.0	$7.0
Other (Income) Expense	$0.0	$0.0	($1.5)	$0.0	$0.0	($1.5)	$0.0	$0.0
Operating Income	($12.4)	($1.9)	($0.4)	($1.9)	($1.9)	($6.1)	($9.0)	($9.5)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.0	$0.0	($0.0)	$0.0	$0.0	($0.0)	$0.0	$0.0
Pre-Tax Income	($12.4)	($1.9)	($0.4)	($1.9)	($1.9)	($6.2)	($9.0)	($9.5)
Income Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($12.4)**	**($1.9)**	**($0.4)**	**($1.9)**	**($1.9)**	**($6.2)**	**($9.0)**	**($9.5)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($1.43)**	**($0.20)**	**($0.04)**	**($0.18)**	**($0.18)**	**($0.61)**	**($0.75)**	**($0.63)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	8.7	9.4	10.2	10.3	10.4	10.1	12.0	15.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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HISTORICAL STOCK PRICE



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