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November 29, 2021
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Appili Therapeutics Inc. (T.APL-TSX)

T.APL: PRESECO Trial Unsuccessful in COVID-19…

Based on our probability adjusted DCF model that takes into account potential future revenues of ATI-2307, ATI-1701, and ATI-1501 APLI.T is valued at CAD$1.00/share. This model is highly dependent upon continued clinical success of the company's pipeline and will be adjusted accordingly based on future clinical results.

Current Price (11/29/21)	CAD$0.16
Valuation	**CAD$1.00**

OUTLOOK

On November 12, 2021, Appili Therapeutics Inc. (APLI.T) announced that the Phase 3 PRESECO trial evaluating favipiravir for the treatment of mild-to-moderate COVID-19 did not achieve statistical significance on the primary endpoint of time to sustained clinical recovery. The company will now turn its attention to its novel clinical-stage antifungal ATI-2307, which we anticipate entering a Phase 2 clinical trial in 2022. In addition, Appili is developing ATI-1701, a vaccine for the prevention of tularemia that the company recently announced positive one-year challenge results from its preclinical efficacy study.

SUMMARY DATA

52-Week High	**$1.43**
52-Week Low	**$0.15**
One-Year Return (%)	**-83.91**
Beta	**N/A**
Average Daily Volume (sh)	**300,770**
Shares Outstanding (mil)	**71**
Market Capitalization ($mil)	**$11**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**21**
Insider Ownership (%)	**33**
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 2019 Estimate	**N/A**
P/E using 2020 Estimate	**N/A**

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

ZACKS ESTIMATES

Revenue
(in millions of CAD$)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2021	0.0 A	0.0 A	0.0 A	0.0 A	0.1 A
2022	0.0 A	0.0 A	0.0 E	0.0 E	0.0 E
2023					0.0 E
2024					0.0 E

Earnings per Share
(in CAD$)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2021	-$0.05 A	-$0.04 A	-$0.07 A	-$0.08 A	-$0.24 A
2022	-$0.12 A	-$0.18 A	-$0.09 E	-$0.09 E	-$0.46 E
2023					-$0.25 E
2024					-$0.20 E

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WHAT'S NEW

Business Update

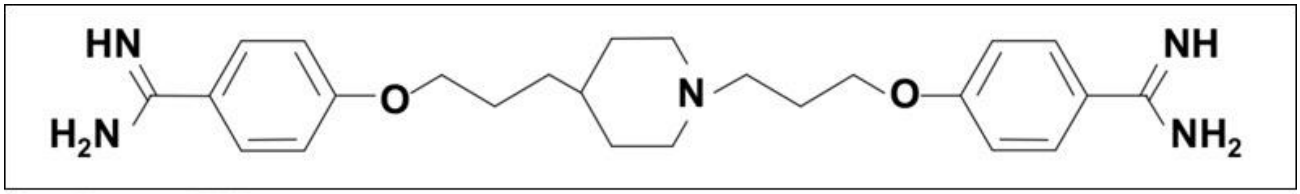
PRESECO Trial Unsuccessful

On November 12, 2021, Appilii Therapeutics, Inc. (T.APLI) announced that the Phase 3 PRESECO (PREventing SEvere COvid-19) trial evaluating favipiravir (Avigan® / Reeqonus™) for the treatment of mild-to-moderate COVID-19 did not achieve statistical significance on the primary endpoint of time to sustained clinical recovery. The PRESECO trial was a randomized, double blind, placebo controlled Phase 3 trial that enrolled 1,231 patients from 38 study sites in the U.S., Mexico, and Brazil.

These results are disappointing and when combined with the results recently announced by both Pfizer and Merck for their respective antiviral compounds, we believe this will end the development of favipiravir in COVID-19.

Update on ATI-2307

In November 2019, Appili acquired ATI-2307 from FUJIFILM Toyama Chemical Co., LTD. It is a broad-spectrum, novel arylamidine antifungal agent that belongs to the same class of aromatic diamidines as pentamidine and furamidine (Mitsuyama *et al*., 2008). It has a highly differentiated novel mechanism of action that could potentially be used to treat infections caused by a number of clinically important and high priority pathogens, including *Cryptococcus*, *Candida*, and *Aspergillus*.



Source: Mitsuyama *et al*., 2008

ATI-2307 has been successfully tested in multiple Phase 1 clinical trials. In addition, the compound has been tested in 80 human subjects in three single ascending dose and/or multiple ascending dose clinical studies conducted in the U.S. in which it was safe and well tolerated at all doses tested.

Appili is currently conducting proof of concept nonclinical studies to evaluate the therapeutic effect of ATI-2307 in rabbit and mouse intracranial *Cryptococcus* infection models and earlier this year published the results of studies evaluating the drugs activity *in vitro* against a panel of clinical isolates (Gerlach *et al*., 2021). The work is being conducted in collaboration with researchers at Duke University and the University of Texas Health Science Center at San Antonio. A portion of the work is being supported by the U.S. National Institute of Allergy and Infectious Diseases (NIAID).

In addition, Appili is evaluating the potential for ATI-2307 as a treatment for invasive *Candida* infections. These infections are caused by a number of *Candida* species, including *Candida albicans* and the newly emerging pathogen *Candida auris*, and are generally treated with an echinocandin or azole. However, an increase in antifungal resistance is decreasing the efficacy of those compounds, and with the highly toxic amphotericin B used for refractory *Candida* infections, there exists the need for safer and more effective treatment options.

Following a recent meeting with Key Opinion Leaders, Appili plans to meet with regulatory authorities in 2022 and submit filings to the U.S. FDA such that Phase 2 clinical trials can initiate in 2022.

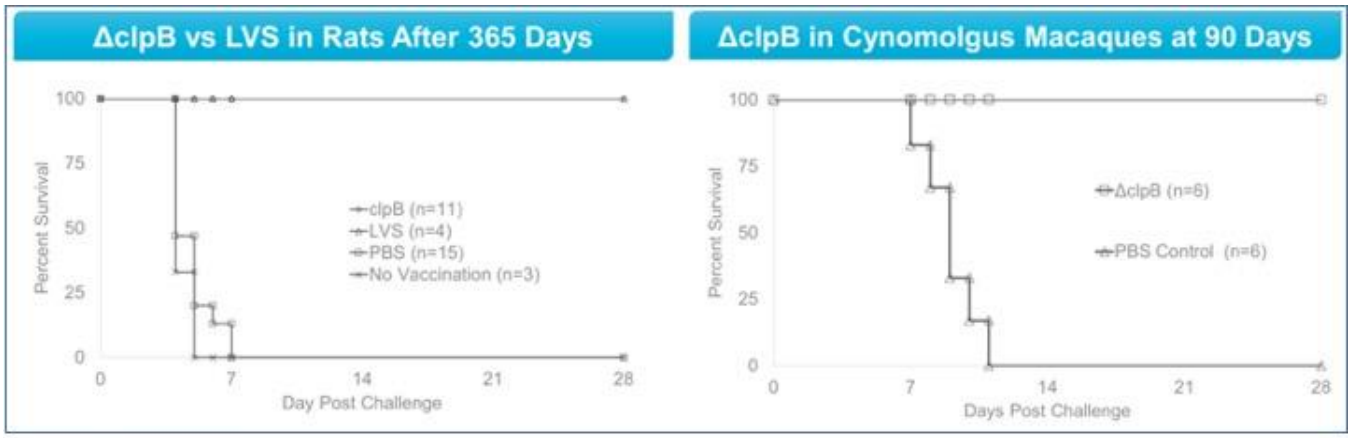
ATI-2307 may be eligible for development under the Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD), which provides a mechanism for accelerated clinical development for antibiotics and antifungals. In addition, ATI-2307 could be eligible for Orphan Drug Designation (ODD) from the FDA if developed as a treatment for cryptococcal meningitis or invasive candidiasis. ODD designation is accompanied by seven years of regulatory exclusivity following FDA approval. ATI-2307 may also be eligible for an additional five years of exclusivity if approved to treat either *Candida* or *Cryptococcus* as both those are qualifying pathogens for Qualified Infectious Disease Product (QIDP) designation. Lastly, the drug may be eligible for a tropical disease Priority Review Voucher (PRV) if it is the first compound approved for cryptococcal meningitis.

ATI-1701 Update

ATI-1701 is a vaccine for the prevention of tularemia caused by *Francisella tularensis*, a pathogen that is a Tier 1 biological threat agent according to the CDC (Dennis *et al*., 2001). Its potential as a bioterror agent is based on the fact that only a very small number of *F. tularensis* cells (10-50) can cause disease and the organism can be aerosolized to infect a large area. Inhalation of *F. tularensis* and development of pneumonic tularemia can lead to breathing difficulties and ultimately be fatal if not treated. Based on its highly infectious nature and ability to cause severe illness, the U.S. government and other governments around the world have made medical countermeasures against *F. tularensis* a high biodefense priority.

Since it unacceptable to test the efficacy of a tularemia vaccine in a human population, ATI-1701 is being developed via the FDA Animal Rule. Products developed via this pathway are required to show efficacy in two animal models, one of which being a non-human primate, along with safety in a healthy adult population.

Appili previously presented data showing that ATI-1701 (denoted clpB) protected rats for 365 days and cynomolgus macaques for 90 days following immunization, as shown in the following figures. This was tested by challenging vaccinated animals with aerosolized *F. tularesnsis*, which resulted in 100% fatality in non-vaccinated rats, rats immunized with the legacy *F. tularensis* vaccine (LVS), and non-vaccinated macaques.



Source: Gelhaus *et al*., 2019

The company recently announced positive one-year challenge results with non-human primates showing a survival rate of 29% (2/7) in the ATI-1701 vaccinated cohort compared to 0% (0/5) in placebo vaccinated controls.

The development of ATI-1701 has been supported through grants received from the US Department of Defense (DoD) Defense Threat Reduction Agency (DTRA), including a US$6.3M grant that was awarded in October 2020 to support advanced development and manufacturing of the vaccine. Appili is continuing progress on manufacturing and IND-enabling activities and we anticipate a Phase 1 safety study in humans initiating in 2023. If approved, ATI-1701 would be eligible for a medical countermeasure PRV.

ATI-1503 Update

The ATI-1503 program is devoted to developing antibiotic compounds that target Gram-negative bacteria, including CDC priority pathogens such as *Enterobacteriaceae*, *Acinetobacter*, and *Pseudomonas*. The program is based off of negamycin, a naturally occurring compound that shows activity against Gram-negative bacteria.

Negamycin was originally isolated from cultures of *Streptomyces purpeofuscus* where it showed activity in immunocompetent mouse models of sepsis caused by Gram-negative pathogens such as *P. aeruginosa* and *Klebsiella Pneumoniae* (Hamada *et al*., 1970). It exerts its antibiotic effect by targeting protein synthesis (Mizuno *et al*., 1970). Negamycin has a number of positive attributes, however the compound itself is not potent enough for development as an antibiotic, with minimum inhibitor concentration (MIC) values of 16-64 μg/mL. To improve upon its characteristics, researchers at AstraZeneca produced analogues of negamycin and a lead compound was identified that showed 4-fold improvement in MIC against a panel of 100 clinical isolates of *P. aeruginosa* (McKinney *et al*., 2015).

Appili has identified two novel and structurally distinct lead molecules based on the negamycin scaffold, which each have low, single-digit MIC values against many Gram-negative bacteria. In addition, these compounds have shown in vivo proof-of-concept against *Klebsiella* and *Escherichia*. The compounds are continuing to be evaluated in multiple in vivo efficacy models, safety screening, and pharmacokinetic evaluations.

ATI-1501 Update

ATI-1501 is a taste-masked liquid oral suspension formulation of the antibiotic metronidazole. This was the company's initial R&D program initiated in the first quarter of 2015. Metronidazole is an antibiotic used to treat various protozoan and anaerobic bacterial infections, including giardiasis, trichomoniasis, and amebiasis (Freeman *et al*., 1997). It is a widely used antibiotic, with more than 10 million oral prescriptions written each year (IQVIA™ 2017).

In December 2019, Appili announced a commercial agreement with Saptalis Pharmaceuticals for ATI-1501, in which Appili will be eligible to receive multiple milestones and royalty payments based on the sale of ATI-1501 in the U.S. Saptalis will be responsible for overseeing the regulatory review, manufacturing, and preparation for the anticipated commercialization of ATI-1501 in the U.S. Saptalis is currently evaluating formulation options to maximize product stability and has requested a Type C meeting with the FDA to discuss potential adjustments to the formulation. We anticipate an NDA being filed in 2022.

Financial Update

On November 12, 2021, Appili announced financial results for the second quarter of fiscal year 2022, which ended September 30, 2021. Net loss for the second quarter of fiscal year 2022 was CAD$11.2 million, or CAD$0.18 per share, compared to a net loss CAD$2.5 million, or CAD$0.04 per share, for the quarter ending September 30, 2020.

R&D expenses for the second quarter of fiscal year 2022 were CAD$8.9 million, compared to CAD$1.1 million for the second quarter of fiscal year 2021. The increase was primarily due to increased expenses associated with the favipiravir clinical trials, salaries and benefits, and stock-based compensation. G&A expenses for the second quarter of fiscal year 2022 were CAD$1.1 million, compared to CAD$1.4 million for the second quarter of fiscal year 2021. The decrease was primarily due to decreased G&A expenses excluding salaries and benefits.

As of September 30, 2021, Appili had approximately CAD$10.0 million in cash and cash equivalents along with approximately US$2.2 million remaining on the PRMRP government grant and approximately US$1.62 million remaining on the DTRA grant. In October 2021, the company raised CAD$7.0 million through a public offering. We estimate the company has sufficient funding through the third quarter of calendar 2022. As of November 12, 2021, Appili had approximately 71.3 million shares outstanding and, when factoring in stock options and warrants, a fully diluted share count of approximately 99.2 million.

Conclusion

We're disappointed by the failure of the PRESECO trial as another effective therapy for COVID-19 would have been helpful as the world attempts to get out of the ongoing pandemic. However, the company will now turn its full attention to ATI-2307 and ATI-1701, with a Phase 2 trial expected to get underway for ATI-2307 in 2022.

Based on the results of the PRESECO trial we have removed favipiravir from our model. In addition, investors should be aware that now that the company's market cap has fallen below CAD$36 million, the Lind Convertible Security may be converted into common shares at the discretion of Lind at any time. With the stock trading near CAD$0.20, the conversion of the approximately CAD$4.0 million face value of the Lind Security could significantly dilute current shareholders. Our valuation is now CAD$1.00 per share, with the majority of that valuation due to ATI-1701 and its potential sale to the U.S. strategic national stockpile and the priority review voucher (PRV) that would be issued upon its approval.

PROJECTED FINANCIALS

Appili Therapeutics Inc. Fiscal Year Ends Mar. 31 / in Canadian dollars	FY2021 A	Q1FY22 A	Q2FY22 A	Q3FY22 E	Q4FY22 E	FY2022 E	FY2023 E	FY2024 E
ATI-2307	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
ATI-1701	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
ATI-1503	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
ATI-1501	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Other Income	$0.1	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Total Revenues	**$0.1**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**
Cost of Sales	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$10.2	$6.1	$10.0	$4.5	$5.0	$25.6	$18.0	$19.0
General & Administrative	$4.8	$1.1	$1.1	$1.5	$1.6	$5.3	$6.0	$6.3
Business Development	$0.7	$0.4	$0.2	$0.2	$0.2	$1.0	$0.9	$1.0
Other (Income) Expense	($1.2)	($0.2)	($0.2)	$0.0	$0.0	($0.4)	$0.0	$0.0
Operating Income	($14.3)	($7.3)	($11.2)	($6.2)	($6.8)	($31.5)	($24.9)	($26.3)
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	($14.3)	($7.3)	($11.2)	($6.2)	($6.8)	($31.5)	($24.9)	($26.3)
Income Taxes	$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	**($14.3)**	**($7.4)**	**($11.2)**	**($6.2)**	**($6.8)**	**($31.6)**	**($24.9)**	**($26.3)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.24)**	**($0.12)**	**($0.18)**	**($0.09)**	**($0.09)**	**($0.46)**	**($0.25)**	**($0.20)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	59.2	62.8	62.8	70.0	80.0	68.9	100.0	130.0

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

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HISTORICAL STOCK PRICE



Source: Stockcharts.com

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