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Appili Therapeutics Inc. (T.APL-TSX)

T.APL: Phase 3 PRESECO Trial Readout in Late Calendar 1Q/Early 2Q 2021…

Based on our probability adjusted DCF model that takes into account potential future revenues of ATI-2307, ATI-1701, ATI-1501, and favipiravir APLI.T is valued at CAD$3.25/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 (02/22/21)	CAD$1.20
Valuation	**CAD$3.25**

OUTLOOK

On February 12, 2021, Appili Therapeutics Inc. (APLI.T) announced financial results for the third quarter of fiscal year 2021 that ended December 31, 2020 and provided a business update. The company is currently conducting the Phase 3 PRESECO (PREventing SEvere COvid-19) trial that is evaluating favipiravir for the early treatment of COVID-19 in the outpatient setting. We currently expect topline results from that trial in late calendar 1Q/early 2Q 2021. While Appili is focusing most of its resources on getting the PRESECO trial completed in an expedited manner, the company is also conducting the PEPCO (post exposure prophylaxis) and CONTROL-COVID (outbreak control in long-term care facilities) trials that could lead to post-approval label expansions.

SUMMARY DATA

52-Week High	**$1.89**
52-Week Low	**$0.50**
One-Year Return (%)	**N/A**
Beta	**1.57**
Average Daily Volume (sh)	**131,470**
Shares Outstanding (mil)	**63**
Market Capitalization ($mil)	**$85**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**54**
Insider Ownership (%)	**42**
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	**Above Avg.**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in millions of CAD$)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2020	0.0 A	0.0 A	0.2 A	0.0 A	0.2 A
2021	0.0 A	0.0 A	0.0 A	0.0 E	0.0 A
2022					0.0 E
2023					0.0 E

Earnings per Share
(in CAD$)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2020	-$0.06 A	-$0.03 A	-$0.04 A	-$0.04 A	-$0.16 A
2021	-$0.05 A	-$0.04 A	-$0.07 A	-$0.05 E	-$0.21 E
2022					-$0.18 E
2023					-$0.19 E

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WHAT'S NEW

Business Update

PRESECO Trial Interim Data in Late Calendar Q1/Early Q2 2021

On January 28, 2021, Appili Therapeutics, Inc. (T.APLI) provided an update on the company's Phase 3 PRESECO ((PREventing SEvere COvid-19) trial that is evaluating favipiravir for the treatment of COVID-19 in the outpatient setting. The trial is currently recruiting patients in 12 out of 20 sites in the U.S. and is pursuing approvals to expand the trial into sites in Mexico, Brazil, and Columbia.

The PRESECO trial is a randomized, double blind, placebo-controlled Phase 3 trial that plans to enroll 826 participants who were recently diagnosed with COVID-19 and have mild to moderate symptoms. The purpose of the trial is to determine if favipiravir can shorten the time to clinical recovery, prevent progression to severe disease, and decrease the period of infectiousness.

Appili is prioritizing resources to accelerate recruitment and data analysis for the PRESECO trial and is planning to use the information gathered from the ongoing CONTROL and PEPCO trials (discussed below) as label expansion studies to evaluate if favipiravir is efficacious as a post-exposure prophylaxis treatment. Based on current enrollment rates for PRESECO, the company anticipates interim data from that trial in late calendar Q1/early Q2 2021 with full enrollment completing in calendar Q2 2021.

PEPCO: This is a randomized, double blind, placebo controlled, multinational Phase 3 trial that will enroll approximately 1,156 participants at 47 centers. The purpose of the study is to determine if favipiravir can prevent the development of COVID-19 in asymptomatic individuals who had direct exposure (within the past 72 hours) to someone with COVID-19. Enrollment will include any individual over the age of 60 along with those 18 years and older with at least one significant underlying health condition.

CONTROL: This is a Phase 2 cluster-randomized, placebo-controlled trial evaluating the effectiveness of favirpiravir to prevent COVID-19 outbreaks in long-term care facilities. They anticipate approximately 760 participants enrolling across 16 long term care facilities, with eight facilities administering favipiravir to its residents and the other eight administering placebo. Facilities are eligible to be enrolled in the trial after two or more residents test positive for SARS-CoV-2 by PCR testing. Following enrollment of the facility, all residents (elderly patients with co-morbidities) and front-line healthcare workers will be administered either favipiravir or placebo with the primary outcome of the trial being outbreak control, defined as no new cases of COVID-19 in residents for 24 consecutive days up to Day 40 after the start of prophylactic treatment.

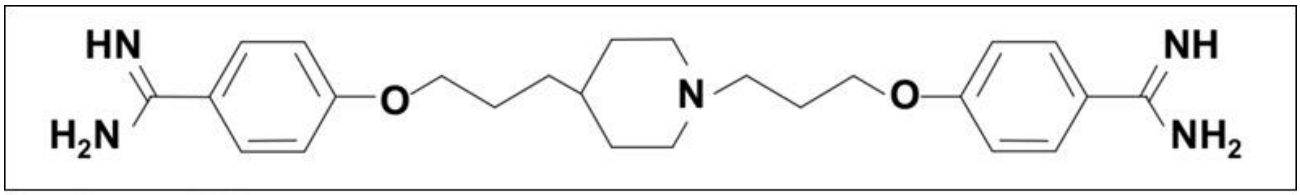
In October 2020, Appili announced that it had entered into a collaboration, development, and supply agreement with Dr. Reddy's Laboratories Ltd. (DRL) and Global Response Aid (GRA) that will work in harmony with a prior global licensing transaction (excluding Japan, Russia, and China) between DRL, GRA, and FUJIFILM Toyama Chemical Co. (FFTC) for the worldwide development, commercialization, and distribution of favipiravir for the potential treatment and prevention of COVID-19.

In December 2020, the consortium announced that Dr. Reddy's Canada filed an application on behalf of the consortium for REEQONUS™ (favipiravir) tablets for the acute treatment of mild to moderate COVID-19 in adult patients under Health Canada's Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19. The consortium was the first in Canada to file an application for oral solid tablets for COVID-19 treatment in Canada such that if successful clinical trial results are obtained favipiravir could be approved for use in an expeditious manner.

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, including a Phase 1 clinical trial in healthy volunteers in Japan that showed the drug was safe and well tolerated (NCT02289599). 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 along with evaluating the drugs activity *in vitro* against a panel of clinical isolates. 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).

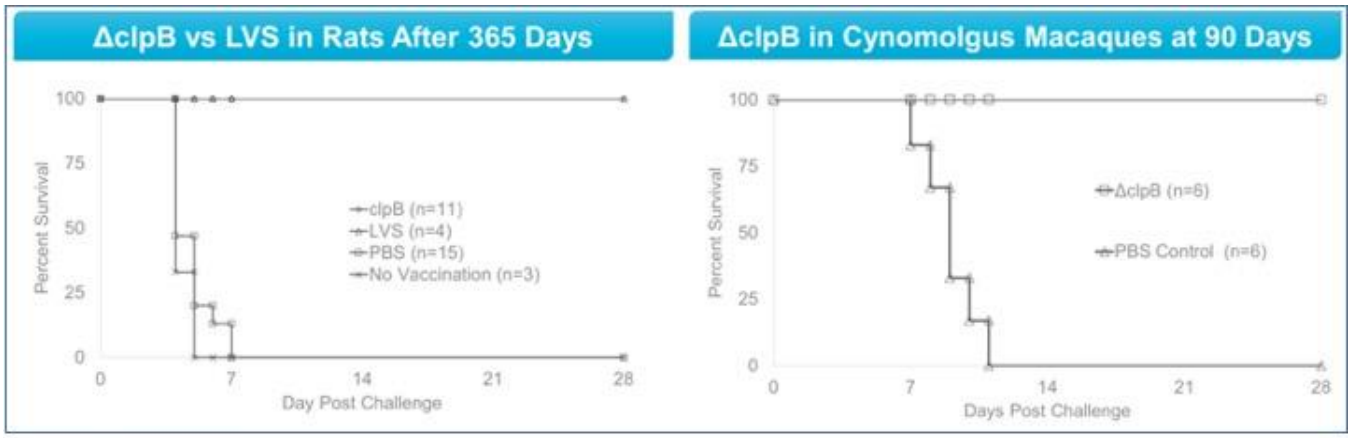
In addition, Appili is evaluating the potential for ATI-2307 as a treatment for invasive *Candida* infections. These infections are caused by a number of *Candida* species, including *Candida albicans* and the newly emerging pathogen *Candida auris*, and are generally treated with an echinocandin or 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.

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. Lastly, ATI-2307 may 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.

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.

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

Appili has performed an additional experiment with non-human primates that were challenged 365 days post-vaccination and analysis from that study is currently ongoing. Once that is complete, we anticipate the initiation of pivotal animal studies as well as Phase 1 human studies potentially starting in 2022.

Since it is no longer acceptable 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.

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.

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. The company is hopeful that a lead development compound can be identified in 2021.

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 February 12, 2021, Appili announced financial results for the third quarter of fiscal year 2021, which ended December 31, 2020. Net loss for the three months ending December 31, 2020 was CAD$4.2 million, or CAD$0.07 per share, compared to a net loss of $1.2 million, or $0.04 per share, for the three months ending December 31, 2019.

R&D expenses for the third quarter of fiscal year 2021 were CAD$3.4 million compared to CAD$0.5 million for the third quarter of fiscal year 2020. The increase was primarily due to favipiravir clinical trial costs, increased expenses for the ATI-2307 program, and increased salaries and benefits. G&A expenses for the third quarter of fiscal year 2021 were CAD$1.1 million compared to CAD$0.9 million for the third quarter of fiscal year 2020. The increase was primarily due to increased audit and legal fees, public relations costs, investor relations costs, and regulatory fees.

As of December 31, 2020, Appili had approximately CAD$20.3 million in cash, cash equivalents, and short-term investments along with approximately US$2.5 million remaining on the PRMRP government grant. As of February 12, 2021, the company had approximately 62.6 million shares outstanding and, when factoring in stock options and warrants, a fully diluted share count of 82.0 million.

Conclusion

We are looking forward to the data from the PRESECO trial, which we anticipate will be in late calendar Q1/early Q2 2021. Multiple successful vaccines have already been approved against COVID-19, however just as influenza is combated with both vaccines and antivirals, so too will doctors need both vaccines and antivirals in their arsenal to battle COVID-19. In addition, news of COVID-19 vaccines having less efficacy against SARS-CoV-2 variants further emphasizes the point that effective antivirals are necessary, particularly those that can be administered at home shortly after a diagnosis is given. As we await the results of the PRESECO trial there are no changes to our model and the valuation remains at CAD$3.25.

PROJECTED FINANCIALS

Appili Therapeutics Inc. Fiscal Year Ends Mar. 31 / in Canadian dollars	FY2020 A	Q1FY21 A	Q2FY21 A	Q3FY21 A	Q4FY21 E	FY2021 E	FY2022 E	FY2023 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	$0.2	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Other Income	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Total Revenues	**$0.2**	**$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	$2.1	$1.6	$1.1	$3.4	$2.0	$8.0	$8.0	$9.0
General & Administrative	$3.3	$1.0	$1.4	$1.1	$1.0	$4.5	$3.3	$3.3
Business Development	$0.9	$0.1	$0.2	$0.1	$0.3	$0.7	$1.0	$1.0
Other (Income) Expense	$0.0	$0.0	($0.2)	($0.3)	$0.0	($0.5)	$0.0	$0.0
Operating Income	($6.1)	($2.7)	($2.5)	($4.3)	($3.3)	($12.8)	($12.3)	($13.3)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.7	$0.1	$0.0	$0.1	$0.1	$0.3	$0.0	$0.0
Pre-Tax Income	($5.4)	($2.6)	($2.5)	($4.2)	($3.3)	($12.5)	($12.3)	($13.3)
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	**($5.4)**	**($2.6)**	**($2.5)**	**($4.2)**	**($3.3)**	**($12.5)**	**($12.3)**	**($13.3)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.16)**	**($0.05)**	**($0.04)**	**($0.07)**	**($0.05)**	**($0.21)**	**($0.18)**	**($0.19)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	34.3	50.2	61.6	62.7	63.0	59.4	67.0	70.0

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

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HISTORICAL STOCK PRICE



Source: Stockcharts.com

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