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August 13, 2021

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Achieve Life Sciences, Inc. (ACHV - NASDAQ)

ORCA-2 Fully Enrolled

Based on our DCF model and a 15% discount rate, ACHV is valued at approximately $58.00 per share. Our model applies a 40% probability of eventual cytisinicline sales based on historical Phase III trial success ratios, trial progress and data generated to date. Our valuation includes geographic contributions from the United States only.

Current Price (8/12/2021)	$7.57
Valuation	**$58.00**

OUTLOOK

Achieve Life Sciences is developing cytisinicline for use as a smoking cessation treatment for approval and commercialization in the United States and RoW. The candidate recently completed a Ph2b optimization clinical trial which provided detailed data in September 2019.

Two Ph3 studies are planned with the first underway and the second based on availability of additional funding. The trials will compare cytisinicline with placebo combined with counseling. The primary endpoint is abstinence at 6 and 12 weeks.

Current products on the market have only limited effectiveness and come with unpleasant side effects including nausea, vivid dreams, insomnia and GI issues. Cytisinicline may fill a void in the prescription and NRT market by reducing nicotine cravings, the severity of withdrawal and the reward associated with smoking along with fewer side effects and shorter treatment duration. There are almost 40 million smokers in the US and over 1 billion globally, providing a substantial population demanding an improved smoking cessation product.

ACHV launched the first of its Ph3 trials in 3Q:20 and began enrolling in earnest in early 2021. We anticipate a 2024 commercialization of cytisinicline.

SUMMARY DATA

52-Week High	**18.26**
52-Week Low	**6.85**
One-Year Return (%)	**-18.3**
Beta	**1.28**
Average Daily Volume (sh)	**250,435**
Shares Outstanding (mil)	**9.45**
Market Capitalization ($mil)	**71.5**
Short Interest Ratio (days)	**3.09**
Institutional Ownership (%)	**18.6**
Insider Ownership (%)	**0.31**
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 2021 Estimate	**N/A**
P/E using 2022 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(In millions of US$)

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

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2020	-$2.15 A	-$1.68 A	-$1.14 A	-$1.11 A	-$5.42 A
2021	-$1.30 A	-$1.53 A	-$0.72 E	-$0.59 E	-$3.89 E
2022					-$2.75 E
2023					-$3.53 E

*2020 quarterly EPS does not sum to full year due to distortion from share issuance

WHAT'S NEW

Second Quarter 2021 Results

Achieve Life Sciences, Inc. (NASDAQ: ACHV) reported second quarter results in a press release and held a conference call after market close on August 12, 2021. The company concurrently filed its Form 10-Q with the SEC.

Highlights for the second quarter ended June 30th and to-date include:

- Publication of ORCA-1 Phase IIb Trial in *Nicotine and Tobacco Research* - April 2021
- Announcement, pricing and closing of $20 million offer - May 2021
- US patent applications allowance - June 2021
- ORCA-2 target enrollment achieved - June 2021
- NIH grant for cytisinicline in e-cigarette cessation - July 2021
- Two patents granted for novel cytisinicline dosing - August 2021

No revenues were reported in the second quarter. Operating expense in 2Q:21 was ($11.3) million yielding a net loss of ($11.3) million or ($1.53) per share.

For the quarter ending June 30, 2021 and versus the year-ago quarter ending June 30, 2020:

- Research & development expense rose 736% to $9.2 million from $1.1 million, attributable to the Phase III ORCA-2 trial now fully enrolled and underway;
- General & administrative expense rose 14% to $2.1 million from $1.8 million due to higher employee expense associated with stock-based compensation, increase in premiums for insurance and clinical trial media and awareness expenses;
- Net loss was ($11.3) million vs. ($2.9) million or ($1.53) and ($1.68) per share, respectively.

As of June 30, 2021, cash and equivalents totaled $42.0 million. This amount compares to a $35.9 million balance in cash and equivalents held at the end of 2020. Achieve carries no debt on its balance sheet. Cash used in operations was ($15.5) million versus ($6.7) million for the six months ended 2021 and 2020, respectively. Cash from financing for the first six months of 2021 was $21.7 million, which includes gross proceeds of $23 million from the May common stock offering.

May 2021 Common Stock Offering

On May 24th Achieve proposed an underwritten public offering of almost three million shares to raise $20 million in proceeds. The market received the offering well and the 15% overallotment was exercised on top of the base amount to raise a gross $23 million in proceeds. The transaction was executed at $7.00 per share for 3,285,714 shares. Net proceeds after issuing costs were $21.3 million. Along with existing cash on the balance sheet, the balance provides a runway until 2023. Oppenheimer acted as the sole book-running manager in the offering and Lake Street Capital Markets acted as the lead manager.

NIH Vaping Grant

Achieve announced that it had been awarded a grant (non-dilutive funding) from the National Institute on Drug Abuse (NIDA) of the National Institutes of Health (NIH) for the evaluation of cytisinicline in cessation of nicotine e-cigarette use. The grant award commenced on August 1, 2021, in an amount of $320,000. This initial infusion will support the completion of regulatory and clinical activities, namely protocol finalization, clinical site identification, and submission of an IND. Upon completion of the milestones, Achieve will then be subject to NIH assessment for the next stage of grant award of $2.5 million. The second tranche of the award will enable initiation of Phase II ORCA-V1, which will target ~150 adult nicotine e-cigarette users in the US. Grant funding is expected to cover approximately 50% of the trial cost. Primary investigators for the grant are Achieve's CMO, Dr. Cindy Jacobs, and Dr. Nancy Rigotti, Professor of Medicine at Harvard Medical School and Director, Tobacco Research and Treatment Center, Massachusetts General Hospital.

Intellectual Property

On June 3rd Achieve announced that the United States Patent and Trademark Office (USPTO) had allowed U.S. Patent Application number 16/993,522 and 17/101,686 covering the novel 3.0 mg three times daily (TID) cytisinicline dosing regimen.

On August 11th, Achieve publicized the granting of two US patents regarding the dosing and administration regimen of cytisinicline. The two patents 11,083,715 and 11,083,716 cover the novel 3 mg TID[1] dosing regimen. The patents could provide marketing exclusivity for cytisinicline until 2040. The claims cover 3 mg TID dosing for the treatment of nicotine addiction and for promoting reduction/cessation in smoking and vaping in treatment naïve and refractory patients who have failed previous cessation treatment attempts.

Chantix Nitrosamine Contamination

In a surprise development, several recognized news sources reported that Pfizer had halted global distribution of Chantix due to higher than recommended levels of nitrosamines. Nitrosamines are carcinogenic organic compounds that have appeared in a number of pharmaceuticals, including several angiotensin II receptor blockers. The FDA had promulgated[2] acceptable levels of nitrosamines in a report published in February in a follow up to a September 2020 guidance document. After internal testing earlier this year, Pfizer found levels that exceeded the recommended values and subsequently halted distribution and recalled several lots of the smoking cessation drug. While Pfizer believes the benefits of Chantix outweigh the risks of the nitrosamines, Canada and South Korea have issued recalls for the drug.

The source of the nitrosamines is likely from the reagents and solvents used in the drug manufacturing process. It is not clear from our vantage point if Achieve's manufacturing process completely sidesteps this issue given the natural source of cytisinicline from the Golden Chain tree; however, Achieve management has been testing for these impurities as a matter of course for some time and reports that they are below the FDA thresholds.

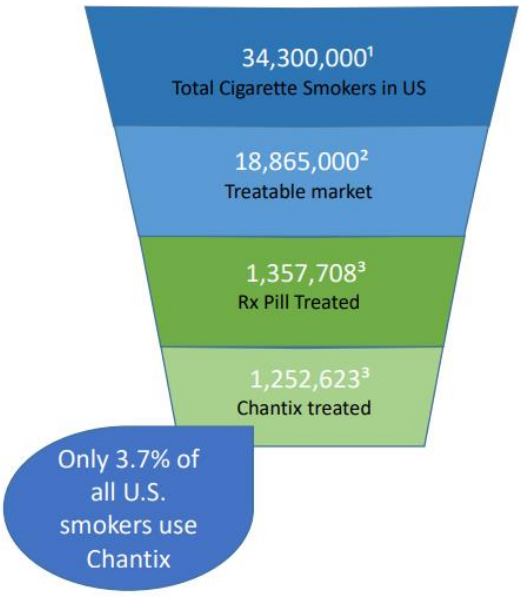
This appears to be a favorable development for Achieve, as it shifts public perception more towards natural products such as cytisinicline and creates doubt about a competing product. Our thesis for Achieve identifies many reasons for an eventual Pfizer buyout of the company given their strong need to replace Chantix and offset the near $1 billion revenue cliff. It also leverages the salesforce that they have in place with active smoking cessation prescriber relationships. Chantix is going off-patent this year and we expect generic competition to soon follow which may be given a boost by this setback for the pharmaceutical giant.

In response to shortages resulting from the recall, the FDA has granted Par Pharmaceuticals approval as a generic competitor to Chantix. Pfizer's Chantix patent expired in November of 2020, and there are others, including Apotex which is importing generic varenicline from Canada to address the shortage. Other generic manufacturers such as Teva and Mylan have also filed to provide a generic version of Chantix.

While Chantix is the predominant smoking cessation therapy, only 3.7% of US smokers use it and 76% of Chantix patients report not completing the full three-month course of treatment.[3] 61% of patients who did not complete the full course of therapy for Chantix or Zyban report stopping due to side effects.[4] Thus, many smokers who wish to quit are still underserved. The availability of generic Chantix may do little to address this as most patients (~80%) do not pay out of pocket for Chantix or buproprion prescription,[5] representing opportunity for cytisinicline.

[1] Three times daily
[2] See page 6 of document for acceptable nitrosamine impurity levels.
[3] IQVIA Prescription Claims Database; 072018-062019
[4] IQVIA Patient Survey, 2019
[5] IQVIA Prescription Claims Database; 072018-062019

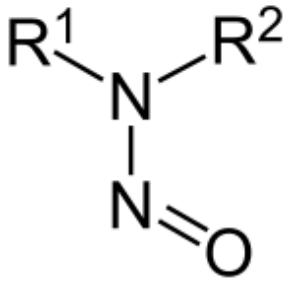
Exhibit I - Chantix Leaves Quitters Underserved[6]



Nitrosamines Background

Nitrosamines, most of which are indirectly carcinogenic in animals, are organic compounds with alkyl and nitroso groups. The chemical structure is represented as $R_2N\text{-}N{=}O$, where R represents an alkyl group [7].

Exhibit II - The Chemical Structure of Nitrosamines[8]



Nitrosamines become carcinogenic only when they are metabolically activated in the body and converted to alkylating agents which can modify DNA bases and induce mutations. This is a pH-dependent process.

The clinical importance of nitrosamines was first discovered by Barnes and Magee when they noticed that dimethylnitrosamine associated with development of liver tumors in rats.[9] Later, it was found that about 90% of the 300 nitrosamines tested were carcinogenic in a wide range of animals including humans.[10,11] The compounds have an organotropic action, meaning some nitrosamino compounds specifically induce tumors in various target organs including lung, nasal cavity, esophagus, stomach, pancreas, colon, urinary bladder, central nervous system.[12]

The major carcinogenic compounds in this group of molecules include:

- N-nitroso-dimethylamine (NDMA)
- N-nitroso-pyrrolidine (NPYR)
- N-nitroso-piperidine (NPIP)
- N-nitroso- morpholine (NMOR)

[6] Achieve Corporate Presentation June 2021
[7] https://en.wikipedia.org/wiki/Nitrosamine
[8] https://en.wikipedia.org/wiki/Nitrosamine
[9] Barnes JM, Magee PN (1954) Some toxic properties of dimethylnitrosamine Brit. J. Ind. Med. 11: 167-174
[10] https://en.wikipedia.org/wiki/Nitrosamine#cite_note-nitrocancer-8
[11] https://doi.org/10.1016/0015-6264(71)90306-3
[12] https://www.fda.gov/media/147331/download

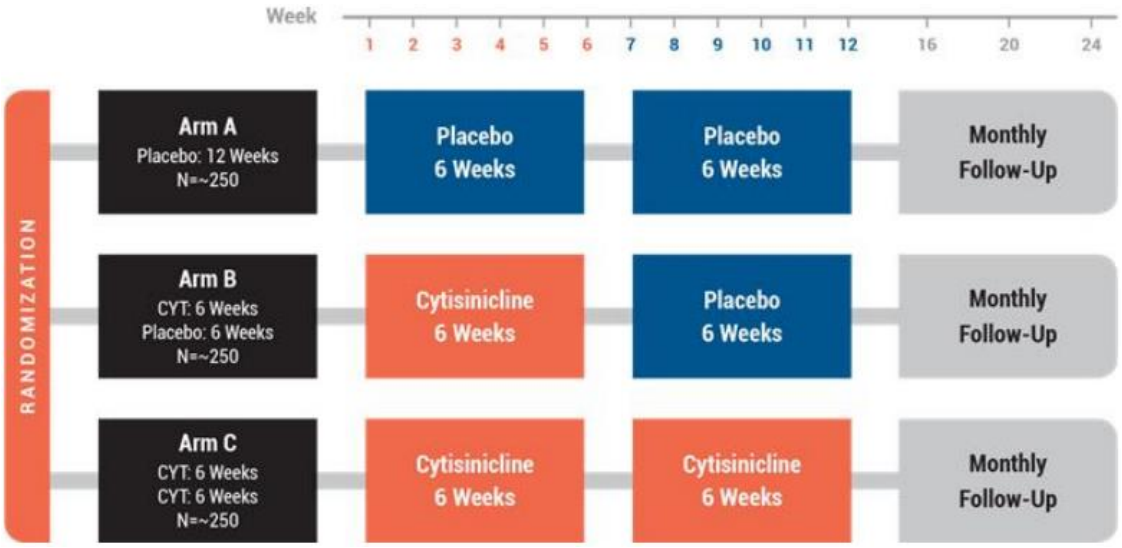
One common way ordinary consumers are exposed to nitrosamines is through tobacco products.[13] Ironically, the cure, at least in Pfizer's case, appears to present the same problems as the smoking addiction it serves to address.

ORCA-2 Phase III Trial

Achieve announced the start of its Phase III ORCA-2 trial on October 7th 2020, targeting enrollment of 750 smokers at 15 clinical sites throughout the United States. The trial is a multi-center, double-blind, randomized, placebo-controlled Phase III study that will enroll adult cigarette smokers who intend to quit smoking. Subjects will be randomized into one of three arms which include 12 weeks of placebo, six weeks of cytisinicline then six weeks of placebo or 12 weeks of cytisinicline. Dosing will be 3.0 mg, three times daily in each of the treatment cohorts. This dosing regimen is expected to be effective against even high nicotine use prior to cessation as cytisinicline efficiently binds nicotinic acetylcholine receptors.

The trial began with a slower than expected enrollment rate due to impacts related to the coronavirus and severe winter weather in the South; however, the rate accelerated at the end of the first quarter and ORCA-2 has now enrolled 810 subjects. There will be a six-month follow up period after the measurement at week 12, and last patient, last visit is anticipated by the end of 2022. Then the data analysis portion will begin and topline results are anticipated to be available by spring 2022.

Exhibit III – ORCA-2 Phase III Trial Design[14]



ORCA-1 Publication

On April 14, 2021, Achieve announced that details for the Phase IIb ORCA-1 trial had been published in the journal *Nicotine and Tobacco Research*. The publication was entitled "A Multicenter, Double-blind, Randomized, Placebo-controlled Phase 2b Trial of Cytisinicline in Adult Smokers (The ORCA-1 Trial)." ORCA-1 evaluated safety and efficacy of cytisinicline in various dosing and administration schedules and enrolled 254 smokers in the US. All subjects treated with cytisinicline in the trial had statistically significant ($p<0.001$) end of treatment abstinence rates compared to placebo. The 3 mg cytisinicline TID arm had a five-fold higher likelihood of quitting ($p<0.001$). No serious or severe adverse events were reported. Adverse events were below 10% in the 3 mg TID arm versus placebo. Most common adverse events were abnormal dreams, insomnia and constipation, at 6% vs 2% in placebo, upper respiratory tract infection, at 6% vs 14% in placebo, and nausea at 6% vs 10% in placebo. Treatment adherence was greater than 94% in all treated arms, and 98% in the 3 mg TID arm.

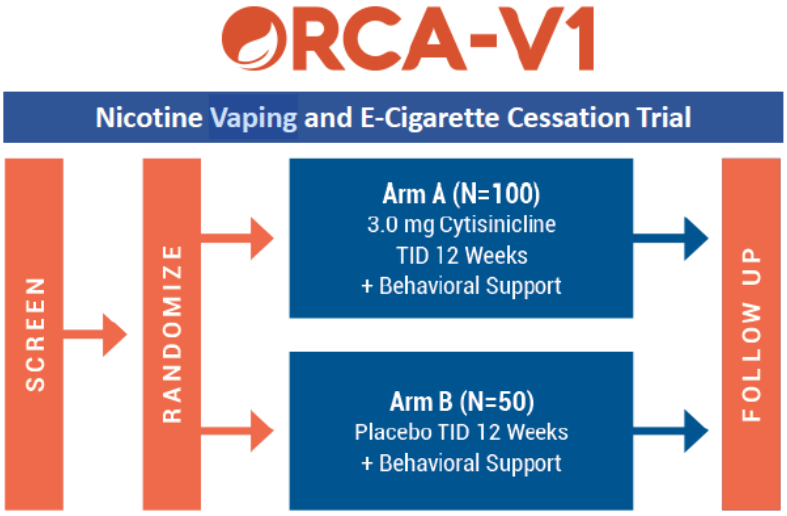
ORCA Vaping Trial

While smoking has shown declines in prevalence in the last decades, it has been replaced by another popular form of nicotine consumption: vaping. Last year, Achieve announced a collaboration with the FreeMind Group to identify non-dilutive funding to support the launch of a clinical trial that will evaluate the effectiveness of cytisinicline in sub-

[13] Hecht, Stephen S. (1998). "Biochemistry, Biology, and Carcinogenicity of Tobacco-Specific N-Nitrosamines". Chemical Research in Toxicology. 11 (6): 559–603. doi:10.1021/tx980005y. PMID 9625726.
[14] Source: Achieve Life Sciences S-1 Filed November 6, 2019.

jects that are vaping and using e-cigarettes. The study will likely include 150 subjects that are vaping, but not smoking. Randomization will be divided into a 2:1 split with 100 receiving twelve weeks of cytisinicline and 50 on placebo. Dosing is expected to follow the regimen evaluated in ORCA-2: 3 mg three times daily. The Phase II study will examine vaping cessation as the endpoint at the six week and twelve week point by measuring cotinine levels.[15] If the trial is successful and generates statistically significant results, it could provide support, along with a successful ORCA-2 trial, to require only one Phase III to obtain approval. Achieve announced that it had secured a non-dilutive grant from NIDA that is expected to support the program through IND submission, and could provide additional support as milestones are met.

Exhibit IV – Anticipated Vaping Trial Structure[16]



Key Events

- Launch of ORCA-2 – October 2020
- $23.0 million gross capital raise – May 2021
- Completion of enrollment in ORCA-2 - June 2021
- NIDA (NIH) grant for ORCA-V1 - July 2021
- ORCA-V1 IND development – 2H:21
- Topline readout of ORCA-2 - 1H:22
- ORCA-V1 launch – 1H:22
- Initiation of ORCA-3 - 2022

Summary

Achieve and the smoking cessation space have remained in the news in recent weeks. Continued progress on the Phase III trial, allowance of patents that provide protection until 2040 and competitor missteps support our continued favorable view of the company and an increase in target price. Additional capital from the share issuance adds more funds to the company coffers and supports the continued and uninterrupted advancement of the Phase III ORCA programs.

Cytisinicline, with its established use in Central and Eastern Europe and directionally superior data in pivotal trials, has a material opportunity to provide for an unmet need in smokers who wish to quit, but are wary of side effects and lack of efficacy in existing alternatives. US patents for Pfizer's Chantix, which represents standard of care in smoking cessation, expired in November 2020,[17] and generic competition has begun, prompted by Chantix product shortages. This provides an opportunity for cytisinicline to come to market, offering both a low-side effect alternative to Chantix and over a decade of intellectual property protection. We maintain our recently increased price target of $58.00 per share.

[15] Cotinine is a metabolite of nicotine & cotinine urine or blood testing is considered highly accurate for assessing nicotine use, including vaping.
[16] Source: Achieve Life Sciences October 2020 Corporate Presentation
[17] Pfizer FY:20 10-K

PROJECTED FINANCIALS

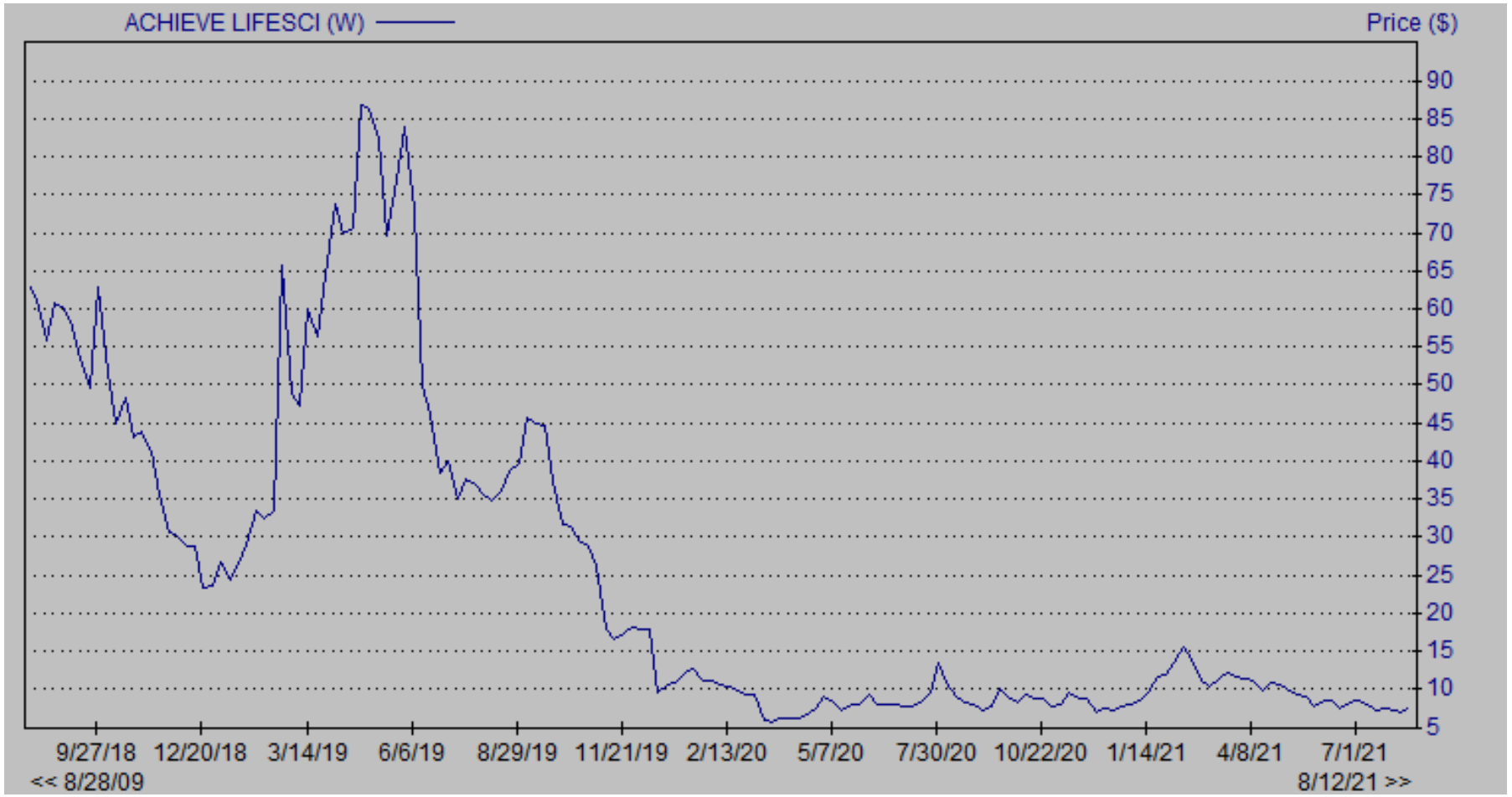
Achieve Life Sciences, Inc. - Income Statement

Achieve Life Sciences, Inc.	2020 A	Q1 A	Q2 A	Q3 E	Q4 E	2021 E	2022 E	2023 E
Total Revenues ($MM)	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.2**	**$0.2**	**$2.6**	**$0.0**
R&D	$6.9	$5.6	$9.2	$4.8	$4.0	$23.7	$21.5	$22.0
G&A	$7.9	$2.3	$2.1	$2.0	$2.0	$8.4	$8.3	$14.0
Operating Income	($14.8)	($8.0)	($11.3)	($6.8)	($5.8)	($31.9)	($27.2)	($36.0)
Total Other Income	$0.0	($0.0)	($0.0)	$0.0	$0.0	($0.0)	$0.0	$0.0
Pre-Tax Income	($14.7)	($8.0)	($11.3)	($6.8)	($5.8)	($31.9)	($27.2)	($36.0)
Taxes & Other	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*$0.0*	*0%*	*0%*
Net Income	($14.7)	($8.0)	($11.3)	($6.8)	($5.8)	($31.9)	($27.2)	($36.0)
Reported EPS	**($5.42)**	**($1.30)**	**($1.53)**	**($0.72)**	**($0.59)**	**($3.89)**	**($2.75)**	**($3.53)**
YOY Growth								
Shares Outstanding	2.719	6.132	7.391	9.500	9.800	8.206	9.900	10.200

Source: Company Filing // Zacks Investment F

HISTORICAL STOCK PRICE

Achieve Life Sciences, Inc. – Stock Price Chart[18]



[18] Source: Zacks Research System

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