Zacks Small-Cap Research

Sponsored – Impartial - Comprehensive

May 17, 2021
John D. Vandermosten, CFA
312-265-9588 / jvandermosten@zacks.com
scr.zacks.com
10 S. Riverside Plaza, Suite 1600, Chicago, IL 60606

Achieve Life Sciences, Inc. (ACHV - NASDAQ)

ORCA-2 Enrollment On Track

Based on our DCF model and a 15% discount rate, ACHV is valued at approximately $50.00 per share. Our model applies a 30% probability of eventual cytisinicline sales based on historical Phase II trial success ratios and data generated to date. Our valuation includes geographic contributions from the United States only.

Current Price (5/14/2021)	$9.41
Valuation	**$50.00**

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 will 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 (%)	**20.6**
Beta	**1.26**
Average Daily Volume (sh)	**95,926**
Shares Outstanding (mil)	**6.16**
Market Capitalization ($mil)	**58.0**
Short Interest Ratio (days)	**7.09**
Institutional Ownership (%)	**24.0**
Insider Ownership (%)	**0.45**
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 2020 Estimate	**N/A**
P/E using 2021 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 E	$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	-$1.16 E	-$1.09 E	-$0.96 E	-$4.51 E
2022					-$3.55 E
2023					-$4.23 E

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

WHAT'S NEW

First Quarter 2021 Results

Achieve Life Sciences, Inc. (NASDAQ: ACHV) reported first quarter results in a press release and held a conference call after market close to discuss details therein on May 13, 2021. The company concurrently filed its Form 10-Q with the SEC.

Highlights for the first quarter, and to-date include:

- Presentation of Smoker and E-Cigarette Quitting Survey at SRNT - February 2021
- Appointment of Dr. Bridget Martell and Dr. Cindy Jacobs to Board - March 2021
- Publication of RAUORA Trial in *Addiction* - March 2021
- Publication of ORCA-1 Phase IIb Trial in *Nicotine and Tobacco Research* - April 2021

Achieve produced no revenues in 1Q:21 and incurred operating expense of ($7.98) million yielding net loss of ($8.00) million or ($1.30) per share.

For the quarter ending March 31, 2021 and versus the year-ago quarter ending March 31, 2020:

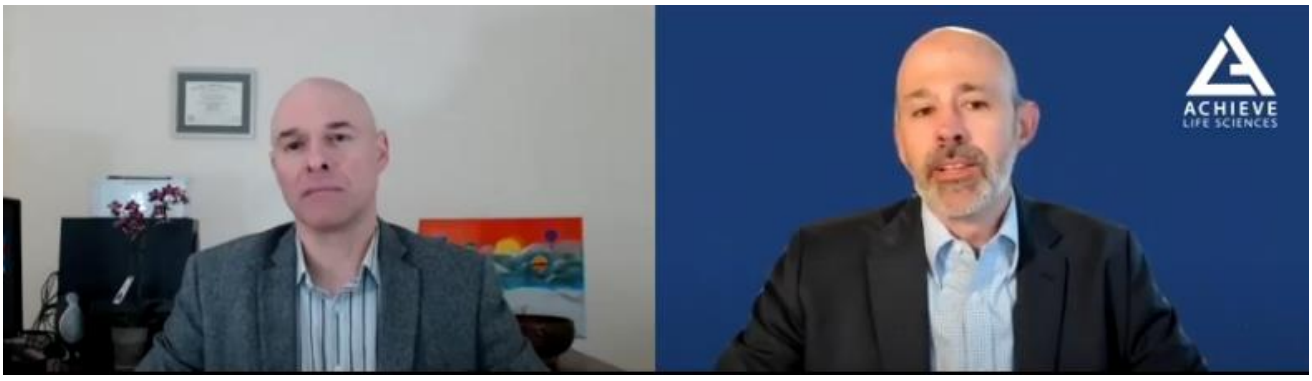
- Research & development expense rose 273% to $5.64 million from $1.54 million attributable to the launch and ongoing enrollment for the Phase III ORCA-2 trial;
- General & administrative expense rose 28.6% to 2.34 million from $1.82 million due to higher stock-based compensation and clinical trial media and awareness expenses;
- Net loss was ($8.00) million vs. ($3.32) million or on a per share basis ($1.30) and ($2.15) with the seeming disconnect between net loss and per share values attributable to an increase in shares outstanding.

As of March 31, 2021, cash and equivalents totaled $29.6 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 $6.45 million, up 45% from the $4.46 million consumed in 1Q:20. After a slow start in 2021, Achieve's Phase III ORCA-2 trial is now on track to be fully enrolled, as scheduled, in mid-2021.

Interview with CEO John Bencich

In April, we held a question and answer session with CEO John Bencich where we reviewed the background on cytisinicline, recent study results and what lies ahead for the company. Follow link here to view.

Exhibit I – Interview with CEO John Bencich[1]



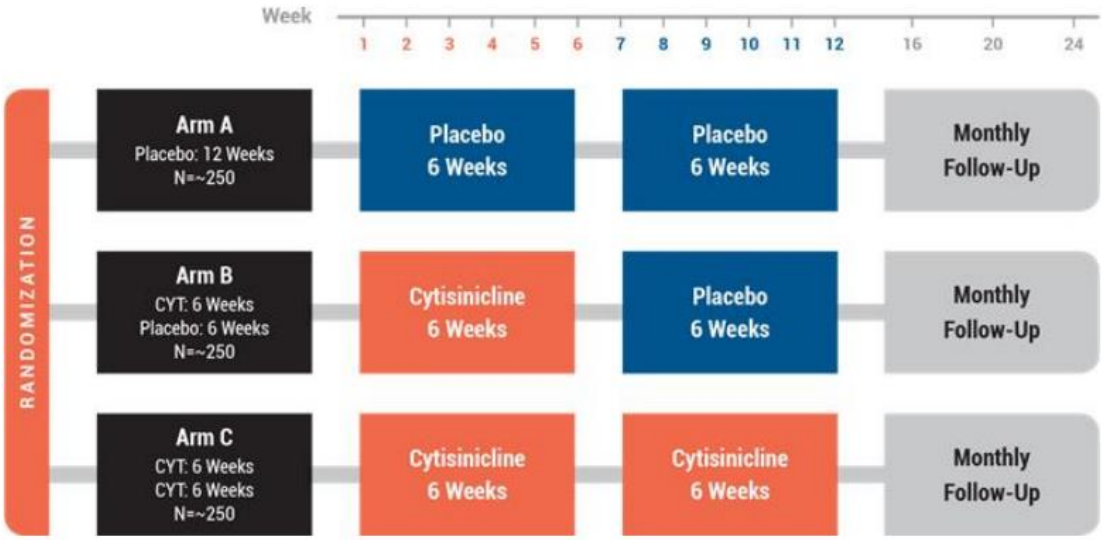
[1] Source: SNN hosted interview with Zacks SCR biotech analyst John Vandermosten and Achieve Life Sciences CEO John Bencich. Achieve Life Sciences Inc. (NASDAQ: ACHV) - Virtual NDR on April 27, 2021 | SNN Network

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 should enroll the targeted 750 subjects by mid-year. Two new sites were added in Atlanta, Georgia and Evansville, Indiana since our last update, bringing the total to 17. There will be a six-month follow up period after the measurement at week 12 measurement which should be complete by the end of the year. Then the data analysis portion will begin and topline results are anticipated to be available by spring 2022.

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



Appointment of Drs. Bridget Martell and Cindy Jacob to the Board

Achieve announced on March 15, 2021 that Drs. Bridget Martell and Cindy Jacobs were appointed to Achieve's Board of Directors. Dr. Cindy Jacobs has served as Achieve's Chief Medical Officer and President before taking on the additional role as Director. She will continue leading the regulatory and clinical development for cytisinicline, leveraging her 30 years of experience in industry.

Dr. Martell brings a background with scientific, clinical and leadership experience. Martell is board certified in both Internal and Addiction Medicine, practicing over 20 years as a physician at Yale. She continues to serve at Yale as an Entrepreneur in Residence at the Office of Cooperative Research and has held leadership positions and executive roles at Pfizer, Kura Oncology and Juniper Pharmaceuticals. Dr. Martell holds a B.Sc. in Microbiology from Cornell University, an M.A. in Molecular Immunology from Boston University, and an M.D. from The Chicago Medical School.

RAUORA Publication

Following the completion of the RAOURA trial in early 2020, topline results were provided in the summer of that year. Further data analysis was conducted from the RAOURA study and a paper was written which was published in the scientific journal *Addiction*. The piece, entitled Cytisine versus varenicline for smoking cessation in New Zealand indigenous Māori: a randomized controlled trial provided additional detail regarding the statistical methods and trial design used and subgroup analysis.

[2] Source: Achieve Life Sciences S-1 Filed November 6, 2019.

The first subject was enrolled in September 2017 and the last follow up occurred in October 2019 for this New Zealand-based smoking cessation project comparing cytisinicline with varenicline. Sample size was lower than the initially anticipated 2,140 subjects due to delays related to ethics and regulatory approvals and slower than anticipated recruitment. Ultimately, 679 subjects were randomized, 337 in the cytisinicline group and 342 in the varenicline group. Continuous abstinence at six months post-quit date were 12.1% for cytisinicline vs. 7.9% for varenicline. However, zero remained within the 95% confidence interval and cytisinicline was not considered superior despite a mean that was better than varenicline.

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.

Presentation of Data on Smoker and E-Cigarette User Attitudes and Perceptions Toward Quitting

Achieve presented three posters on February 25, 2021 at the Society for Research on Nicotine & Tobacco (SRNT) Annual Meeting, held virtually this year. The posters featured survey data on smoker and e-cigarette user behavior. A recap of the survey results are discussed in our recent article.

The posters were entitled:

- "A Survey in the United States of Attitudes to Nicotine Cessation in Smokers: Smokers' Satisfaction with Available Treatments" (PH-293)
- "A Survey in the United States of Attitudes to Nicotine Cessation in Vapers: Reasons for Choosing to Vape" (PH-294)
- "A Survey in the United States of Attitudes to Nicotine Cessation in Vapers: Their Plans to Quit Vaping" (PH-295)

Dr. Anthony Clarke, Chief Scientific Officer for Achieve, presented data from Achieve's 15-minute online survey in adults aged 19-64 who were current daily smokers or smokers who had quit in the past year. In total, 1,122 current and former smokers participated in the survey with 986 current smokers and 136 recent quitters. All participants had also used an FDA-approved prescription pill (varenicline or bupropion) and/or nicotine replacement therapy at least once in a prior quit attempt.

Of those that attempted to quit using a prescription pill, the full 12-week course was not completed in a majority of cases. 53% completed less than one month of therapy, with about half of those completing three weeks or less.

Side-effects were reported in 61% of respondents as a key reason for non-compliance. In those who had not used a prescription pill, fear of side effects was reported by 49% of responders. Lack of efficacy was reported by 27% of those using prescription medicine and by 42% of those using non-prescription medicine. The results indicated that the satisfaction and perceived efficacy of available cessation treatments was low.

Exhibit III - Perceived Effectiveness and Satisfaction with Cessation Available Treatments[3]

	Effectiveness	Satisfaction
Chantix (varenicline)	29%	30%
Zyban (bupropion)	22%	24%
e-cigarettes	30%	33%
Behavioral counselling	28%	30%
R NRT	22%	23%
OTC NRT	17%	18%

Less than a third of respondents who attempted to quit using prescription pills reported perceived efficacy and satisfaction. E-cigarettes were comparable in efficacy, trending superior, although as revealed by Achieve's other survey in vape users, e-cigarettes are not effective in addressing the underlying nicotine addiction.

In addition to the data from the aforementioned survey in smokers, Dr. Anthony Clarke also presented data from another survey regarding vape user behavior and quit intentions. 508 individuals completed the survey between February 29 and March 12, 2020. The population comprised 249 past smokers, 247 dual users, and 12 never smokers.

The most common reason cited to begin vaping was to quit smoking. A quarter of vapers planned to quit vaping in the next three months, a third in the next three to six months, and 43% in the next 12 months. Almost three quarters of dual users expressed interest in a new prescription treatment to help them quit. Finally, 84% of dual users and 50% of past smokers consulted their primary care physician for advice on cessation.

In the press release announcing the presentations and posters at SRNT, John Bencich, Achieve's CEO, commented that the combined evidence indicated the substantial need for a new therapeutic option for smokers who largely wish to quit but face the limitations of current standard of care. Bencich reminded investors that Achieve's lead candidate, cytisinicline, has demonstrated a favorable tolerability profile and a lack of common side effects that may help smokers adhere to treatment and overcome their addiction.

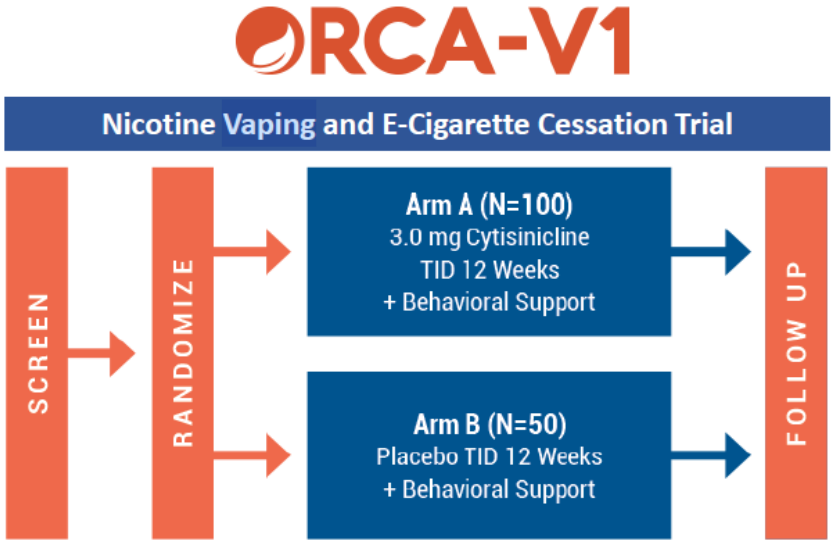
ORCA Vaping Trial

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 subjects 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.[4] If the trial is successful and generates statistically significant results, it could provide support, along with a successful ORCA-2, to require only one Phase III to obtain approval. Achieve continues to explore funding opportunities for Phase II ORCA-V1, and expects to share additional details on its application status later this year.

[3] A Survey in the United States of Attitudes to Nicotine Cessation in Smokers: Smokers; Satisfaction with Available Treatments. Clarke, Xinos, Stewart. Achieve Life Sciences - SRNT 2021

[4] Cotinine is a metabolite of nicotine, and cotinine urine or blood testing is considered highly accurate for assessing nicotine use, including vaping.

Exhibit IV – Anticipated Vaping Trial Structure[5]



Key Events

- SRNT poster presentations - February 2021
- Completion of enrollment in ORCA-2 – mid-year 2021
- Additional detail on funding application status for vaping trial – 2021
- Possible vaping trial ORCA-VI – 2021/2022
- Topline readout of ORCA-2 – 1H:22
- Initiation of ORCA-3 - 2022

Summary

Highlights from Achieve's first quarter 2021 included the presentation of survey data for attitudes and perceptions towards quitting at the SRNT, appointment of Drs. Bridget Martell and Cindy Jacobs to the Board and publications of the RAUORA and ORCA-1 studies in *Addiction* and *Nicotine and Tobacco Research*.

After the turn of the year, enrollment for ORCA-2 advanced at a slower pace than anticipated due to the pandemic and winter weather. Management has taken steps to drive enrollment to the study including adding extra sites and anticipates full enrollment by mid-2021. Following completion of ORCA-2, Management expects ORCA-3 to initiate sometime in 2022. Vaping presents yet another opportunity for cytisinicline, and non-dilutive funding opportunities are currently being explored, with an update expected later this year.

Cytisinicline, with its established use in Central and Eastern Europe and potentially 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,[6] and generic competition is expected to mount within a year or two. This gives an opportunity for cytisinicline to come to market, offering both a low-side effect alternative to Chantix and several years of intellectual property protection. We maintain our price target of $50.00.

[5] Source: Achieve Life Sciences October 2020 Corporate Presentation
[6] Pfizer FY:20 10-K

PROJECTED FINANCIALS

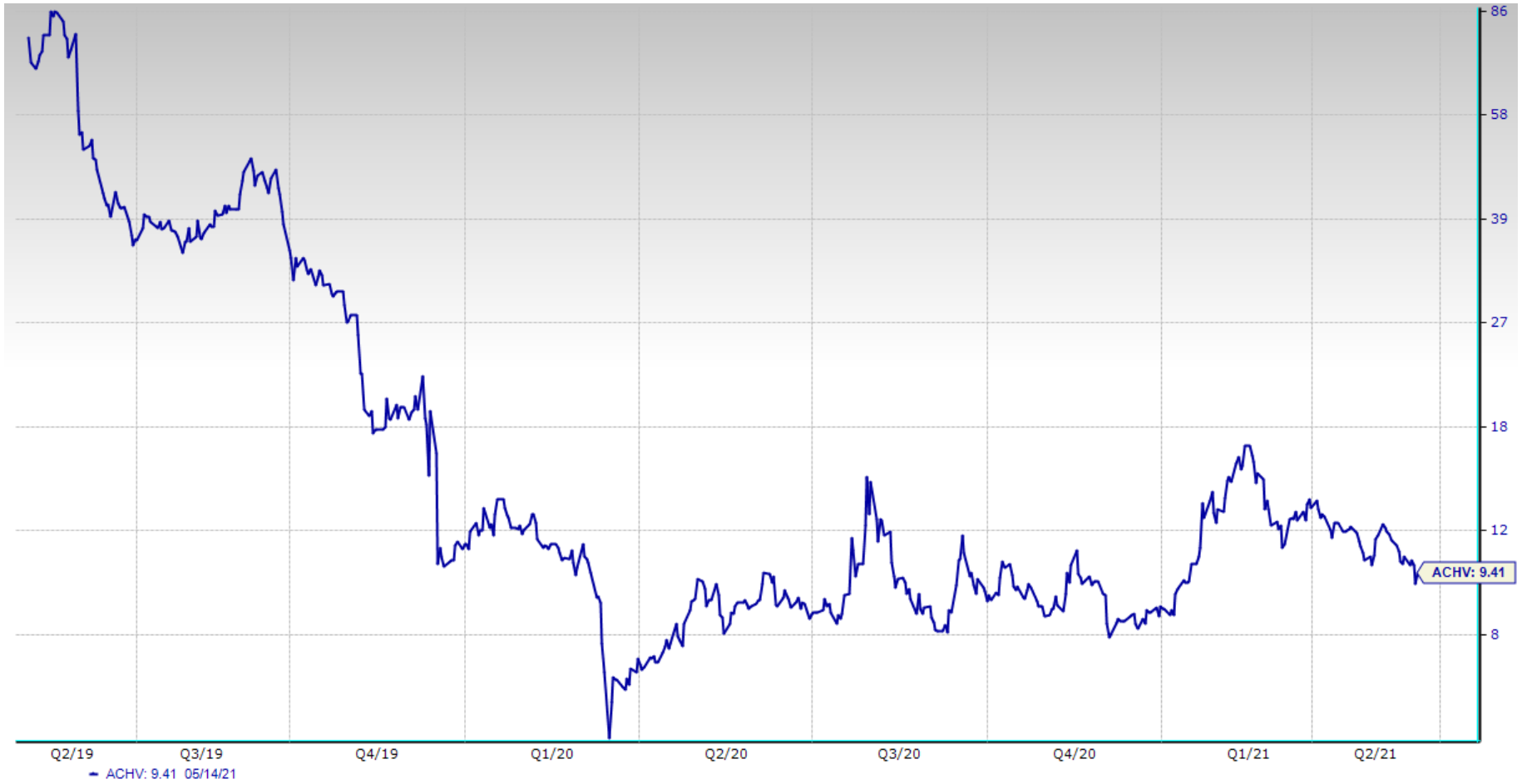
Achieve Life Sciences, Inc. - Income Statement

Achieve Life Sciences, Inc.	2020 A	Q1 A	Q2 E	Q3 E	Q4 E	2021 E	2022 E	2023 E
Total Revenues ($MM)	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**
R&D	$6.9	$5.6	$5.2	$4.8	$4.0	$19.6	$21.5	$22.0
G&A	$7.9	$2.3	$2.0	$2.0	$2.0	$8.3	$8.3	$14.0
Operating Income	($14.8)	($8.0)	($7.2)	($6.8)	($6.0)	($28.0)	($29.8)	($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)	($7.2)	($6.8)	($6.0)	($28.0)	($29.8)	($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)	($7.2)	($6.8)	($6.0)	($28.0)	($29.8)	($36.0)
Reported EPS	**($5.42)**	**($1.30)**	**($1.16)**	**($1.09)**	**($0.96)**	**($4.51)**	**($3.55)**	**($4.23)**
YOY Growth								
Shares Outstanding	2.719	6.132	6.220	6.240	6.260	6.213	8.400	8.520

Source: Company Filing // Zacks Investment R

HISTORICAL STOCK PRICE

Achieve Life Sciences, Inc. – Stock Price Chart[7]



[7] Source: Zacks Research System

DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

I, John Vandermosten, hereby certify that the views expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the recommendations or views expressed in this research report. I believe the information used for the creation of this report has been obtained from sources I considered to be reliable, but I can neither guarantee nor represent the completeness or accuracy of the information herewith. Such information and the opinions expressed are subject to change without notice.

INVESTMENT BANKING AND FEES FOR SERVICES

Zacks SCR does not provide investment banking services nor has it received compensation for investment banking services from the issuers of the securities covered in this report or article.
Zacks SCR has received compensation from the issuer directly or from an investor relations consulting firm engaged by the issuer for providing non-investment banking services to this issuer and expects to receive additional compensation for such non-investment banking services provided to this issuer. The non-investment banking services provided to the issuer includes the preparation of this report, investor relations services, investment software, financial database analysis, organization of non-deal road shows, and attendance fees for conferences sponsored or co-sponsored by Zacks SCR. The fees for these services vary on a per-client basis and are subject to the number and types of services contracted. Fees typically range between ten thousand and fifty thousand dollars per annum. Details of fees paid by this issuer are available upon request.

POLICY DISCLOSURES

This report provides an objective valuation of the issuer today and expected valuations of the issuer at various future dates based on applying standard investment valuation methodologies to the revenue and EPS forecasts made by the SCR Analyst of the issuer's business.
SCR Analysts are restricted from holding or trading securities in the issuers that they cover. ZIR and Zacks SCR do not make a market in any security followed by SCR nor do they act as dealers in these securities. Each Zacks SCR Analyst has full discretion over the valuation of the issuer included in this report based on his or her own due diligence. SCR Analysts are paid based on the number of companies they cover. SCR Analyst compensation is not, was not, nor will be, directly or indirectly, related to the specific valuations or views expressed in any report or article.

ADDITIONAL INFORMATION

Additional information is available upon request. Zacks SCR reports and articles are based on data obtained from sources that it believes to be reliable, but are not guaranteed to be accurate nor do they purport to be complete. Because of individual financial or investment objectives and/or financial circumstances, this report or article should not be construed as advice designed to meet the particular investment needs of any investor. Investing involves risk. Any opinions expressed by Zacks SCR Analysts are subject to change without notice. Reports or articles or tweets are not to be construed as an offer or solicitation of an offer to buy or sell the securities herein mentioned.