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Achieve Life Sciences, Inc. (ACHV - NASDAQ)

The ORCA Has Launched: Target to $50

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. Our valuation includes geographic contributions from the United States only.

Current Price (11/13/2020)	$9.71
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 begin enrolling in earnest by beginning of year 2021. We anticipate a 2024 commercialization of cytisinicline.

SUMMARY DATA

52-Week High	**28.00**
52-Week Low	**4.60**
One-Year Return (%)	**-41.5**
Beta	**1.82**
Average Daily Volume (sh)	**206,696**
Shares Outstanding (mil)	**3.62**
Market Capitalization ($mil)	**35.1**
Short Interest Ratio (days)	**1.3**
Institutional Ownership (%)	**28.4**
Insider Ownership (%)	**5.0**
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-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of US$)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	$0.0 A	$0.0 A	$0.0 A	$0.0 A	$0.0 A
2020	$0.0 A	$0.0 A	$0.0 A	$0.0 E	$0.0 E
2021					$0.0 E
2022					$0.0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	-$17.57 A	-$10.08 A	-$9.07 A	-$5.91 A	-$39.76 A
2020	-$2.15 A	-$1.68 A	-$1.14 A	-$1.32 E	-$5.80 E
2021					-$6.75 E
2022					-$5.96 E

*2019 quarterly does not sum to full year due to distorting effects of share issuance

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WHAT'S NEW

Third Quarter 2020 Review

Achieve Life Sciences, Inc. (NASDAQ: ACHV) reported third quarter results in a press release which was followed by a conference call held after market close on November 12, 2020. The company concurrently filed its 10-Q with the SEC. During the third quarter and to date, key events included the RAUORA study read out, the presentation of two studies at SRNT-E, the raise of additional capital, executive promotions including John Bencich to CEO and, most importantly, the launch of the Phase III ORCA-2 trial.

Third Quarter 2020 Financial Performance

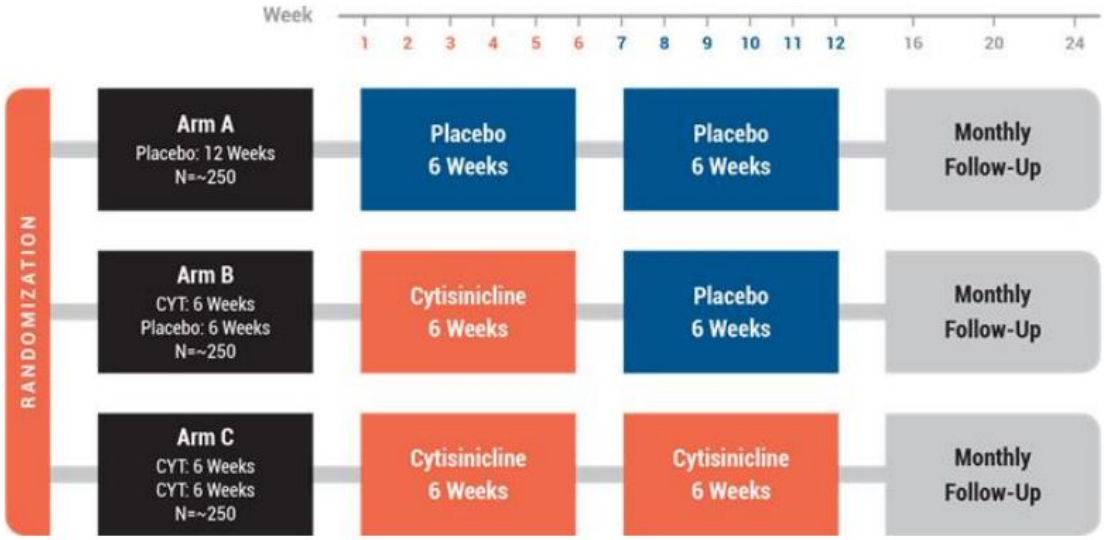
Research and development expenses totaled $1.9 million in 3Q:20, a 4% increase compared with 3Q:19 due to the completion of the ORCA-1 trial last year. General and administrative expenses for the quarter were also $1.9 million, near flat with last year's levels as lower travel related expense was offset by higher public relations and insurance expense. Net loss for 3Q:20 was ($3.8) million or ($1.14) per share on a weighted average share count of 3.29 million.

Cash burn was ($4.3) million for the third quarter, compared with ($3.1) million in the comparable prior year period. Cash and equivalents and short-term investments as of September 30, 2020 were $22.4 million, rising by over $10 million compared to 2Q:20. Financing cash flows during the quarter were $14.6 million, reflecting contributions from the July Registered Direct Offering and the August Public Offering.

Phase III Trial

Achieve announced the start of its Phase III ORCA-2 trial on October 7th which is expected to enroll 750 smokers at 15 clinical sites throughout the United States. The trial will be 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. The trial has begun with metered enrollment to ensure all of its moving parts are running smoothly. The ramp is expected to begin in earnest following the New Year to coincide with traditional resolutions to stop smoking. Management anticipates enrollment to be complete by the end of the first quarter 2021.

Exhibit I – ORCA-2 Phase III Trial Design[1]



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

The primary endpoints for the ORCA-2 study will be the rate of smoking abstinence at the end of 6- and 12-week treatment periods compared to placebo. Abstinence will be defined as no smoking during the last four weeks of treatment using weekly CO biochemical verification. Secondary endpoints will be based upon continued smoking abstinence until week 24 from the end of treatment and identify a reduction in the risk of relapse for subjects on the 6 week treatment regimen compared to the 12 week. Efforts have been made to prepare sites to comply with COVID-19 restrictions. All required non-clinical submissions necessary to start the trial have been completed.

RAOURA Study

In June, topline results for the New Zealand RAUORA[2] study were made available without quantification. The trial achieved statistical significance demonstrating that cytisinicline and behavioral support were at least as effective as varenicline[3] plus behavioral support at six months. Cytisinicline showed significantly fewer reported adverse events compared with varenicline in the study.

Dr. Natalie Walker, who led the RAUORA trial, presented "Is Cytisine At Least as Effective as Varenicline for Smoking Cessation? Findings from a Non-Inferiority Trial in Indigenous New Zealanders and their Extended Family." The study reported favorable results and achieved statistical significance in demonstrating that cytisinicline and behavioral support were at least as effective as varenicline plus behavioral support at six months. Cytisinicline subjects experienced significantly fewer reported adverse events compared with varenicline in the study. Adding to the topline announcement in June, final results showed that the trial met its pre-specified, non-inferiority endpoint of no less than 10% lower quit rate compared to varenicline. Not only did the trial meet its endpoint, but the trend was toward superiority with an Absolute Risk Difference of 4.29. Cytisinicline's 4.29% improvement in quit rates fell within a 95% confidence interval of -0.22 to 8.79. If the lower end of the confidence interval had not fallen below zero, the trial would have demonstrated superiority. We think that if a larger population size was enrolled in the trial, that cytisinicline could have generated statistical superiority. Trial highlights include:

- Cytisinicline subjects were 55% more likely to quit smoking at 6 months compared to varenicline subjects
- Cytisinicline treated subjects presented significantly fewer overall adverse events

Continuous abstinence at 6 months, verified by exhaled carbon monoxide, was 12.1% for cytisinicline compared to 7.9% for varenicline. Subjects in the cytisinicline arm were approximately 1.5x more likely to have quit smoking and have maintained this status by 6 months compared to those in the varenicline arm as evidenced by 1.55 Relative Risk on an intent to treat basis. Equally noteworthy were the significantly fewer adverse events in cytisinicline-treated subjects ($p < 0.001$). 111/337 cytisinicline subjects compared to 138/342 experienced adverse events with less nausea and fewer vivid dreams in those treated with cytisinicline versus varenicline at 22.5% vs 39.1% and 7.2% vs 17.4%, respectively.

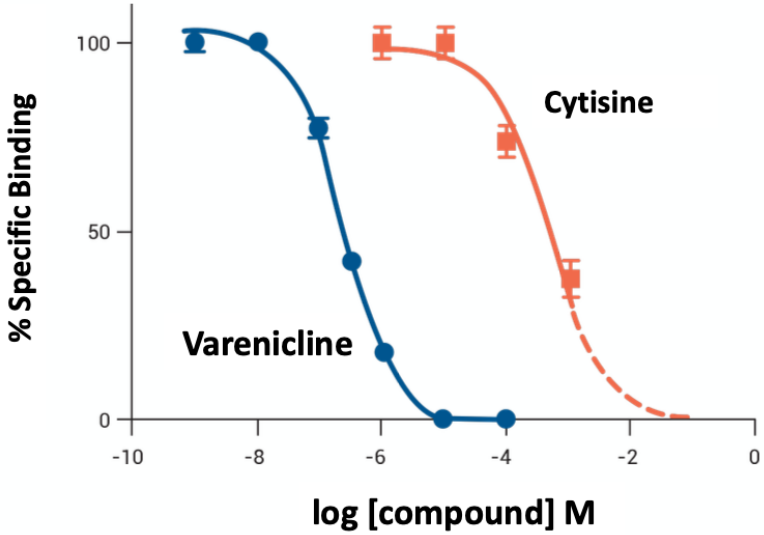
5-HT_3 Receptor Binding Assay Study

On September 18, 2020, Achieve presented details of its 5-HT_3 receptor binding assay study at the Society for Research on Nicotine and Tobacco European (SRNT-E) Annual Meeting. It addressed Achieve's smoking cessation candidate cytisine's (cytisinicline's) lower binding affinity to the 5-HT_3 receptor.

The 5-HT_3 receptor report provided insight into a potential explanation for cytisinicline's lack of nausea and vomiting side effects compared to varenicline. Varenicline has been confirmed as a potent and full agonist for the 5-HT_3 receptor. The receptor pharmacology study conducted by Professor Sarah Lummis and Dr. Kerry Price at the University of Cambridge Department of Biochemistry evaluated *in vitro* binding characteristics of cytisinicline and its competitor varenicline to the human 5-HT_3 receptor. These receptors in the brain stem, when activated by an agonist, are known to directly lead to nausea and vomiting. The study was done using a radioligand antagonist displacement design. Human embryonic kidney (HEK) 293 cells were first cultured under controlled conditions, transfected with cDNA coding for the 5-HT_{3A} receptor subunit and then later incubated with the radioligand before displacing with either cytisinicline or varenicline. 1 uM quipazine was used as a control. Results reported an IC_{50} of 0.50 mM for cytisinicline and 0.25 µM for varenicline, representing a 2000-fold greater agonist binding affinity to the 5-HT_3 receptor for varenicline compared to cytisinicline. More cytisinicline was required to displace the radioligand compared to varenicline indicating cytisinicline's weaker bond with 5-HT_3. Cytisinicline's weaker bond explains the lack of nausea and vomiting-related side effects versus varenicline.

[2] Rauora is the Māori word for rescue
[3] Branded Chantix from Pfizer in the United States

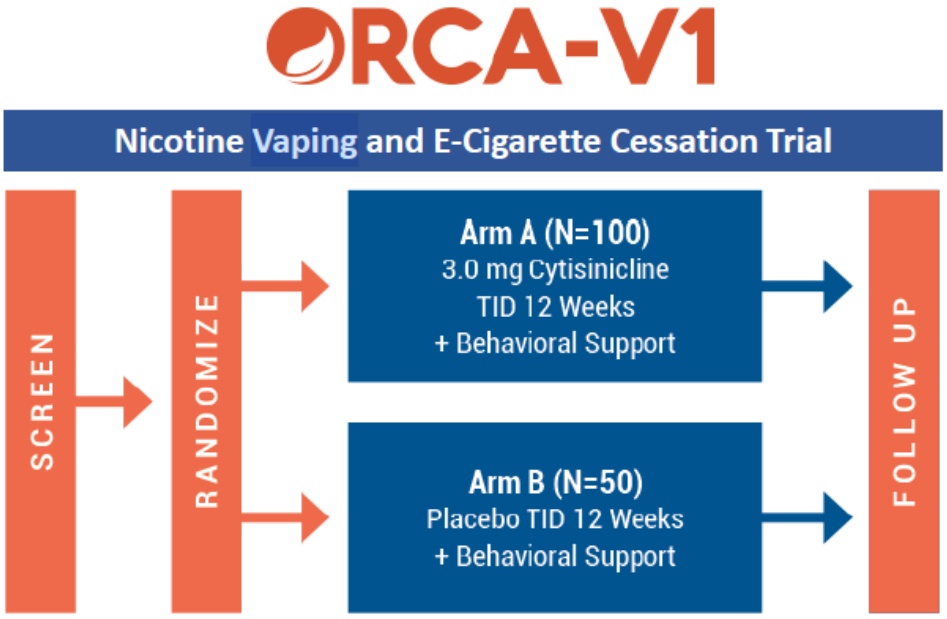
Exhibit II – Displacement Curves for Cytisine (Cytisinicline) vs Varenicline[4]



ORCA Vaping Trial

Achieve introduced details regarding the possible vaping and e-cigarette cessation trial. 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. The Phase II study will look at vaping cessation as the endpoint at the six week and twelve week point. If the trial is successful and generates statistically significant results, it could provide support, along with a successful ORCA-2, to justify one Phase III to obtain approval.

Exhibit III – Vaping Trial Structure[5]



[4] Lummis SCR, Price KL, Clarke A, Cytisine's lower potency at 5-HT_3 receptors may explain its lower incidence of nausea and vomiting than varenicline, September 28, 2020, SRNT-E Annual Meeting
[5] Source: Achieve Life Sciences October 2020 Corporate Presentation

Capital Raises

During the third quarter, Achieve completed a registered direct offering of 731,707 shares at $8.20 per share on July 1, 2020. This effort raised gross proceeds of $6.0 million and net funds of $5.5 million. On August 3rd, 2020, Achieve announced a public offering of 712,000 shares and pre-funded warrants for $10.50 per unit. The effort is expected to raise $7.5 million gross and $6.8 million in net proceeds. The underwriter has an option to purchase 93,000 additional shares.

Subsequent to the end of the quarter, on October 20, Achieve terminated its At-The-Market (ATM) Offering Agreement that it signed with H.C.Wainwright in June 2019. No sales were made under this facility.

Valuation

We increase our target price to $50 per share for Achieve based on an increase in likelihood of success now that cytisinicline has successfully started in a Phase III study and based on the favorable results from the RAUORA study. We think that the results of the New Zealand trial demonstrated a benefit that will be replicated with statistical significance in ORCA-2 which is expected to read out mid-2021.

Key Events

- Presentation of additional analyses of ORCA-1 at SRNT New Orleans – March 2020
- Complete animal toxicity study – 2Q:20
- RAUORA Data Presentation at SRNT Virtual – September 2020
- Second chronic toxicology study submission to FDA – 4Q:20
- Launch Phase III trial – 4Q:20
- Completion of enrollment in ORCA-2 – 1H:21
- Topline readout of ORCA-2 – Mid-2021
- Possible vaping trial ORCA-VI – 2021/2022

Summary

We believe that the historical use of cytisinicline lends support to its safety and efficacy which we anticipate will be confirmed in the upcoming Phase III trials. Now that the Phase III ORCA-2 trial has started, we expect rapid enrollment at the start of the New Year and a read out in mid-2021. Achieve is developing an attractive asset that has demonstrated efficacy in smoking cessation in a number of trials including the recently read out RAUORA study and the recently completed Phase IIb ORCA-1. One of the key attributes of cyticinicline compared to alternatives is its favorable side effect profile which was elucidated by the comparative 5-HT_3 receptor binding assay study. We think prospective partners with a primary care salesforce and other infrastructure already in place will be interested in acquisition. Suitors could include Pfizer, which will need a replacement for Chantix, GSK, which has both Zyban and NRT offerings, and even Perrigo, Johnson & Johnson and Amarin who all have primary care salesforces in place in smoking cessation and would benefit from layering on a complementary product. If Phase III trials are able to show materially improved success over what varenicline has achieved, we anticipate even higher sales than what we forecast in our model and potentially more interest from big pharma. The next milestones on the horizon are the continued enrollment of ORCA-2 and its expected readout in mid-2021. Based on our conservative estimates and updated probability of success, we increase our valuation of Achieve to $50.00 per share.

PROJECTED FINANCIALS

Achieve Life Sciences, Inc. - Income Statement

Achieve Life Sciences, Inc.	2019 A	Q1 A	Q2 A	Q3 A	Q4 E	2020 E	2021 E	2022 E
Total Revenues ($MM)	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**
R&D	$9.7	$1.5	$1.1	$1.9	$3.0	$7.5	$19.0	$21.5
G&A	$6.9	$1.8	$1.8	$1.9	$1.9	$7.4	$8.0	$8.3
Operating Income	($16.5)	($3.4)	($2.9)	($3.8)	($4.9)	($14.9)	($27.0)	($29.8)
Interest Income	$0.0					$0.0	$0.0	$0.0
Total Other Income	$0.1	$0.0	($0.0)	($0.0)	$0.0	$0.0	$0.0	$0.0
Pre-Tax Income	($16.4)	($3.3)	($2.9)	($3.8)	($4.9)	($14.9)	($27.0)	($29.8)
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	($16.4)	($3.3)	($2.9)	($3.8)	($4.9)	($14.9)	($27.0)	($29.8)
Reported EPS	**($39.76)**	**($2.15)**	**($1.68)**	**($1.14)**	**($1.32)**	**($5.80)**	**($6.75)**	**($5.96)**
YOY Growth								
Shares Outstanding	0.412	1.547	1.744	3.289	3.700	2.570	4.000	5.000

Source: Company Filing // Zacks Investment Research, Inc. Estimates

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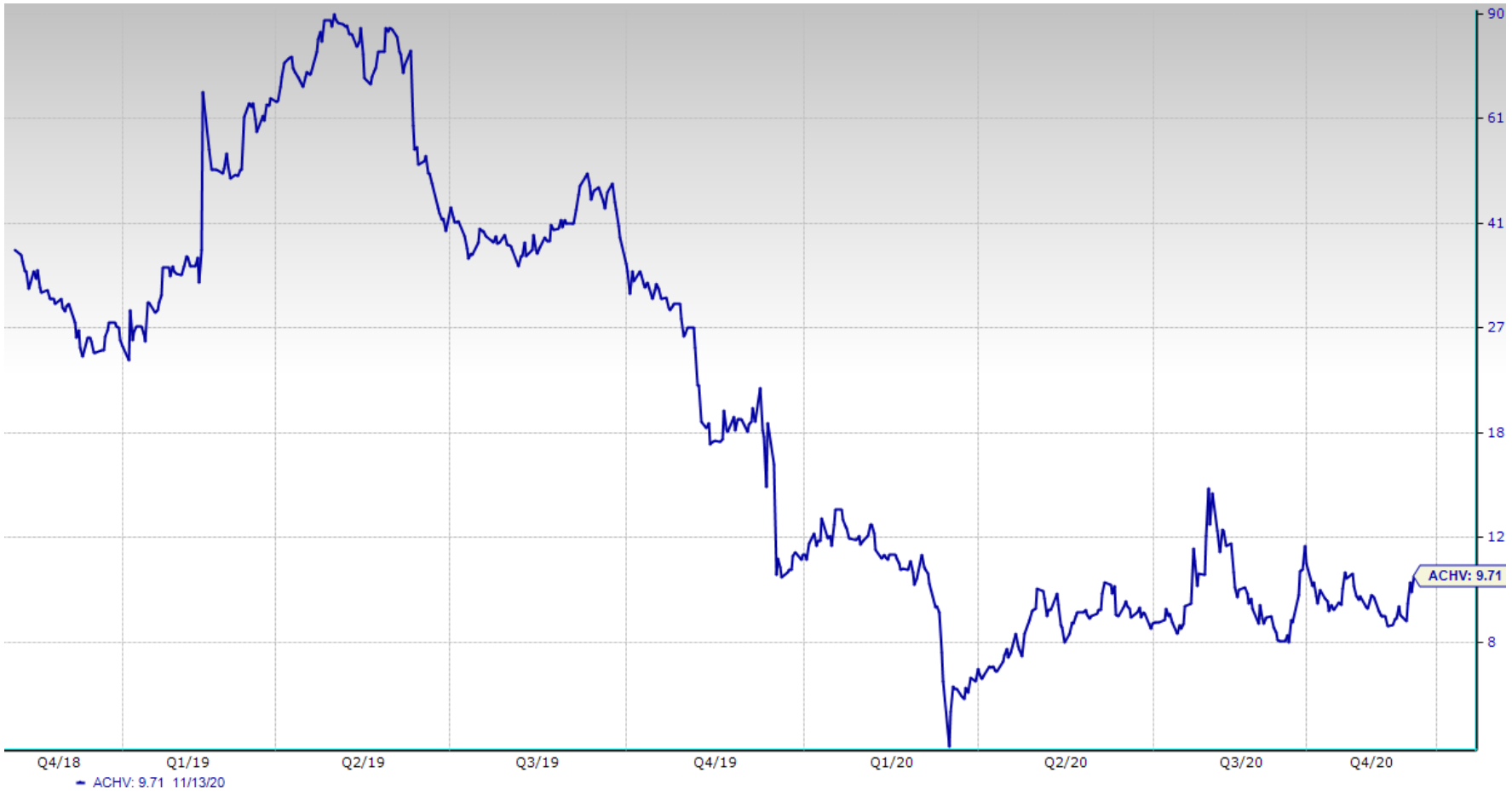
HISTORICAL STOCK PRICE

Achieve Life Sciences, Inc. – Stock Price Chart[6]



[6] Source: Zacks Research System

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