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May 25, 2023

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Achieve Life Sciences, Inc. (ACHV: NASDAQ)

ACHV: ORCA-3 Topline

We employ a DCF model and a 15% discount rate to generate our valuation. Our model applies a 70% 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 only from the United States.

Current Price (5/24/2023)	$6.02
Valuation	**$56.00**

OUTLOOK

Achieve Life Sciences is developing cytisinicline for use as a smoking cessation treatment in the United States and rest of world. Topline results from ORCA-2 were reported in April 2022 and for ORCA-3 in May 2023. Results exceeded expectations on safety & efficacy parameters.

Both Phase III trials compare cytisinicline with placebo combined with counseling. The primary endpoint is abstinence at 6 & 12 weeks for the last 4 weeks of treatment. A Phase II trial in vaping cessation (ORCA-V1) reported topline in April 2023.

Existing cessation products provide limited effectiveness and produce unpleasant side effects including nausea, vivid dreams, insomnia & GI issues. Cytisinicline may fill a void in the prescription & NRT market by reducing nicotine cravings, severity of withdrawal & reward associated with smoking along with fewer side effects & 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. We anticipate a 2025 commercialization of cytisinicline.

SUMMARY DATA

52-Week High	**10.30**
52-Week Low	**2.00**
One-Year Return (%)	**-9.9**
Beta	**1.5**
Average Daily Volume (sh)	**164,216**
Shares Outstanding (mil)	**18.0**
Market Capitalization ($mil)	**108.6**
Short Interest Ratio (days)	**3.2**
Institutional Ownership (%)	**33.1**
Insider Ownership (%)	**8.5**
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 2023 Estimate	**N/A**
P/E using 2024 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)
2022	$0.0 A	$0.0 A	$0.0 A	$0.0 A	$0.0 A
2023	$0.0 A	$0.0 E	$0.0 E	$0.0 E	$0.0 E
2024					$0.0 E
2025					$97.1 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2022	-$0.80 A	-$1.09 A	-$1.35 A	-$0.83 A	-$4.00 A
2023	-$0.50 A	-$0.40 E	-$0.37 E	-$0.32 E	-$1.59 E
2024					-$1.64 E
2025					$2.16 E

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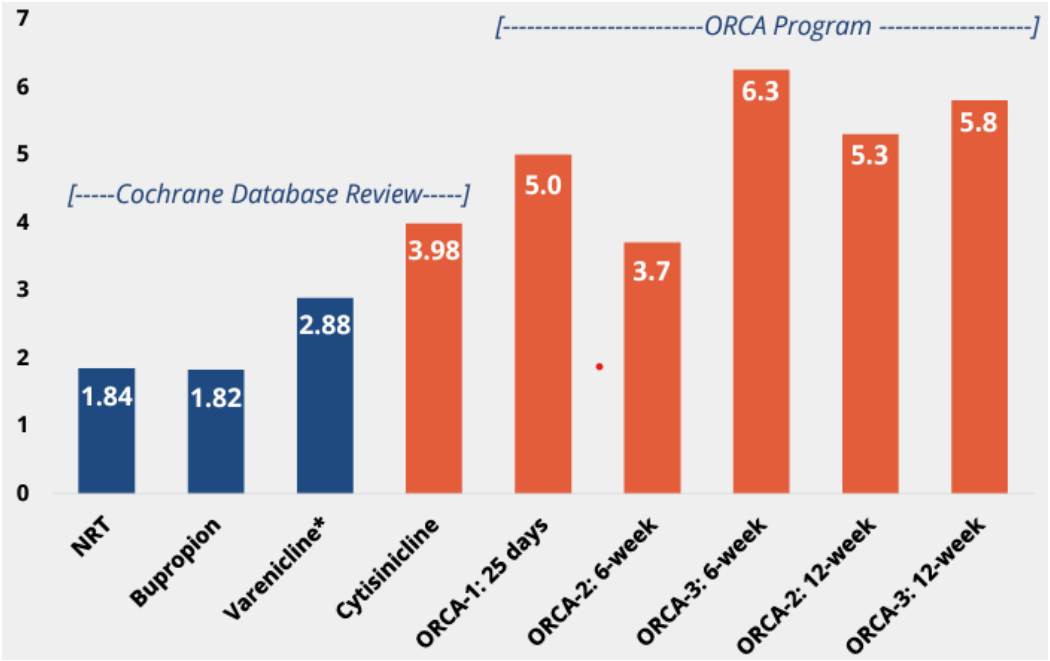
WHAT'S NEW

ORCA-3 Topline Results

Achieve Life Sciences, Inc. (NASDAQ: ACHV) reported topline results from the second Phase III pivotal trial of cytisinicline on May 23, 2023. Results were discussed with analysts and investors in a conference call held that morning. On average, odds ratios were lower than that achieved in ORCA-2, but still well ahead of other alternatives and previous regimens of cytisinicline. The data provided from the ORCA-3 trial are strongly supportive of safety, efficacy and FDA approval. Based on the favorable results, we increase our target price to $56 per share.

Exhibit I – Odds Ratios for Smoking Cessation Alternatives[1]



Achieve reported statistically significant results from the ORCA-3 trial, with a marked improvement in cessation from the six and twelve week dosing regimens both in terms of odds ratio and quit rate. Adverse events were only slightly more elevated for the cytisinicline arms compared with the placebo arms. See below for a summary of topline performance for the ORCA-3 trial:

Exhibit II – ORCA-3 Primary Endpoints[2]

ORCA-3 (n=792)	Abstinence Rate - Last Four Weeks	
Treatment	Six Weeks	Twelve Weeks
Cytisinicline	14.8%	30.3%
Placebo	6.0%	9.4%
Odds Ratio	2.85	4.4
p-value	0.0008	<0.0001

Exhibit III – ORCA-3 Secondary Endpoints[3]

ORCA-3 (n=792)	Abstinence Rate Following Treatment	
Treatment	Six Weeks	Twelve Weeks
Cytisinicline	6.8%	20.5%
Placebo	1.1%	4.2%
Odds Ratio	6.25	5.79
p-value	0.0006	<0.0001

[1] Source: Achieve Life Sciences ORCA-3 Phase III Topline Data accompanying presentation, May 23, 2023
[2] Source: Analyst compilation of data from Achieve Life Sciences ORCA-3 Phase III Topline Data, May 23, 2023
[3] Source: Analyst compilation of data from Achieve Life Sciences ORCA-3 Phase III Topline Data, May 23, 2023

About two-thirds of cytisinicline subjects experienced mild to moderate adverse events, which was only slightly ahead of the placebo arm rate. Primary adverse events recorded were insomnia, abnormal dreams, headaches and nausea. Notably, nausea was generally lower in the cytisinicline arms vs. placebo, which supports patients' use of therapy to conclusion as opposed to stopping early due to discomfort. Achieve's Chief Medical Officer, Dr. Jacobs, provided context regarding the discontinuation rates noting that historical data for varenicline ranged from 35% to 45% with about 12% - 13% due to adverse events. This compares to cytisinicline that has a ~21% discontinuation rate with about 2% - 3% due to adverse events.

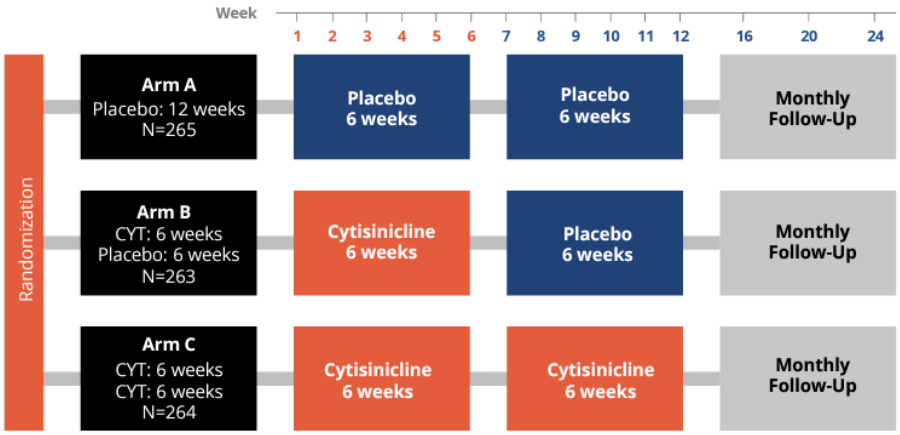
Exhibit IV – ORCA-2 & 3 Most Commonly Reported Adverse Events (>5% Overall)[4]

Adverse Event (AE)	Placebo		6-week CYT		12-week CYT	
	ORCA-2	ORCA-3	ORCA-2	ORCA-3	ORCA-2	ORCA-3
At least 1 TEAE	166 (61.5%)	164 (62.6%)	172 (63.9%)	170 (64.6%)	184 (68.1%)	168 (64.5%)
Insomnia	13 (4.8%)	20 (7.6%)	23 (8.6%)	29 (11.0%)	26 (9.6%)	31 (11.9%)
Abnormal Dreams	8 (3.0%)	15 (5.7%)	22 (8.2%)	24 (9.1%)	21 (7.8%)	20 (7.7%)
Nausea	20 (7.4%)	19 (7.3%)	16 (5.9%)	25 (9.5%)	15 (5.6%)	18 (6.9%)
Headache	22 (8.1%)	16 (6.1%)	18 (6.7%)	20 (7.6%)	21 (7.8%)	22 (8.5%)

ORCA-3 Trial Design

ORCA-3 reported topline results on May 23, 2023. The trial targeted enrollment of 750 subjects across 15 clinical trial sites, randomized into three arms and ultimately enrolled 792 subjects with 265 in the placebo group, 263 in the six week arm and 264 in the twelve week arm. Subjects were administered 3 mg three times per day (TID). As with the first Phase III trial, the primary outcome measure for ORCA-3 is biochemically verified continuous abstinence during the last 4 weeks of treatment in the 6 and 12-week cytisinicline treatment arms compared to placebo. Each treatment arm was compared independently to the placebo arm. Secondary outcome measures will be conducted to assess continued abstinence rates through six months from the start of study treatment.

Exhibit V – ORCA-3 Clinical Trial Design[5]



Multiple Primary Endpoints:
- Biochemically verified smoking cessation during the last 4 weeks of treatment
  - Arm B: Weeks 3-6
  - Arm C: Weeks 9-12

Secondary Endpoint:
- Continuous smoking cessation from end of treatment through 6 months

Statistics:
- >95% power for the 24-week comparisons

Next Steps

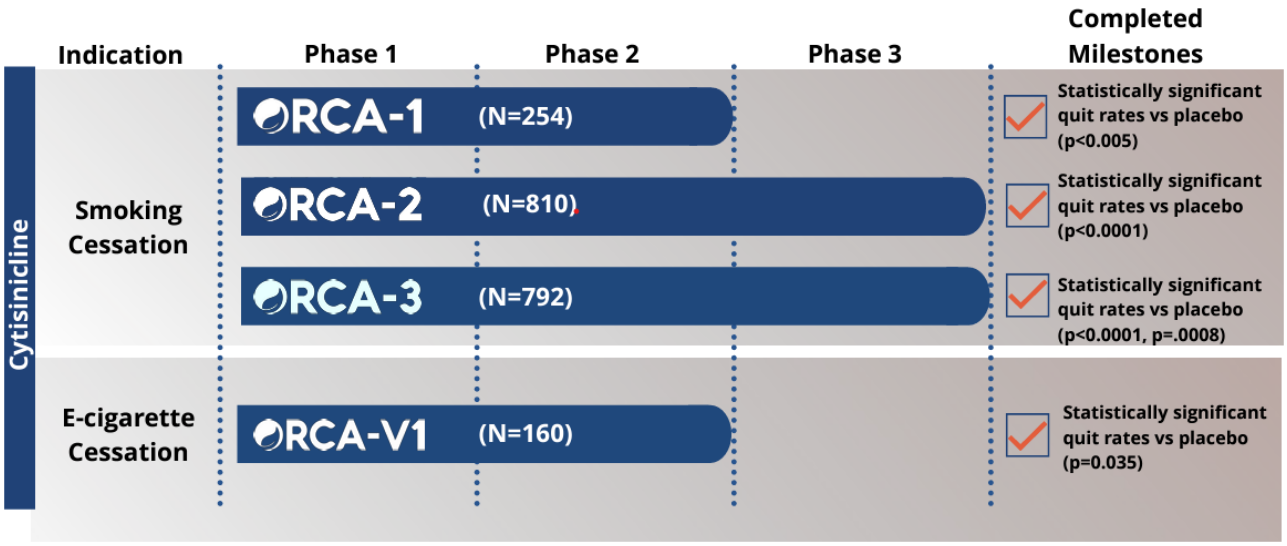
Next steps for the cytisinicline program call for management to schedule a pre-new drug application (NDA) meeting with the FDA. Based on management's estimates, this meeting will be requested in the next weeks and could take up to four months to get on the FDA calendar. Achieve prefers a teleconference to review the agency's desires as opposed to a written communication for enhanced communication in order to present the best application possible. The teleconference is expected to add to what would normally be a shorter turnaround for a pre-NDA meeting.

[4] Source: Achieve Life Sciences ORCA-3 Phase III Topline Data accompanying presentation, May 23, 2023
[5] Source: Achieve Life Sciences ORCA-3 Phase III Topline Data accompanying presentation, May 23, 2023

A clinical study report (CSR) must be compiled and Achieve must complete several ancillary and pharmacokinetic studies that will be ready by the end of the year and submitted along with the ORCA data. Following the scheduling of and participation in the pre-NDA meeting, we expect to see refined estimates for timing of the NDA submission. When the submission is made, Achieve will seek a label for both the six week and twelve week treatment regimens.

Discussions with partners are expected to expand now that the data from ORCA-3 are available. Based on management's comments, we feel as if there are already multiple contenders for the asset, and that more will enter the fray now that the critical pivotal data is available.

Exhibit VI – Cytisinicline Development Program[6]



Valuation

We update our valuation to reflect the positive results from the ORCA-3 trial. We increase our probability of success to 70%. The increase is further supported by the recent report of vaping trial results in the ORCA-V1 trial, which demonstrated favorable odds ratios, quit rates and safety. The change in valuation is attributable to the change in probability of success. As we move closer to submission and further clarity of the path forward for cytisinicline become clear, we will update our revenue estimates, timing and valuation accordingly. Our new target is $56 per share.

Milestones

- Addition of regulatory and Chemistry, Manufacturing and Control (CMC) personnel – 1Q:23
- SRNT Conference – March 2023
- Mock FDA inspections with Sopharma – 2022/2023
- ORCA-V1 results – April 2023
- ORCA-3 results – May 2023
- Completion of cytisinicline supportive studies
    - PK study, renal impairment
    - PK study, steady state concentration of 3mg, 3x per day
    - QT interval prolongation
- Cytisinicline NDA filing – 1H:24

[6] Source: Achieve Life Sciences ORCA-3 Phase III Topline Data accompanying presentation, May 23, 2023

Summary

Achieve Life Sciences has completed both pivotal studies for cytisinicline in combustible cigarettes in its ORCA-2 and ORCA-3 trials. Results have exceeded other smoking cessation therapy success rates and provide a less difficult adverse event profile. There are a few odds and ends that need to be wrapped up including completion of ancillary trials for its cytisinicline product prior to an anticipated new drug application (NDA) next year. As Achieve now has pivotal data in hand, it can offer potential partners a compelling product and we anticipate negotiations with them will step up as the year progresses.

Following the ORCA-3 results, we increase our valuation to $56 per share. Achieve represents an outstanding value with numerous comparative clinical trials run on the cytisinicline, a deep understanding of the safety profile of the drug compared to other products, favorable efficacy results from trials already run and clear boundaries for the commercialization opportunity given the performance of varenicline. The latest data even further support the safety profile of cytisinicline which in some cases is better in the active arm than in the placebo arm. We see even greater opportunity for cytisinicline compared with varenicline given the likelihood of gaining approval to treat nicotine addiction in vaping and higher penetration in markets outside of the United States, especially Asia.

PROJECTED FINANCIALS

Achieve Life Sciences, Inc. - Income Statement

Achieve Life Sciences, Inc.	2022 A	Q1 A	Q2 E	Q3 E	Q4 E	2023 E	2024 E	2025 E
Total Revenues ($MM)	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$97.1**
R&D	$30.1	$5.5	$4.2	$3.8	$3.0	$16.5	$10.0	$8.0
G&A	$10.7	$3.0	$3.0	$3.0	$3.0	$12.0	$22.0	$28.0
Sales Expenses	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$6.0	$8.2
Operating Income	($40.8)	($8.6)	($7.2)	($6.8)	($6.0)	($28.6)	($38.0)	$52.9
Operating Margin								*54.5%*
Interest Income	$0.2	($0.4)	$0.0	$0.0	$0.0	($0.4)	$0.0	$0.0
Total Other Income	($1.7)	($0.0)	$0.0	$0.0	$0.0	($0.0)	$0.0	$0.0
Pre-Tax Income	($42.4)	($9.0)	($7.2)	($6.8)	($6.0)	($29.0)	($38.0)	$52.9
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%*
Net Income	($42.4)	($9.0)	($7.2)	($6.8)	($6.0)	($29.0)	($38.0)	$52.9
Reported EPS	**($4.00)**	**($0.50)**	**($0.40)**	**($0.37)**	**($0.32)**	**($1.59)**	**($1.64)**	**$2.16**
Shares Outstanding	10.593	17.9	18.1	18.3	18.5	18.204	23.2	24.5

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

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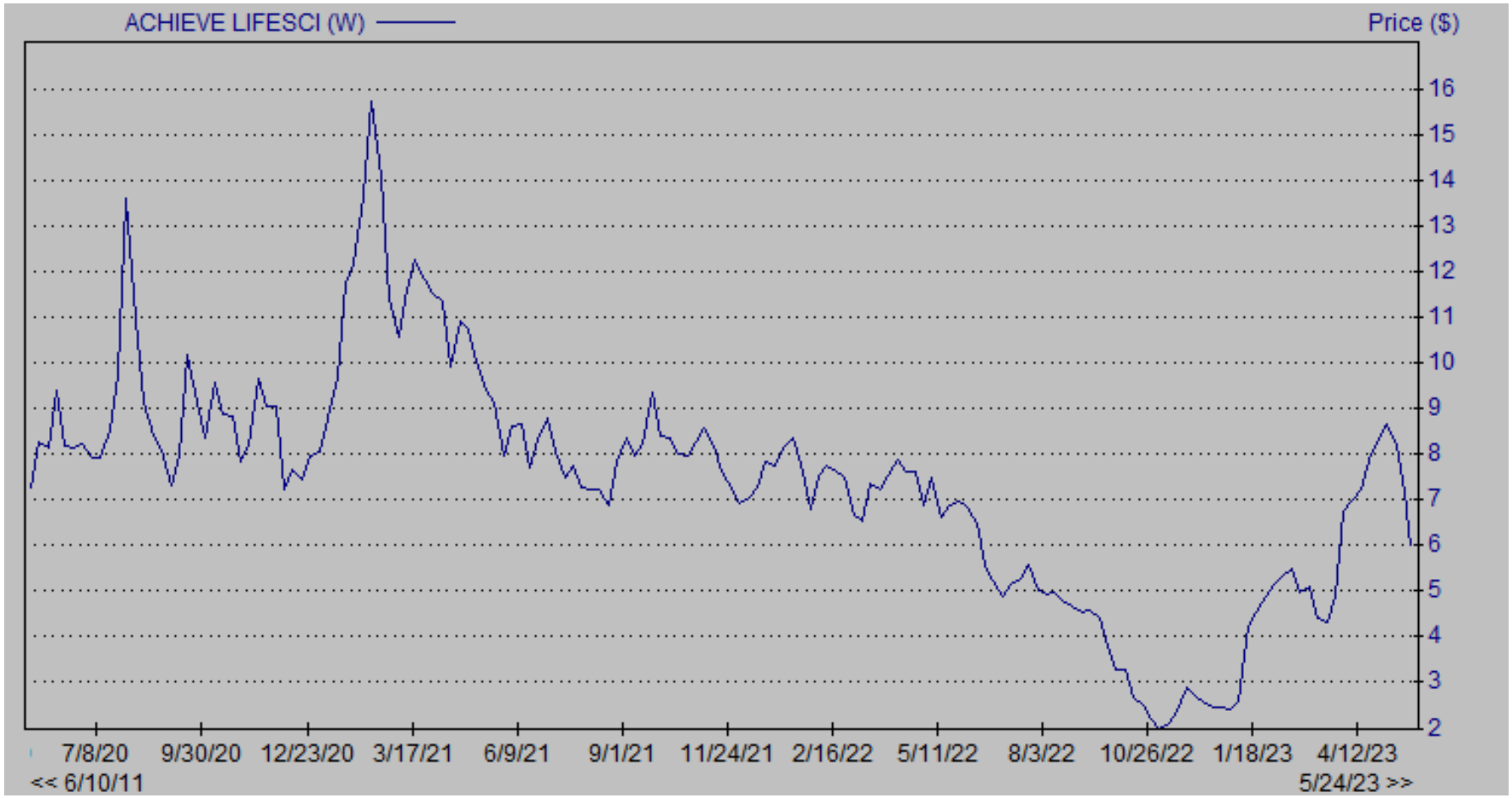
HISTORICAL STOCK PRICE

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



[7] Source: Zacks Research System

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