Achieve Life Sciences: An Excellent Drug Addressing a Large Market will Drive 5x Returns

Achieve Life Sciences (ACHV) went public via a shell company in 2017 to commercialize the smoking cessation drug Cytisinicline. Cytisinicline is derived from a plant-based compound and has a long history of use in Eastern Europe, but had not been tested in the U.S. Achieve's central task is to usher the drug through clinical trials and the FDA approval process. Phase 3 trials are done. The company must complete a long-term safety trial before submitting the New Drug Application (NDA), likely a 1H25 event. I expect the company to be sold to a larger entity with sales and distribution around the same time.

Achieve's life as a publicly traded company has not been smooth. Company travails are clearly evident in the long-term stock chart. Much of the downside volatility over the last few years has been caused by capitalization issues and how they have been handled. Most recently, the FDA made an unexpected request for data in December 2023 injected further uncertainty regarding timing of the NDA submission and created financial uncertainties as well. The FDA requirements and financing issues have recently been resolved.

The combination of these factors has resulted in what is now a ~$150M market capitalization for the company. Therein lies the opportunity.

The clinical trial process has gone extremely well and the drug addresses a large market**. Completed Phase 3 trials show Cytisinicline to increase the odds of quitting 4-6x over a placebo, superior to other treatment options**. A competitive product in generic production currently generates ~$450M in sales annually, despite serious side-effects. A key differentiator of Cytisinicline is that the drug is well tolerated and has an excellent safety profile.

I believe the stock is at an inflection point. Clinical trials have produced excellent results, the path to the NDA filing is clear, the company is financed to completion, and there are ongoing discussions with potential "commercial partners" or prospective buyers, likely Big-pharma.

I believe a buy-out in 2025 is a likely event.

My estimate is that the company could sell for between $20 and $40 per share. **If I am correct, the current uncertainty and low capitalization is a set-up for investors to make 4-9x their investment over the next year.**

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Cytisinicline: Achieve's Smoking Cessation Drug

Cytisinicline is a plant-derived compound that has been used for smoking cessation in Eastern Europe for several decades. Achieve has an agreement with the drug's manufacturer to commercialize the product for certain western markets, of which the U.S. is the largest. As part of the commercialization process, Achieve created a new dosage formulation, for which it retains the intellectual property. Achieve is also responsible for funding the clinical trials.

In 2Q23, the company released excellent results from part two of their Phase III trials. It was supposed to be the last hurdle before submitting the new drug application. However, the FDA request has created uncertainty around the timing of the submission.

The current timeline indicates that the NDA will likely be submitted in IH25. **If approved, Cytisinicline would be the first new smoking cessation drug since Pfizer's Chantix launched in 2006.**

Understanding Chantix and the generic Varenicline is important to frame how important Achieve's drug could become to the medical community and the potential value to Achieve shareholders.

Smoking remains a significant health problem in the U.S. The CDC estimates that there were approximately 28.3 million adult smokers in the country in 2021. There are limited medical options for helping smokers quit. Common aids include nicotine replacement therapy, including gum and patches; Wellbutrin, an anti-depressant is also used. Both have low efficacy.

Pfizer's Chantix, released almost two decades ago, provided the most hope for smokers. It was effective, but the drug was plagued with significant side-effects, which included:

- Headache and nausea, severe enough to cause a significant number of patients to discontinue taking the drug before finishing the course of treatment
- Vivid dreams and insomnia
- Suicidality was such that the drug was issued a black box warning by the FDA. Pfizer eventually succeeded in having the warning removed in 2016.

It is estimated that approximately 30% of all users of Chantix (Varenicline) experienced nausea and 12% of trial participants quit prior to finishing the course of treatment. I suspect high incidence of side-effects may also deter physicians from prescribing the drug more widely, both initially as Chantix as well as the current generic versions.

In 2021, Pfizer withdrew Chantix from the market due to contamination issues. Thus far, the drug has not been reintroduced.

Pfizer's withdrawal paved the way for Endo Pharmaceutical's generic version, which was launched in 2021. As of 4Q23, there were three generic versions available. In Lupin Ltd's December 2023 announcement of FDA approval of its generic version, the company stated **that current annual sales for the drug are $430M annually.**

The Chantix/Varenicline data and experiences are highly suggestive of what may be expected for Cytisinicline. There is significant market demand for smoking cessation products, as evidenced by both Chantix's $1B in sales in 2019 and current generic sales ramp. Generic sales are particularly impressive considering the well-known problems with the drug.

The market for smoking cessation products remains robust, despite the lack of a good pharmaceutical treatment. Using generic sales data, I estimate that the current market represents approximately 1 million

courses of treatment prescribed. **It is conceivable that a more efficacious drug with a superior safety profile could increase the size of the prescription market.**

Cytisinicline: A Better Drug

Cytisinicline could breathe new life into efforts to medically reduce smoking. Clinical trials indicate that Cytisinicline is significantly better than Chantix. The drugs clinical trials are base-lined against a placebo. However, prescribing physicians will likely compare it to Varenicline. Additionally, it is a useful benchmark to consider when estimating the market size.

In the exhibit below, Cytisinicline's adverse reaction profile is compared with Varenicline's.

Comparative Safety Profiles

Comparative Analysis of Safety Events

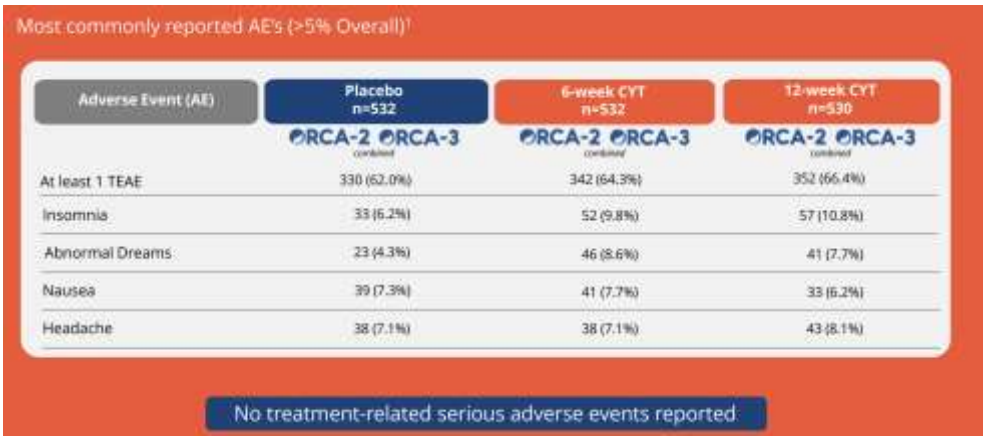
	Cytisinicline[1]	Varenicline (Chantix®)[2]
Treatment Time	**6-12 weeks**	**12 weeks**
Adverse Events		
Nausea	7.0%	27.8%
Insomnia	10.3%	12.7%
Abnormal Dreams	8.2%	12.5%
Headache	7.6%	12.2%

Source: Achieve December 2023 investor presentation.

Cytisinicline exhibits a significantly improved safety profile, particularly relative to nausea, the most problematic adverse event.

The exhibit below shows the Cytisinicline's safety profile from its trials versus a placebo. Note that trial although adverse reactions to the placebo are less than with Cytisinicline, they are not zero. The negative reactions are also symptoms of nicotine withdrawal.

Comparative Safety Profiles



Source: Achieve December 2023 investor presentation.

In addition to being well-tolerated by patients, Cytisinicline is effective. The exhibit below shows the odds ratios of quitting for various smoking cessation treatments.

Comparative Odds of Quitting

Source: Achieve December 2023 investor presentation.

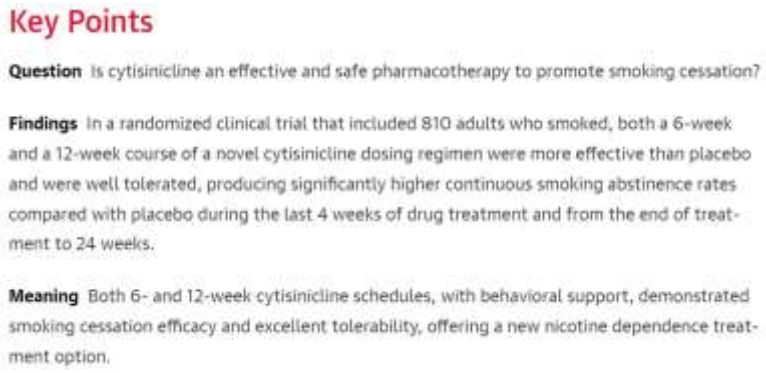
Achieve's trial results are shown under the ORCA program[1]. The results are clearly superior to the placebo as well as other therapies.

Achieve released the preliminary results for the second part of its Phase III trial results on May 23, 2023. The study indicated that cessation rates during weeks 9 through 12 were 30.3% for Cytisinicline compared to 9.4% for placebo. **The use of Cytisinicline generated a 4.4x increase in odds for continuing smoking abstinence at 6-months.**

[1] Ongoing Research of Cytisinicline for Addition. https://orcaprogram.com/orca-3/.

Following the release of the results, the Journal of American Medical Association or JAMA published an editorial on Achieve's results. The prestigious journal was highly supportive and encouraged by the results. The key points are shown below.

JAMA Editorial



Key Points

Question Is cytisinicline an effective and safe pharmacotherapy to promote smoking cessation?

Findings In a randomized clinical trial that included 810 adults who smoked, both a 6-week and a 12-week course of a novel cytisinicline dosing regimen were more effective than placebo and were well tolerated, producing significantly higher continuous smoking abstinence rates compared with placebo during the last 4 weeks of drug treatment and from the end of treatment to 24 weeks.

Meaning Both 6- and 12-week cytisinicline schedules, with behavioral support, demonstrated smoking cessation efficacy and excellent tolerability, offering a new nicotine dependence treatment option.

Source: JAMA.

I view the positive tone of the JAMA article as an indication of the medical community's desire for new treatment options and the excitement an effective new drug could generate.

The editorial notes that 50% of adult smokers in the U.S. have attempted to quit at least once each year. Around 7% of those were smoke-free after 6-months. A recent survey cited in JAMA concluded noted that approximately 28.8% of those attempting to quit used some form of nicotine replacement therapy, and only 10.8% used some form of pharmacological therapy, which would include varenicline. That in itself is interesting, given that the exhibit above shows varenicline to be significantly more effective than replacement therapies. I believe the low usage of pharmacological therapies, at least in part, speaks to the poor patient tolerance of varenicline. **If this is true, I would expect the approval of a new drug that is well-tolerated and more effective to result in more prescriptions than the market currently generates.**

The Market Opportunity and Company Value

The JAMA editorial data suggests that approximately 14M adult smokers attempt to quit every year, with about 1.4M of those taking prescribed medications – varenicline or bupropion. This roughly corresponds to varenicline data of $430M market at an average cost of ~$475 per course of treatment, which implies ~900K courses of treatment prescribed. I use this base data and assumptions regarding drug price and market share to estimate Achieve's revenue opportunity. I then apply what I think is an appropriate multiple of sales to estimate the potential return to stockholders.

When estimating investor returns, I do so in the context of a company sale. The smoking cessation market is well-understood. As a result, I believe the purchase decision is basically driven by discounted cash flow, price, as opposed to assessing a new market. In my opinion, Achieve does not make sense as a stand-alone entity post-drug approval. Achieve does not have either the sales infrastructure or the capital to build it. Cytisinicline would make an excellent addition to the portfolio of a big-pharma company, one with a significant marketing budget and distribution reach.

Market Size and Value per Share

	Total Courses Prescribed	
	1,000,000	**1,500,000**
Market	**Achieve Prescriptions**	
Share	**Low**	**High**
35%	350,000	525,000
50%	500,000	750,000
60%	600,000	900,000

	Price/treatment course	
	Low	**High**
Revenue at share $M	650	900
35%	228	473
50%	325	675
60%	390	810

Multiple of	**Enterprise Value**	
Sales	**Low**	**High**
2.0x	428	888
3.0x	**642**	**1,332**
4.0x	855	1,777
5.0x	1,069	2,221

	Low	**High**
EV $M	*642*	*1,332*
Debt $M	*16.50*	*16.50*
Equity Value $M	***625***	***1,316***

	Per Share Value	
Shares (M)	**Low**	**High**
35	***$18.33***	***$38.07***
32	***$20.05***	***$41.64***
30	***$21.39***	***$44.42***

Source: Company filings and estimates.

I assume that the courses of treatment prescribed will be between 1M and 1.5M and Achieve's market share will range from 35-60%.

Varenicline currently sells for ~$475 for a treatment course. I assume as a new, patented drug, Cytisinicline will sell at a premium. I assume a 35-90% premium or $650 to $900 for a treatment course.

The table to the left shows total revenue associated with the price ranges at the different levels of market share. At 35% market share, revenue is $230-$470M.

To obtain the undiscounted enterprise value, I apply a multiple of sales from 2-5x, as shown to the left. For the purpose of valuing the stock, I assume a multiple of 3x sales for a total enterprise value of $642-$1.3B.

Subtracting the value of the debt from the gross enterprise value leaves the value of the equity.

I estimate that there are currently 34M shares on a fully diluted basis if warrants and debt outstanding are converted. **The stock value is ~$20-40 per share or a return of 4.4-9x the current price of $4.66.**

What's Ailing the Stock?

If Cytisinicline is the first new drug in 20-years and could be the best pharmacological treatment for a large market, why the poorly performing stock and low valuation? The answer is a combination of factors, some of which look like management errors, others unforeseen events. The chart and exhibit below puts the current stock price in context.

Looking at a longer-term chart shows that there has been shortage of **financial drama since Achieve merged with Oncogenex in 2017** after a failed trial. However, for our purposes, it is the near-term events that both explain the current valuation and define what I think is an exceptional short to medium-term opportunity.

ACHV Stock Chart with Notation

Source: Yahoo Finance and Dalrymple Finance.

Achieve Event Timeline

Chart Number	Recent Events Date	Price	Event	Comment
1	3/10/2022	$6.73	4Q22 conference call	$43.1M of cash, sufficient to "provide a runway into 2023"
2	4/27/2022	$7.43	First Phase 3 trial results released	Reports 6-8x increased odds of quitting using cytisinicline
3	5/12/2022	$6.39	1Q22 conference call	Discuss trial results. $36.4M cash "sufficient to provide a runway into 2023".
4	8/11/2022	$5.20	2Q22 conference call	$29.4M of cash - "we believe we have sufficient cash to bring us into 2023
5	11/14/2022	$2.20	3Q22 conference call	$18.2M of cash - "expect the cash burn to remain elevated here in the fourth quarter"
6	11/15/2022	$2.32	Private placement	$18.9M in cash raised in a stock plus 1/2 warrant coverage deal. " Sufficient to last until the end of 2023"
7	3/10/2023	$4.44	Silicon Valley Bank	SVB was Achieve's bank and the stress and eventual failure pressured the stock in early 2023
8	3/30/2023	$6.32	New board members	
9	5/23/2023	$6.21	Second confirmatory Phase 3 Results	6x increase in odds of of abstinence after 6-months
10	5/25/2023	$5.65	$16.5M registered direct offering	2Q23 call - "cash runway well into 2024"
11	12/12/2023	$3.15	8-K on letter from FDA	Vague, negative surprise of FDA asking for additional safety data
12	2/29/2024	$4.40	News on FDA resulution and financing	Dilution from financing, but clear path to NDA submission

Source; Company documents, Yahoo Finance and Dalrymple Finance.

Going through the notations on the chart essentially shows that what have been important and impressive scientific milestones have been periodically interrupted by serious errors in raising capital. **The current valuation reflects the difficulty management has had implementing an effective long-term funding strategy, which has provided ample opportunities to trade around financings and a skeptical investor base.**

While company capitalization has been difficult, the scientific side has done well. Execution on the drug's development and clinical trials have produced excellent results.

Much of the stock's movements, though not all, on the chart can be explained by cash balances and expected burn. As of March 2022, Achieve had enough cash to "provide a runway into 2023". In other words, the company would need funding to go beyond the end of the year.

At the time of the call, the company knew that clinical trial results would be released within the next month or two. I would guess that management thought the clinical results would be good, and the stock would naturally go up from the ~$6.50-7.00 level it was at just pre-release. It didn't. The stock went down.

Perhaps management was waiting for the stock to rebound, but as the year went on cash balances shrunk and running out of cash became a real risk. It is no surprise the stock crumbled.

In November 2022, around the time of the 3Q22 call, the stock had declined ~-72% from a peak of around $8 in April to the low $2s. Two hedge funds came to the rescue and raised ~$19M for the company.

After a significant recovery in early 2023, the Silicon Valley Bank debacle hit the company. SVB was both its lender and deposit holder. Around the same time, the company announced several new board members. Board level changes were the result of the new investors flexing their ownership muscle. It was a positive development for shareholders, though the market impact may have been muted due to the SVB problems. **New board members included investment veterans, and importantly, a former healthcare investment banker. I view the addition of in-house banking expertise as a strong signal as to intent to sell the company.**

When SVB issues dissipated and implications of new board members digested, the stock ran to ~$10 per share, only to collapse ~40% just prior to the announcement of excellent results for clinical trials. **Trial results were followed by a stock offering just two days later.**

The stock's collapse from $10 on May 11th to $5.65 on May 25th, the day the registered direct offering was done suggests that some investors knew the company was going to raise cash and exploited the situation.

The stock did not recover from that decline until November 2023 when it moved from a low of $3.75 to ~$6.00. Then details from the FDA letter knocked the stock back down to almost $3. This 8-K filing details the FDA letter, which, seemingly out of nowhere, said they would like to see safety data for those relapse and use the drug multiple times. However, they did not specify how that data needed to be gathered before submitting the NDA or could be done concurrently. **Those issues have been resolved and the company has reached an agreement with the FDA on how the data will be gathered and studies.**

The FDA snag has essentially caused a 1-year delay, putting of the NDA filing from 1H24 to 1H25. The recent financing, while dilutive, brought in some new investors, including Franklin Templeton Investments. I view the strong commitment from Frankin, a long-term investor, as a good addition to the shareholder base. **Further, Sopharma, the developer of the drug and Achieve's manufacturing partner put money in as well. I likewise view that as a strong vote of confidence.**

One of the financing issues raised by the FDA-induced delay, is the Silicon Valley Bank loan. Achieve was given an extension provided the NDA is filed by the end of 2Q24. That will not happen. Theoretically, Silicon Valley may make the loan due at the end of 2024. However, there is a reasonable chance that they extend it again given the recent funding. If they don't, I believe that Achieve can repay the $16.5M loan, making it a non-event.

Timeline and Investment Set-Up

Achieve's milestone timeline includes completion of phase 3 trials, and most recently the resolution of FDA questions and resulting finance needs. Dialog with potential commercial partners have been running in parallel to these events. On the company's 3Q23 conference call, CEO John Bencich said: "our continued belief is that this asset belongs in the hands of a single global partner". I interpret that as a sale of the Achieve to a Big-pharma company.

The stock is in the set-up phase. It has recovered much of the value lost after the FDA comment revelation, suggesting investors have become more comfortable with near-term events.

The next milestone should be an announcement containing details on new study. I believe the company will recruit from the pool of study participants from the previous studies. Following that, investors need to track progress towards preparing the NDA and timing of the filing.

From this point it is a waiting game. As milestones are passed, I expect the value of the company to increase as reasons for discounting are eliminated.

While there is significant upside to the stock, it is admittedly likely a binary outcome. Any glitch will likely be met with a swift decline in the stock, and if the company is not sold, it may well be a zero. That said, the trial results for the drug are very compelling, and the smoking cessation market is very large. As such, I expect the company to attract a Big-pharma buyer.

I believe there is a good probability that the company is sold for $25 or more per share over the next year, creating the opportunity to make 5x or more on one's investment.

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