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Achieve Life Sciences, Inc. (ACHV - NASDAQ)

Target Up On Longer Patent Life

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 (6/25/2021)	$8.35
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 (%)	**0.00**
Beta	**1.28**
Average Daily Volume (sh)	**170,492**
Shares Outstanding (mil)	**9.45**
Market Capitalization ($mil)	**78.9**
Short Interest Ratio (days)	**1.34**
Institutional Ownership (%)	**17.1**
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 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

Achieve Life Sciences, Inc. (NASDAQ: ACHV) has experienced a considerable of activity since our first quarter update published several weeks ago. We saw a $23 million capital raise, the allowance of new patents and contaminant troubles related to Pfizer's (NYSE: PFE) smoking cessation product, Chantix.

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. Oppenheimer acted as the sole book-running manager in the offering and Lake Street Capital Markets acted as the lead manager.

This event was followed by positive news regarding the company's patent portfolio. 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.

And 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[1] 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 stopped 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.

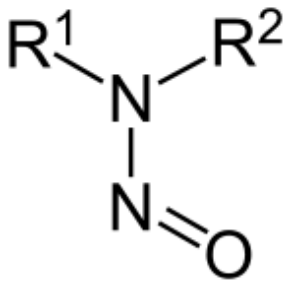
The source of the nitrosamines is likely from the reagents and solvents used in the drug manufacturing process. It is not clear from our vantage point if Achieve's manufacturing process completely sidesteps this issue given the natural source of cytisinicline from the Golden Chain tree; however, Achieve 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.

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 [2].

Exhibit I - The Chemical Structure of Nitrosamines[3]



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.

[1] See page 6 of document for acceptable nitrosamine impurity levels.
[2] https://en.wikipedia.org/wiki/Nitrosamine
[3] https://en.wikipedia.org/wiki/Nitrosamine

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.[4] Later, it was found that about 90% of the 300 nitrosamines tested were carcinogenic in a wide range of animals including humans.[5,6] 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.[7]

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)

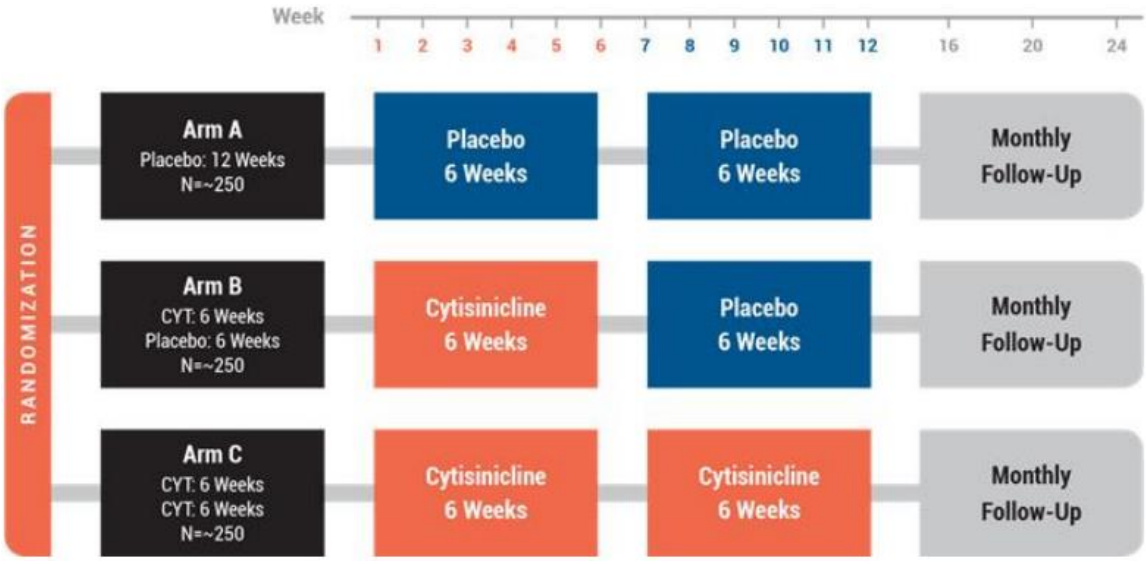
A common way ordinary consumers are exposed to nitrosamines is through tobacco products.[8] Ironically, the cure, at least in Pfizer's case, appears to present the same problems as the smoking addiction it serves to address.

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 should enroll the targeted 750 subjects by mid-year. Two new sites were added in Atlanta, Georgia and Evansville, Indiana in the first part of the year, bringing the total to 17. There will be a six-month follow up period after the measurement at week 12, which should be complete by the end of 2022. 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[9]



[4] Barnes JM, Magee PN (1954) Some toxic properties of dimethylnitrosamine Brit. J. Ind. Med. 11: 167-174
[5] https://en.wikipedia.org/wiki/Nitrosamine#cite_note-nitrocancer-8
[6] https://doi.org/10.1016/0015-6264(71)90306-3
[7] https://www.fda.gov/media/147331/download
[8] 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.
[9] Source: Achieve Life Sciences S-1 Filed November 6, 2019.

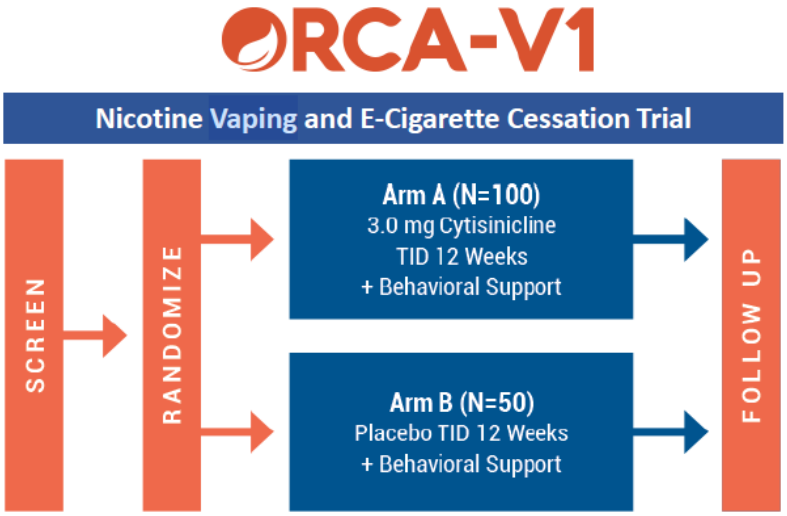
ORCA-1 Publication

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 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.[10] 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 continues to explore funding opportunities for Phase II ORCA-V1, and expects to share additional details on its application status later this year.

Exhibit III – Anticipated Vaping Trial Structure[11]



Valuation

We make several adjustments to our model to reflect recent events related to the capital raise, progress in the Phase III study, patent protection and anticipated penetration rates. Favorable impacts from adjustments to the probability of success and extended patent protection were slightly offset by a higher share count. We increased our anticipated success rate to 40% from 30% to reflect the progress made so far in the first of two Phase III studies. Our model also reflects the extended patent protection stemming from the recently allowed dosing and administration patents related to the 3.0 mg dose administered three times daily. Combined with the control over the supply chain, we see high barriers to entry from a possible competitor and extend our forecast of full penetration until 2040 versus the five year exclusivity previously forecast. As a reminder, we identify two markets in the United States: the broad primary care market, which we anticipate will involve commercialization by a partner and a specialty-focused market that would include smoking cessation centers, pulmonologists and oncologists to be commer-

[10] Cotinine is a metabolite of nicotine, and cotinine urine or blood testing is considered highly accurate for assessing nicotine use, including vaping.
[11] Source: Achieve Life Sciences October 2020 Corporate Presentation

cialized by Achieve. We anticipate first sales in 2024 and a four year ramp to peak sales by 2028 which endure until 2040. Peak sales are represented by 3.4% penetration for each market (6.8% combined) into the addressable market of approximately 26 million. This yields approximately 1.8 million courses of therapy sold per year. We see this level of penetration into each of the primary care and specialty markets persisting until 2040 which coincides with the expiration of the recently allowed patents.

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

Achieve and the smoking cessation space have remained in the news in the weeks following our first quarter update. 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,[12] and generic competition is expected to mount within a year or two. 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. Based on the changes discussed in the valuation section, we increase our target price to $58.00 per share.

[12] Pfizer FY:20 10-K

PROJECTED FINANCIALS

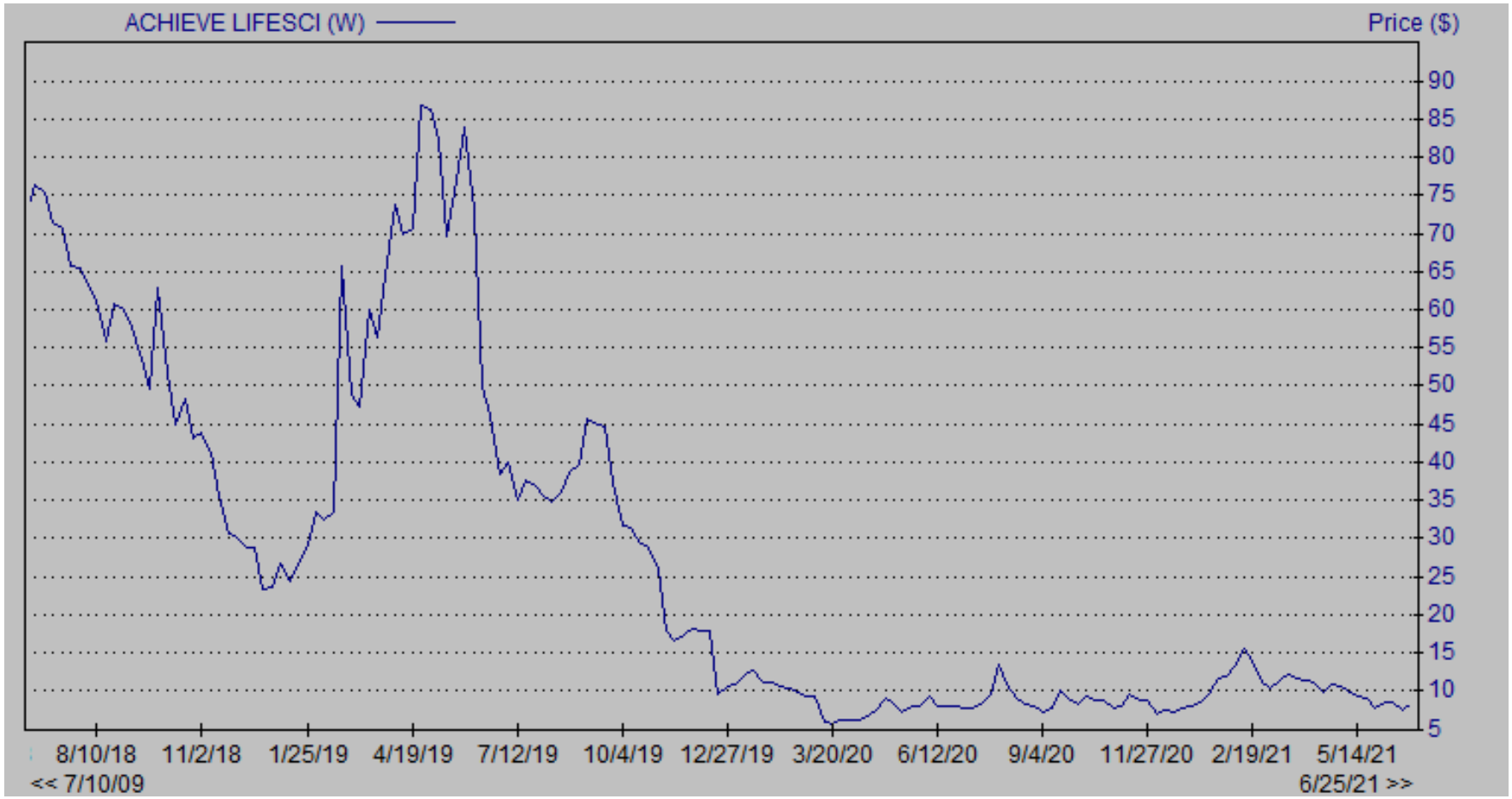
Achieve Life Sciences, Inc. - Income Statement

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[13]



[13] Source: Zacks Research System

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