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NASDAQ:ACHV

Corporate Presentation
April 2021

Forward Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements regarding the timing of planned clinical development activities of cytisinicline; the projected path toward potential regulatory approval; the safety, efficacy and commercial potential of cytisinicline; the potential market for cytisinicline; the benefits of cytisinicline relative to competitors; the anticipated benefits of cytisinicline; plans, objectives, expectations and intentions with respect to future operations. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. Achieve Life Sciences, Inc. (“we,” “us,” “our,” or “the Company”) may not actually achieve its plans or product development goals in a timely manner, if at all, or otherwise carry out the intentions or meet the expectations or projections disclosed in these forward-looking statements. These statements are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described in the forward-looking statements, including, among others, general business and economic conditions, including risk related to the impact on our business of the COVID-19 pandemic or similar public health crisis; the need for and ability to obtain additional financing; the risk that cytisinicline may not demonstrate the hypothesized or expected benefits; the risk that cytisinicline will not receive regulatory approval or be successfully commercialized; the risk that new developments in the smoking cessation landscape require changes in business strategy or clinical development plans; the risk that the Company's intellectual property may not be adequately protected; other risks associated with the process of developing, obtaining regulatory approval for and commercializing drug candidates that are safe and effective for use as human therapeutics; and the other factors described in the risk factors set forth in the Company's filings with the Securities and Exchange Commission from time to time, including its Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q. The Company undertakes no obligation to update the forward-looking statements contained herein or to reflect events or circumstances occurring after the date hereof, other than as may be required by applicable law.

Cytisinicline: A Potential New Treatment for Millions of Smokers

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Exclusively focused on the development and commercialization of cytisinicline for smoking cessation & nicotine addiction

Robust Historical Data

- More than 10,000 participants in cytisinicline clinical trials to date
- Completed 3 investigator-led Phase 3 clinical trials in over 2,700 patients
- Over 20 years of in-market experience in over 20 million patients under brand name TABEX®
- Over 15 million cases in European safety database

Strong Execution

- NIH partnership to complete IND enabling studies
- Completed Phase 1/2 repeat-dose PK/PD study
- Phase 2b ORCA-1 trial completed in Q2 2019 showing statistically significant quit rates (N=254)
- Pivotal Phase 3 ORCA-2 trial launched in Q4'20
- NDA plans already reviewed with FDA

sopharma

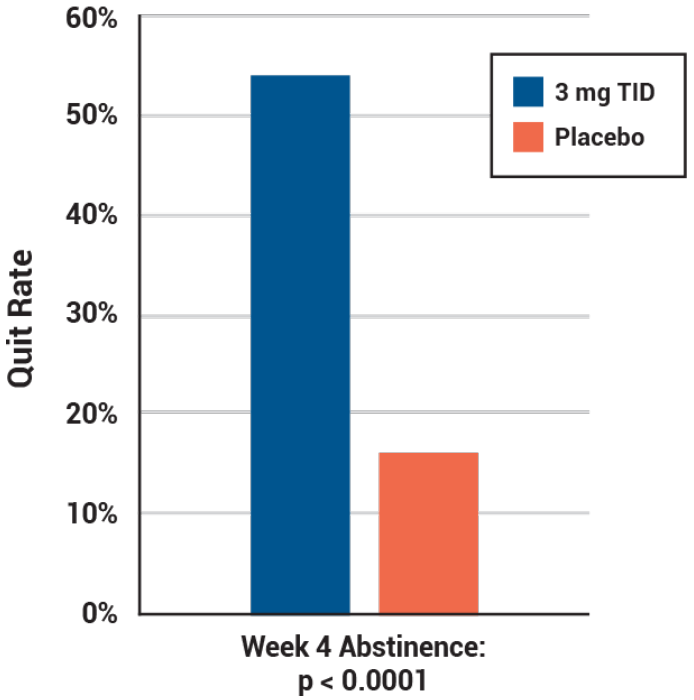
NIH National Institutes of Health

* *Achieve acquired the global rights to cytisinicline from Sopharma AD* excluding certain countries in Central and Eastern Europe, Scandinavia, North Africa, the Middle East and Central Asia, as well as Vietnam

Cytisinicline – Differentiated With Strong Value Proposition

Well-differentiated Product Profile	▪ Single & short course of treatment ▪ Dual-acting, highly selective MOA – improved tolerability ▪ Naturally-derived treatment
Strong, Extensive Foundation of Clinical Evidence	▪ Favorable safety & efficacy from 3 prior Phase 3 trials in >2,700 patients ▪ More than 20M patients treated to date ▪ ORCA-1 study reinforces historical efficacy and safety data
Significant Market & Growth Potential	▪ 1.1B smokers worldwide[1] – more than 34M in U.S.[2] ▪ Smoking cessation market ~ $13 billion and growing[3] ▪ Most prescribed Rx (CHANTIX® - varenicline) sales of ~$919M in 2020[4] ▪ New treatment options required – nothing new in > 10 years
Addresses Global Public Health Epidemic	▪ Smoking and tobacco use is the leading cause of preventable death, responsible for ~8M lives lost annually worldwide[1] ▪ Nearly 30% of all cancer deaths in the U.S. are attributable to cigarette smoking[5]

Quit Rates for 3 mg TID vs Placebo



1. World Health Organization (WHO). WHO Report on the Global Tobacco Epidemic, 2019
2. Centers for Disease Control and Prevention (CDC). Tobacco Product Use Among Adults – United States, 2017
3. Coherent Market Insights, in its March 2017 report "Smoking Cessation and Nicotine De-addiction Products Market"
4. PFE Q4 & 2020 YE Results
5. American Cancer Society November 2015

®Registered trademark of Pfizer Inc.

High Unmet Need for New Treatments

Treatment options are limited with nothing new in over a decade

- Chantix (varenicline) and ZYBAN® (bupropion hydrochloride)
  - Both are oral drugs given on average for 12 weeks
  - Safety has been a concern with both treatments including historical black box warnings
- Nicotine replacement less effective and creates costly, substitute addiction

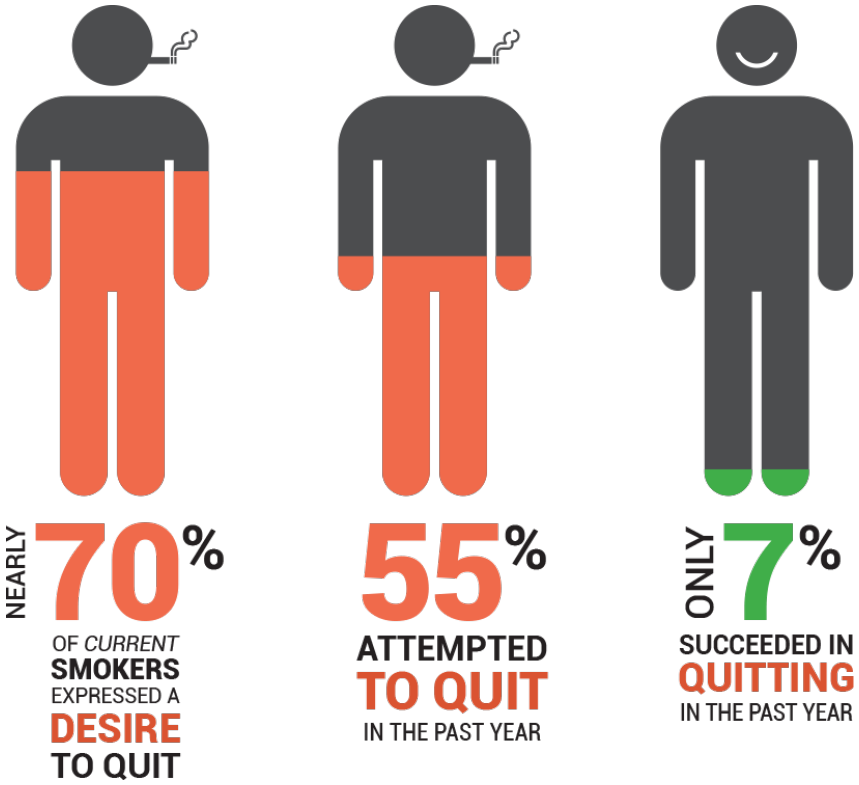
Quitting is Hard! Multiple attempts and treatments are typical

- 68% of current smokers have expressed a desire to quit, 55% attempted to quit in the past year but only ~7% succeeded[1]
- ~4 out of 5 patients relapse six months post initiation of treatment with Chantix[2]
- Estimated 8–11 attempts before quitting permanently[1]

Cigarette smoking rates have not declined in 3 years

- Smokers in the U.S. has remained flat at ~34M since 2017[1]

According to the Centers for Disease Control & Prevention:

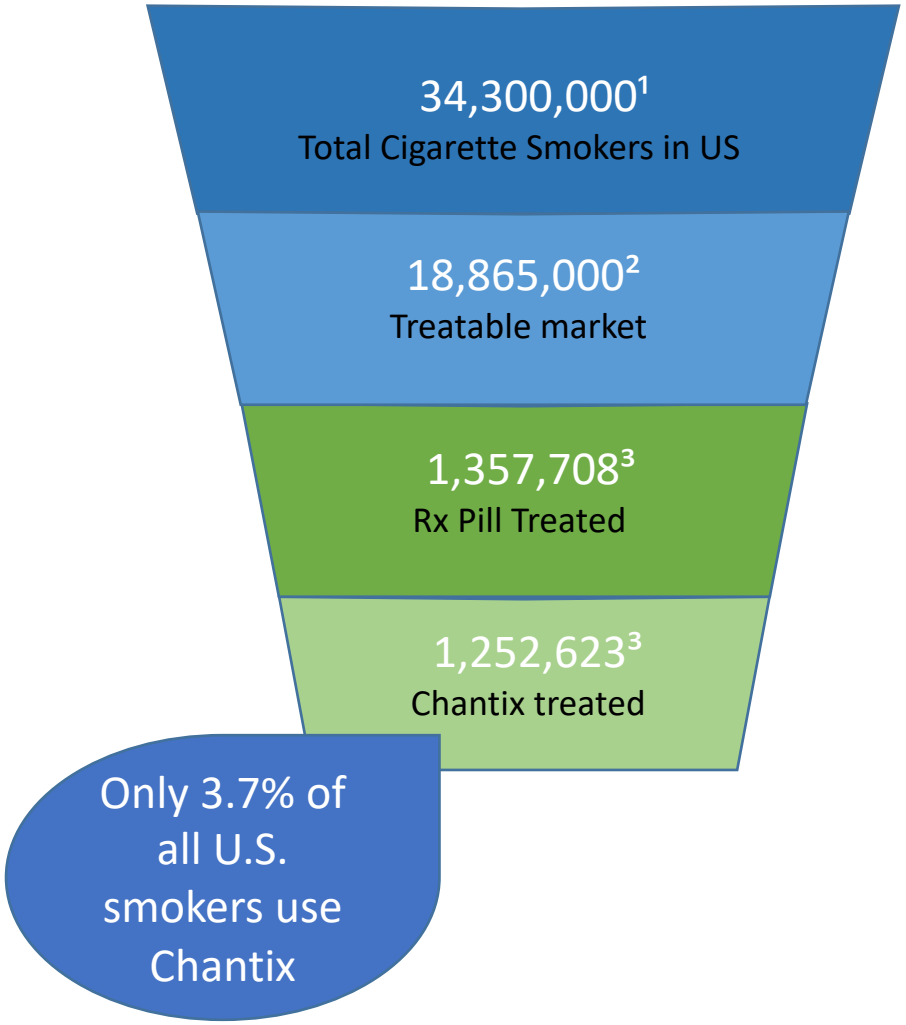


®Registered trademark Glaxo Group

[1]Centers for Disease Control & Prevention, Quitting Smoking Among Adults – United States, 2000-2015

[2] EAGLES: Anthenelli et al; Lancet; 2507-20, June 18, 2016

Significant Opportunity to Expand Smoking Cessation Treatment Utilization with Cytisinicline



Why so low market penetration of current treatment options?

- **Favorable reimbursement for all smoking cessation medications**
  - ACA mandates coverage for smoking cessation medications including multiple quit attempts and counseling services[4]
  - Most patients (~80%) pay $0 for their Chantix or bupropion prescription[3]
- **#1 reason smokers report not using Chantix or Zyban are concerns about side effects[5]**
  - 76% of Chantix patients do not complete 3-month course of treatment[3]
  - 61% of patients surveyed who do not complete full prescription of Zyban or Chantix stated they stopped due to side effects[5]
- **69% of Rx patients indicated they would try a new prescription smoking cessation treatment[5]**

1. Centers for Disease Control and Prevention. Current Cigarette Smoking Among Adults—United States, 2017. Morbidity and Mortality Weekly Report 2018;67(44):1225-32 [accessed 2019 Jan 30].
2. Centers for Disease Control and Prevention. Quitting Smoking Among Adults—United States, 2000-2015. Morbidity and Mortality Weekly Reports January 6, 2017 / Vol. 65 / No. 52
3. IQVIA Prescription Claims Database; 072018-062019, 4. ACA CMS Website, 5. IQVIA Patient Survey, 2019

Proven Leadership Team

Achieve co-founders have a proven track record of value creation for shareholders.

Brabant Pharma Mr. Stewart: CEO Dr. Clarke: CSO	→	***Transaction Value*** ***SOLD $130M***	→	ZOGENIX NASDAQ:ZGNX $1.3B market cap *Fintepla: FDA Approved treatment for Dravet syndrome seizures*
Huxley Pharmaceuticals Mr. Stewart: CEO Dr. Clarke: CSO	→	***SOLD $58M***	→	BIOMARIN® NASDAQ:BMRN $15B market cap *Firdapse: Only FDA Approved treatment for Lambert-Eaton Myasthenic Syndrome*
Amarin Corporation Mr. Stewart: Co-Founder & CEO Dr. Clarke: VP of Clinical Research & Regulatory Affairs	→	***Company Founded***	→	Amarin Corporation NASDAQ:AMRN $2.8B market cap *Vascepa: Only FDA Approved prescription for treatment for high levels of triglycerides*

Note: Market capitalizations as of February 24, 2021

The Cytisinicline Difference

Dual-Acting, Highly-Targeted MOA
Single & Short Treatment
Very Well-Tolerated

Dual-Acting MOA Specifically Targets $\alpha_4\beta_2$ Nicotine Receptors

Activity 1: Partial Agonist

Cytisinicline binds to the receptor partially stimulating dopamine release

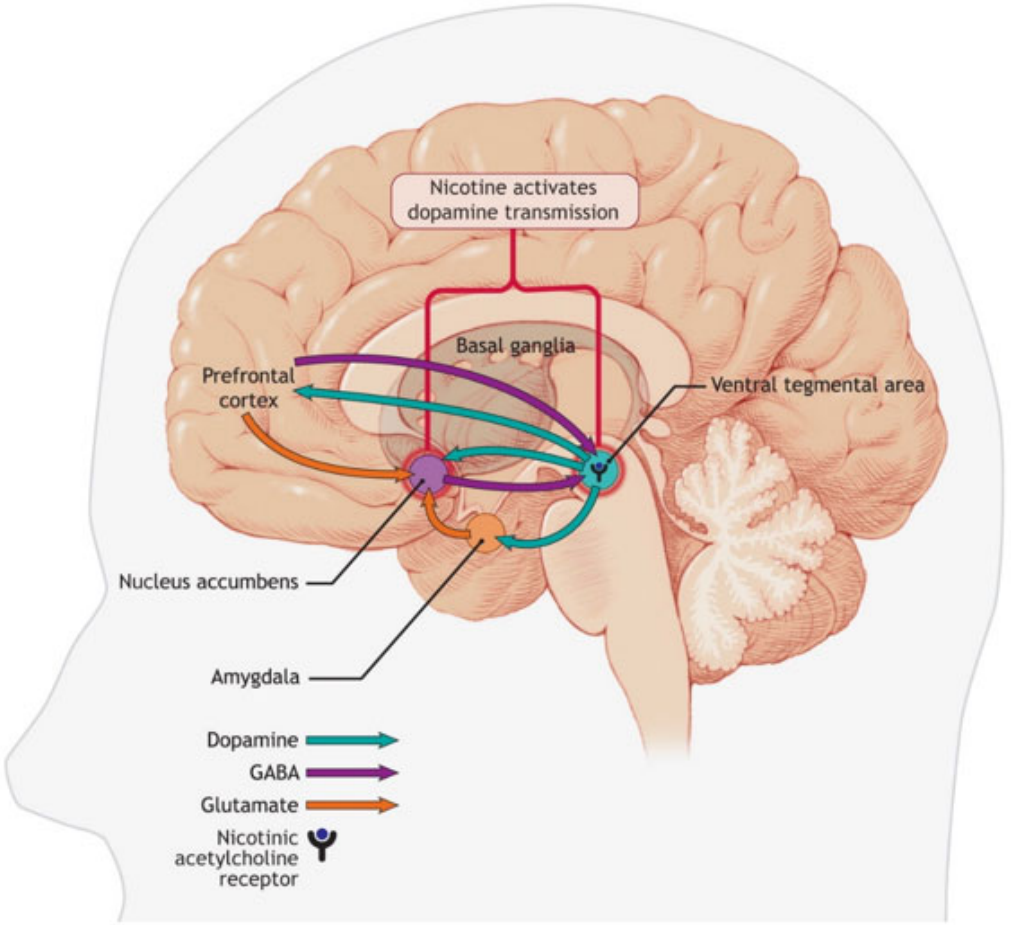
- Reduces nicotine cravings
- Reduces the severity of withdrawal symptoms

Activity 2: Partial Antagonist

Cytisinicline binding to the receptor prevents the binding of nicotine

- Removes the “nicotine-induced” reward and satisfaction associated with smoking

Activation of the central nervous mesolimbic dopamine system is believed to be the neuronal mechanism underlying reinforcement and reward experienced by smoking



Cytisinicline vs. Chantix® MOA

	Cytisinicline[1]	Varenicline (Chantix®)[2]
Selective Receptor Targeting*	More selective	Less selective
	$\alpha_4\beta_2$	$\alpha_4\beta_2$
		α_7
		5-HT_3

- Cytisinicline has high affinity & selective binding to $\alpha_4\beta_2$ receptors in brain
- Varenicline's activity at "off-target" receptors could be responsible for its adverse event profile
- Majority of varenicline patients do not fill second and third month scripts[3]

**Coe J et al. J. Med. Chem. 2005, 48:3474-3477; Papke RL et al. JPET. 2011, 337:367–379; Slater YE et al. Neuropharm. 2003, 44:503–515; Lummis SCR et al. JPET. 2011, 339:125–131.*

1. Data on file; Achieve Life Sciences based on meta analysis of 5 cytisinicline GCP trials, including ORCA-1
2. Cahill K et al; Cochrane Database of Systematic Reviews 2016, Issue 5
3. IQVIA Prescription Claims Database; 072018-062019

Cytisinicline vs. Chantix® Favorable Adverse Event Profile

	Cytisinicline[1]	Varenicline (Chantix®)[2]
Treatment Time	25 days	12 weeks
Adverse Events (95% CI)		
Nausea/Vomiting	4.4%	27.8%
Sleep Disorder/Abnormal Dreams	3.3%	12.5%
Insomnia	1.3%	14.2%
Headache	2.0%	12.7%

- Shorter course of treatment
- Lower overall rate of side effects
- Head-to-head data from the RAUORA trial showed significantly fewer adverse events on cytisincline compared to Chantix ($p<0.001$)

1. Data on file; Achieve Life Sciences based on meta analysis of 5 cytisinicline GCP trials, including ORCA-1
2. Cahill K et al; Cochrane Database of Systematic Reviews 2016, Issue 5

Cytisinicline Clinical Development

Cytisinicline: Extensive & Impressive Foundation of Clinical Evidence

Three investigator-led Phase 3 clinical trials conducted in more than 2,700 patients published in *NEJM

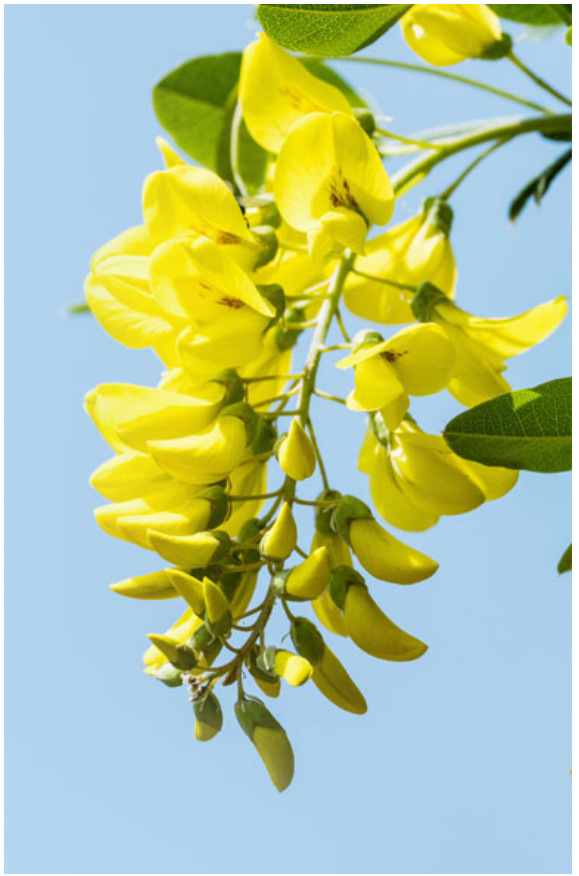
- Phase 3 TASC* trial – cytisinicline versus placebo (n=740)
- Phase 3 CASCAID** trial— cytisinicline versus NRT (n=1,310)
- Phase 3 RAUORA trial – cytisinicline versus varenicline (Chantix®) (n=679)***
- In both TASC and CASCAID, cytisinicline demonstrated superior quit rates and RAUORA demonstrated superior safety **(p-values<0.01)**

Successful completion of Phase 1 and Phase 2 studies

- Fed-fasted study (n=26)
- Repeat dose PK/PD study (n=26)
- ORCA-1 Dose Selection study (n=254)
  - Cytisinicline demonstrated superior quit rates vs. placebo **(p-value<0.005)**

Path to NDA already reviewed with FDA

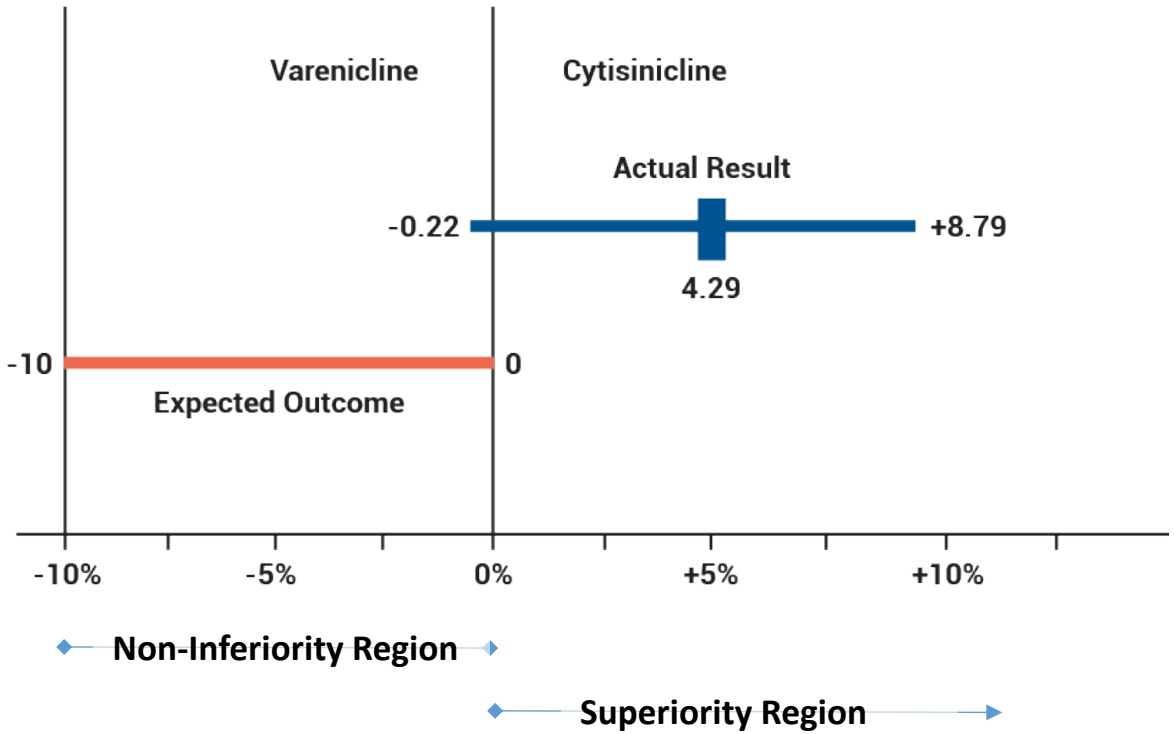
- End of Phase 2 meeting held with FDA
- Efficacy endpoints and pivotal trial designs reviewed by the FDA



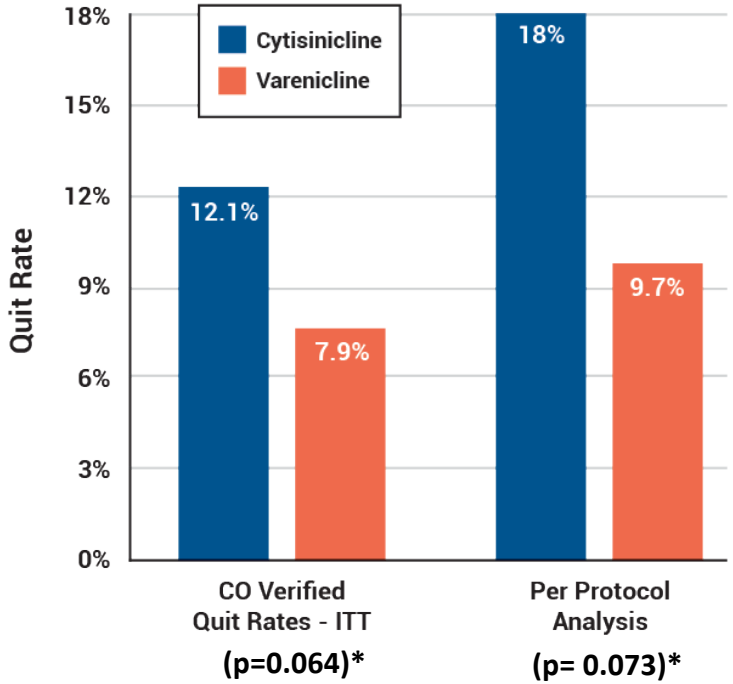
*West et al; N Engl J Med; 365:13 Sept 29, 2011
** Walker et al; N Engl J Med; 371:25 Dec 18, 2014
*** Walker et al; Addiction; March 2021
®TABEX – Registered trademark of Sopharma AD, Chantix® is a registered trademark of Pfizer, Inc

6 Month Quit Rates Trended Towards Superiority for Cytisinicline

Risk Difference at 6 Months



6 Month Quit Rate



*P values calculated based on chi-square analysis of quit rates

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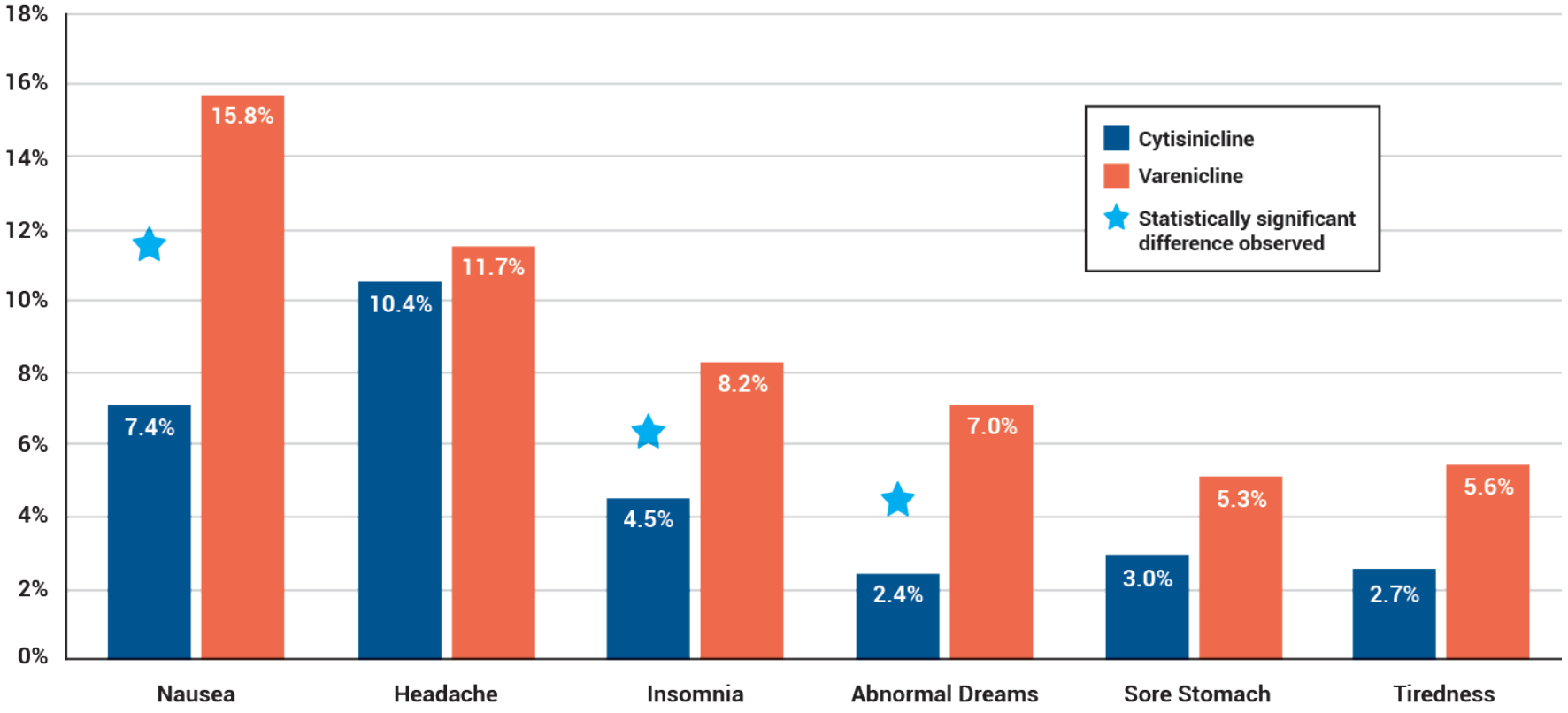
He taniko taku.

Significantly Fewer Overall Adverse Events For Subjects Treated with Cytisinicline (p=0.001)

Adverse Events (>5% of Subjects)

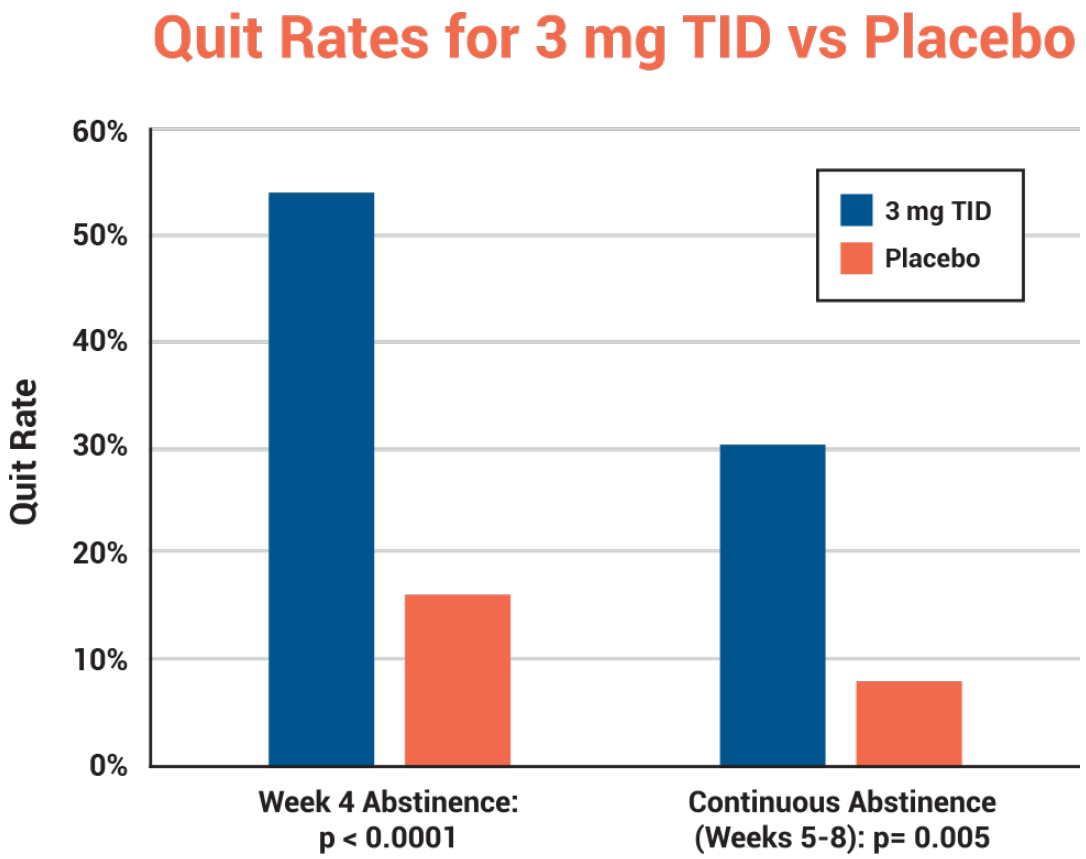


- **Cytisinicline had overall significantly fewer adverse events than varenicline (p<0.001)**
- Varenicline showed significantly increased nausea, abnormal dreams & insomnia (p<0.05)

Achieve analysis of adverse event data based on Mantel-Haenszel chi-square test comparing rates in the cytisinicline and varenicline arms (# subject affected/#subjects exposed)

Nau te kakahu i whatu.
He taniko taku.

ORCA-1 Dose Selection Study Results: Statistically Significant Efficacy Observed for 3.0 mg TID

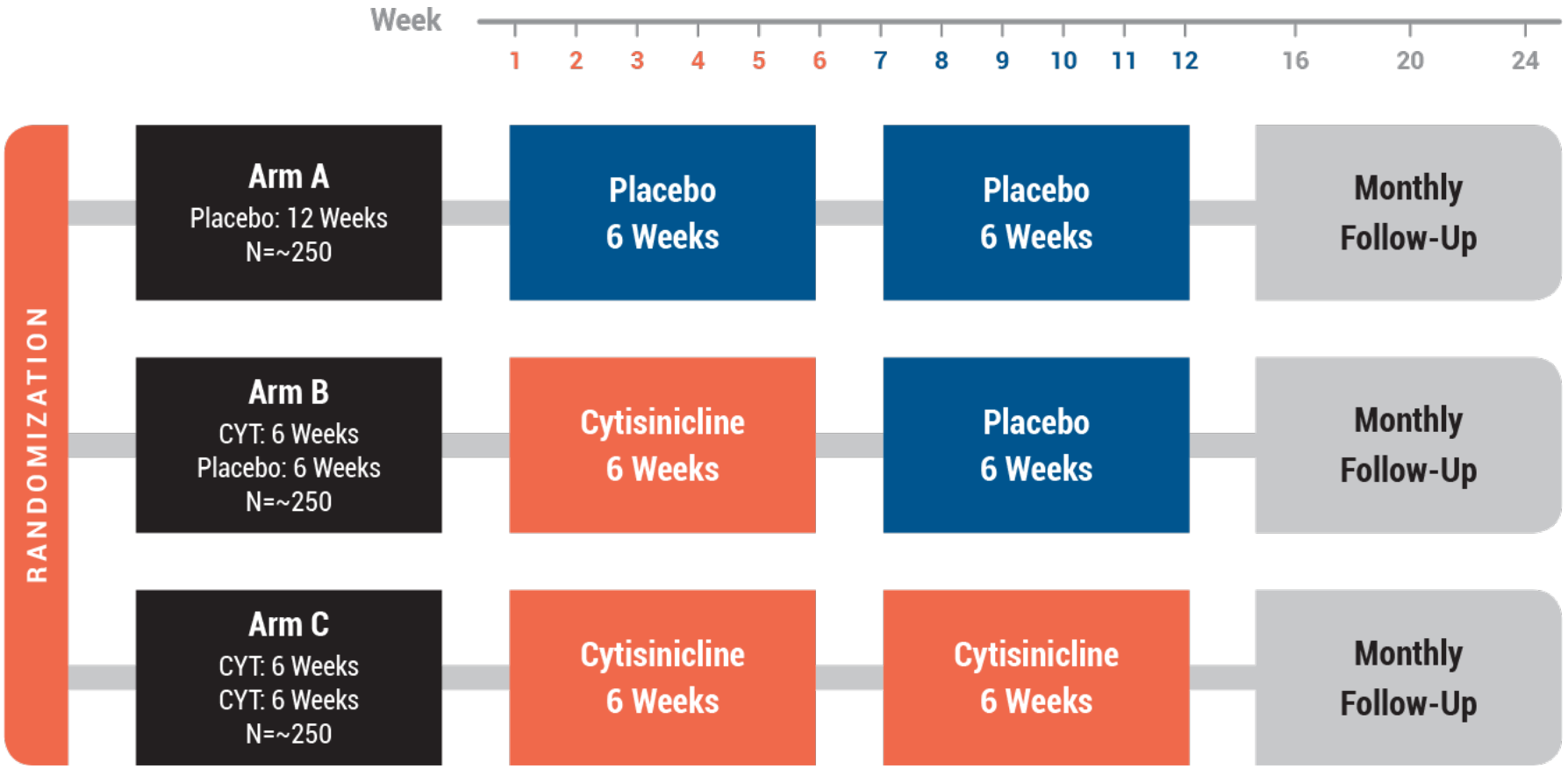


Characteristic	3.0 mg CYT (N=50)	Placebo (N=51)	P Value
Reduction in expired CO[1]	80%	38%	p = 0.003
Week 4 Abstinence [2]	54%	16%	p < 0.001
Continuous Abstinence (Weeks 5-8)[3]	30%	8%	p = 0.005

- Statistically significant quit rates demonstrated at both end of treatment and weeks 5 through 8 (the FDA approvable endpoint)
- CO confirmed end of treatment quit rates on Cytisinicline exceeded Chantix, Zyban & NRT quit rates at both week 4 and week 12 (end of treatment) in latest EAGLES study[4]
- Adherence to study treatment was 98% in the 3.0 mg TID arm
- Cytisinicline was generally well-tolerated with no serious adverse events reported
- 3.0 mg dose with TID administration selected to move forward to Phase 3 development

1. Average % reduction expired CO from Baseline by Day 26
2. Biochemically confirmed quit on Day 26 (no cigarettes smoked and expired CO<10 ppm)
3. Biochemically confirmed on Day 26 and weeks 5, 6, 7, & 8 (no cigarettes smoked and expired CO<10 ppm)
4. EAGLES: Anthenelli et al; Lancet; 2507-20, June 18, 2016

ORCA-2 Phase 3 Study Design



Objective: Evaluate safety and efficacy of 3.0 mg of cytisinicline vs placebo administered TID over 6 & 12 weeks
All subjects to received standardized behavioral support and will be followed up to 24 weeks

Population: Smokers of ≥10 cigarettes/day and expired air CO > 10 ppm

Multiple Primary Endpoints:

- Biochemically verified continuous abstinence during the last 4 weeks of treatment
  - Arm B: Weeks 3-6
  - Arm C: Weeks 9-12

Secondary Endpoint:

- Continuous abstinence from end of treatment through week 24

Statistics:

- >95% power for the 24-week comparisons

Cytisinicline Planned Development Program & Milestones

Activity	Anticipated Timing	
ORCA-1 Additional Phase 2b Results Presented	Q1 2020	✓
RAUORA Topline Study Results: Cytisinicline vs Chantix	Q2 2020	✓
RAUORA Full Study Results: SRNT-E Conference	Q3 2020	✓
ORCA-2 Phase 3 Trial Initiation	Q4 2020	✓
ORCA-2 Study Enrollment Completed	Mid 2021	
ORCA-2 Last Patient Treated	2H 2021	
ORCA-2 Phase 3 Top Line Data Results	1H 2022	

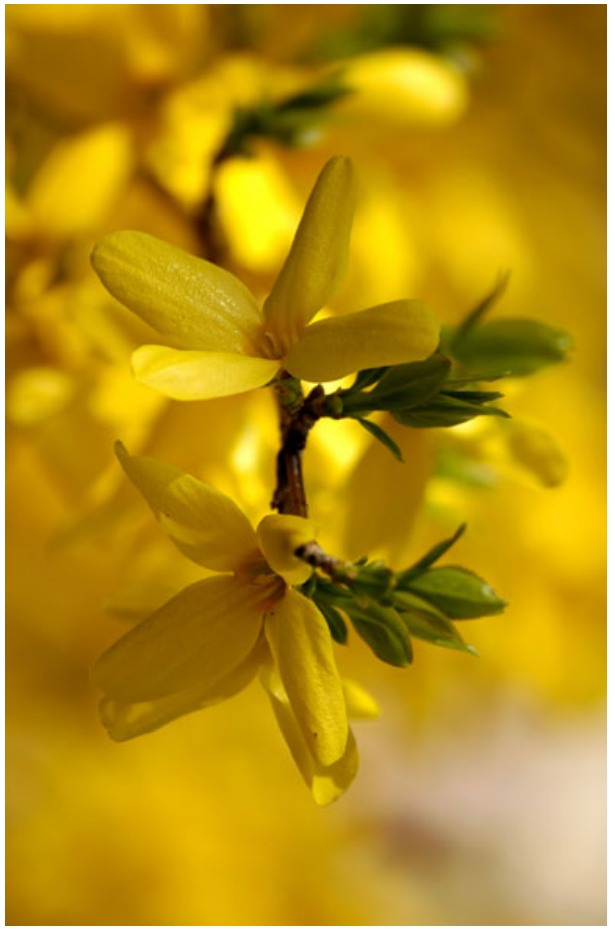
ORCA Ongoing Research of Cytisinicline for Addiction

RAUORA
Nau te kakahu i whatu.
He taniko taku.

Capitalization

- Cash, cash equivalents and investments of ~$35.9M as December 31, 2020
- No debt
- Capitalization (as of December 31, 2020):

Common Shares Outstanding	**6,111,735**
Pre-Funded Warrants ($0.001)	**142,857**
Warrants (WAEP $6.60)	**660,050**
(WAEP $7.29)	**235,856**
(WAEP $8.75)	**50,000**
(WAEP $81.56)	**205,726**
Outstanding under equity award plans	**227,442**
Fully Diluted Shares	**7,633,666**



Investment Highlights

Cytisinicline well-positioned to address global tobacco public health epidemic

- Addresses tobacco & nicotine addiction, leading cause of cancer and cardiovascular disease-related death
- Differentiation from currently available products, with history of black box warnings, has positive implications for improved safety and efficacy

Large market opportunity and patient need

- ~$13B nicotine addiction market, with sales of leading product Chantix of >$900M in 2020*

Compelling foundation of clinical evidence with regards to both safety and efficacy

- Three completed Phase 3 trials, with over 2,700 patients, supports safety and efficacy of cytisinicline

Clear path to market

- Recent FDA interactions provide clear direction for NDA requirements in U.S.

Proven management team

- Management team has a history of leading successful biopharma companies, including through acquisition

**PFE Q4 & 2020 YE Results*

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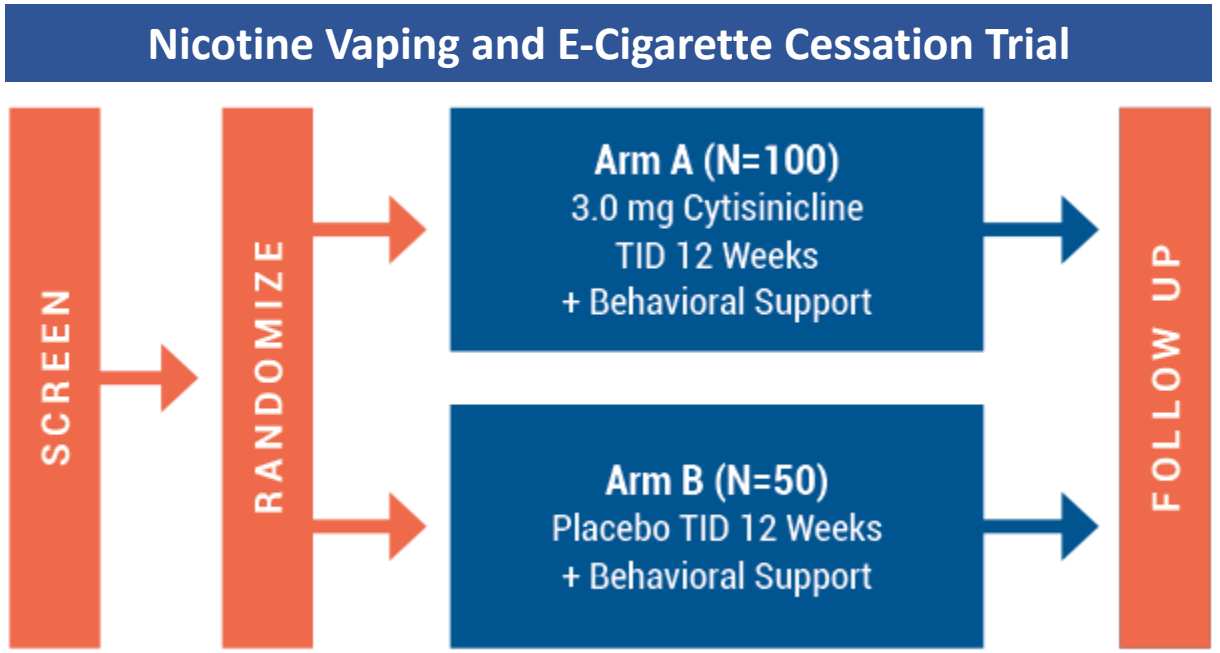
Thank You!

Vaping & E-cigarette Cessation – Market Expansion Opportunity

- 13.7M+ adult U.S. vape/e-cigarette users[1]
- No currently approved treatments specifically address vaping cessation
- Achieve/IQVIA survey of 500+ subjects supports intention to quit[2]
  - 74% of past smokers intend to quit in the next 3-12mos.
  - Of vapers who aim to quit in the next 3mos., 65% would try a new, natural Rx
- Exploring non-dilutive financing of Phase 2, ORCA-V1 study

ORCA-V1



Multi-center, double-blind, randomized, placebo-controlled, Phase 2 study of daily nicotine e-cigarette users who intend to try to quit vaping.

1.JAMA Intern Med., Trends in e-Cig Use in Adults in U.S., Sept 8, 2020; E1- E4, 2. ACHV/IQVIA Vaping Survey, March 2020

Next Steps for Phase 3 Cytisinicline Development

- 3.0 mg TID dosing selected for P3 development
  - Best safety & efficacy demonstrated in ORCA-1
- Extend dosing period from 25 days to 42 days (6 weeks)
  - Potential to further increase quit rates over those seen in ORCA-1
- Evaluate abstinence rates during the last 4-weeks of treatment
  - Previously not able to measure on treatment given 25 day schedule
- Evaluate re-treatment course or 12 weeks total
  - Adds additional safety data (as requested by FDA)
  - Allows evaluation for reduction in risk of relapse

ORCA-1 Phase 2b Dose Selection Study

Objective:

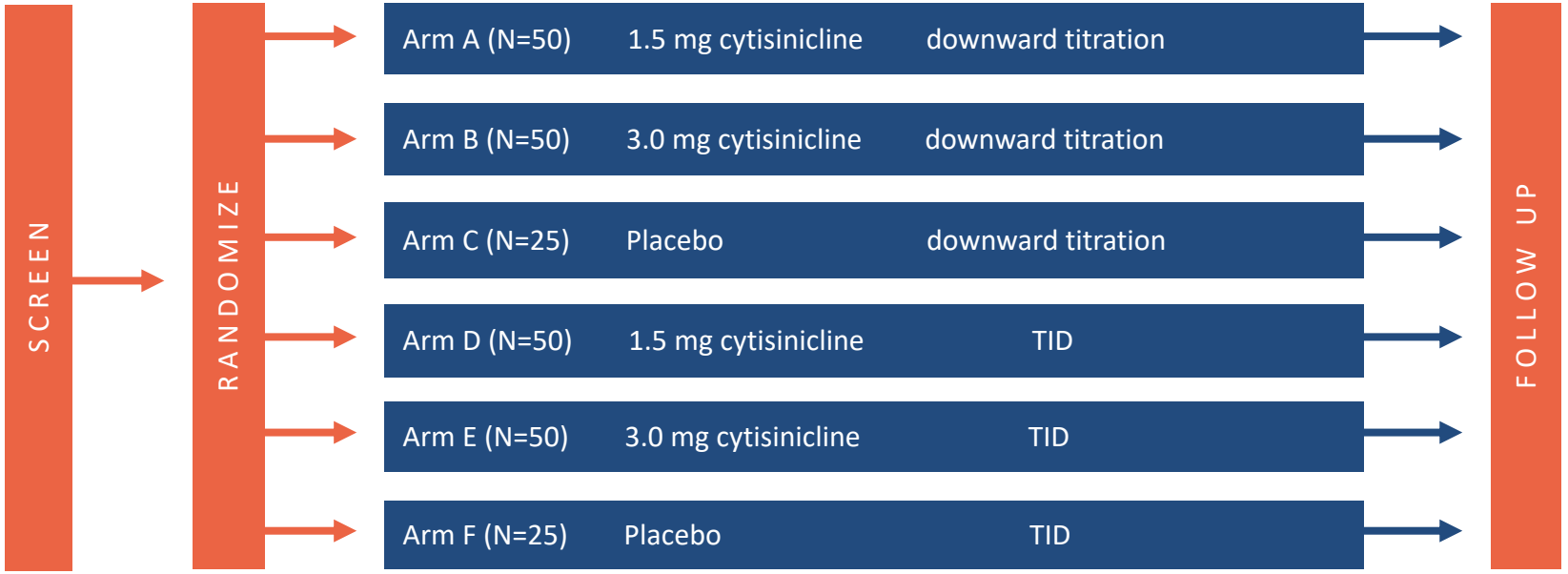
- To optimize Phase 3 trial planning for dosing, scheduling, compliance and efficacy rates in U.S.
- Evaluate safety and efficacy of 1.5mg and 3mg of cytisinicline vs placebo administered over 25 days
- All subjects to receive standardized behavioral support and will be followed up out to 8 weeks

Population:

Smokers of ≥10 cigarettes/day and expired air CO > 10 ppm

Endpoints:

- Biochemically verified abstinence
- Reduction in self reported cigarettes smoked during treatment

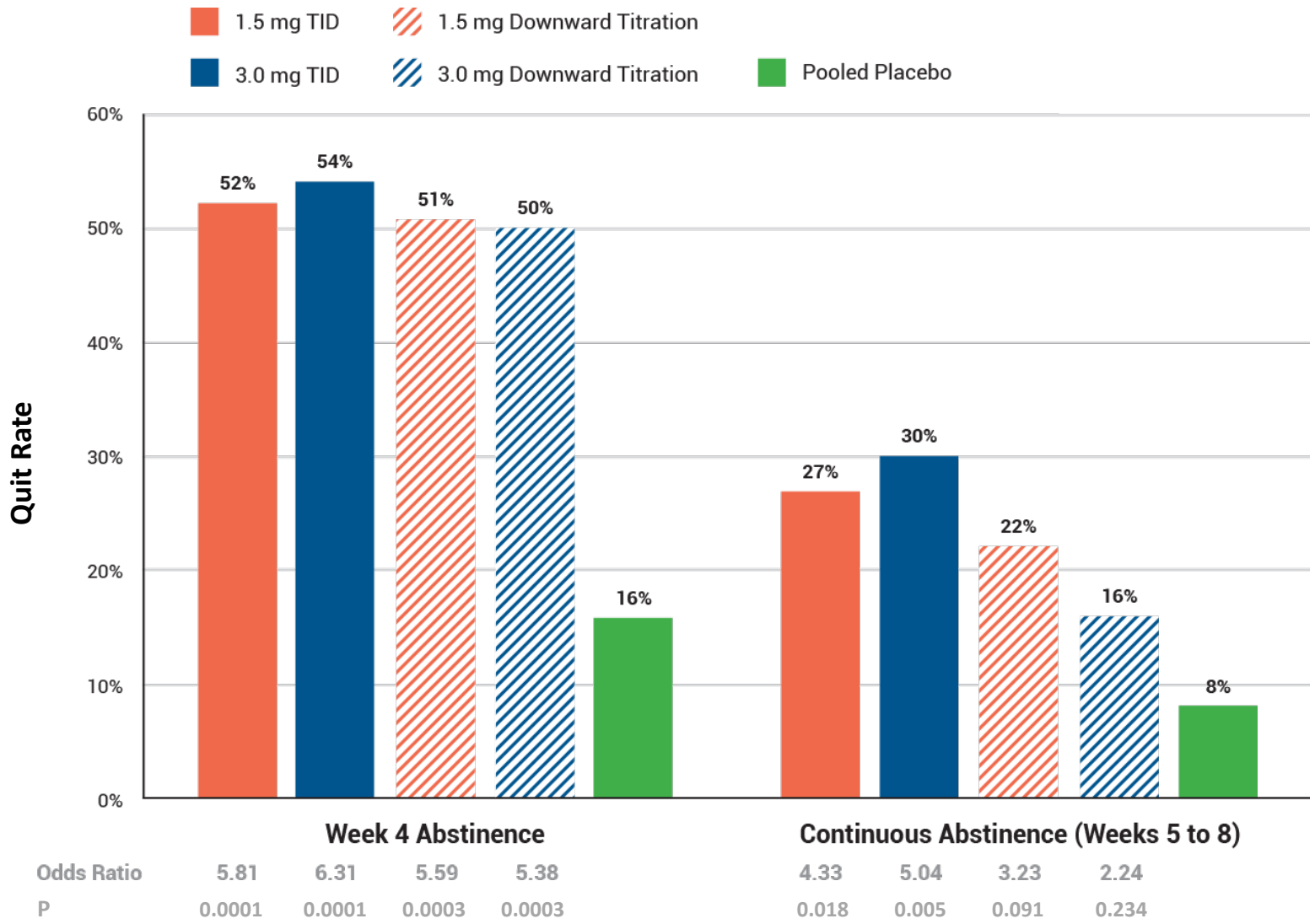


ORCA Ongoing Research of Cytisinicline for Addiction

ORCA-1 Dose Selection Study Results: Baseline Subject Demographics

	TID		Downward Titration			
	1.5 mg (n=52)	3.0 mg (n=50)	1.5 mg (n=51)	3.0 mg (n=50)	Pooled Placebo (n=51)	ALL (n=254)
Smoking duration (mean years)	30.9	30.0	33.3	33.2	33.0	32.1
Daily smoking (median cigarettes)	20	18	20	20	20	20
Prev. quit attempts (mean)	4.7	3.8	5.4	3.8	4.9	4.5
Previous treatments						
Varenicline	21 (40%)	18 (36%)	21 (41%)	13 (26%)	19 (37%)	92 (35%)
Bupropion	9 (17%)	7 (14%)	9 (18%)	3 (6%)	12 (24%)	40 (16%)
NRT	27 (52%)	25 (50%)	23 (45%)	19 (38%)	28 (55%)	122 (48%)
Patch	22 (42%)	16 (32%)	21 (41%)	12 (24%)	26 (51%)	97 (38%)
All other NRT						
e-cigarettes	19 (37%)	13 (26%)	15 (29%)	11 (22%)	18 (35%)	76 (30%)

ORCA-1 Dose Selection Study Results: Significant Increase in Quit Rates Across All Cytisinicline Arms



- All cytisinicline arms demonstrated statistically significant end of treatment quit rates (>= 50%; p<0.001)
- TID administration outperformed the downward titration groups at both end of treatment and weeks 5-8
- 3.0 mg dose with TID administration selected to move forward to Phase 3 development

Investigator-Led Phase 3 Trials of Cytisinicline

	Design	Comparator	Key Endpoints	Results
TASC	N=740 Aged 18 or over; randomized 1:1 Double-blind, placebo-controlled Minimal behavioral support	Placebo 25-day cytisinicline dosing regimen or matched placebo	6 & 12-month quit rates biochemically confirmed	**Cytisinicline 3.4 times more likely to result in smoking cessation after 12 months (p=0.001)** No overall difference in the rate of side effects in the two trial arms
CASCAID	N=1,310 Aged 18 or over; randomized 1:1 Open-label, active-controlled, non-inferiority Moderate behavioral support	NRT 25-day cytisinicline dosing regimen or 8-week NRT (patch &/or gum or lozenge)	1, 2 & 6-month quit rates	Cytisinicline 1.43 times more likely than NRT to result in smoking cessation after 6 months (p=0.002) **6-month quit rate equivalent to the 24-week quit rates in the varenicline EAGLES trial (n=8,144) published in The Lancet in June 2016** Cytisinicline generally well tolerated, although self-reported adverse events were higher in the cytisinicline arm compared with the NRT arm No serious treatment-related adverse events with cytisinicline

TASC: West et al; N Engl J Med; 365:13 Sept 29, 2011
CASCAID: Walker et al; N Engl J Med; 371:25 Dec 18, 2014

Investigator-Led Phase 3 Trials of Cytisinicline (cont.)

	Design	Comparator	Key Endpoints	Results
RAUORA	N=679 Māori (indigenous NZ) ≥ 18 years of age Single blind, non-inferiority Minimal behavioral support	varenicline (Chantix®) 12-week treatment for both arms	6-month biochemically confirmed quit rates Non-inferiority margin of 10% (cytisinicline quit rates no worse than 10% less than Chantix)	Primary endpoint of non-inferiority was met for cytisinicline with a trend towards superior efficacy Cytisinicline demonstrated higher quit rates and smokers were 1.55 times more likely to quit at 6 months compared to varenicline **Cytisinicline-treated subjects experienced a lower rate of adverse events compared to varenicline (RR=0.56, p<0.001)**

Nau te kakahu i whatu.
He taniko taku.

Sourced: Walker et al; Addiction; March 2021

Broad Product Protection

PATENT APPLICATIONS

- Several patent families pursued globally including formulation, method of use, extraction
- Issued patents – new cytisinicline salt formulation
- Ongoing discovery and other development work in providing additional IP opportunities

REGULATORY EXCLUSIVITY

- U.S. – 5 years for NCE under Hatch-Waxman
- Europe –Up to 10 years possible in countries where cytisinicline is not already approved
- Orange Book cytisinicline specification

EXCLUSIVE API SUPPLY

- Sopharma exclusive supply agreement
- 4-6 year API lead time for Laburnum
- 100% (-)- enantiomer of cytisinicline
- Synthetic 100% (-)- cytisinicline not currently viable
- Extraction know-how / trade secrets filed as pending patent

SECOND GENERATION CYTISINICLINE

- University of Bristol exclusive license agreement
- Next generation highly targeted cytisinicline derivatives for other indications

ORCA-1 Dose Selection Study Results: Confirmation of Safety & Tolerability

Most commonly reported (>5%) side effects from ORCA-1:

Adverse Event	3.0 mg TID (n=50)	Pooled Cytisinicline (n=203)	Placebo (n=51)
At least 1 AE	42%	46%	47%
Upper Respiratory Tract Infections	6%	6%	14%
Nausea	6%	6%	10%
Abnormal Dreams	6%	9%	2%
Insomnia	6%	7%	2%
Constipation	6%	2%	2%
Headache	4%	5%	4%

- Cytisinicline was generally well-tolerated across all treatment groups
- Overall low incidence of adverse events
- No serious or severe adverse events reported
- Low rates of AE's compares favourably to currently approved smoking cessation products