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LIFE SCIENCES

Corporate Presentation

NASDAQ: ACHV | April 2024

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; and expectations regarding cash forecasts. 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 inflation, rising interest rates, instability in the global banking sector and risks related to the COVID-19 pandemic or similar public health crisis; risks related to the Russian military action in Ukraine and other regional conflicts; 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.

Company Overview

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

1. Well-positioned to address global tobacco public health epidemic
2. Proven management team
3. NDA submission targeted for first half of 2025
4. Large market opportunity and patient need
5. Broad IP portfolio patent protection to 2040
6. Strong cash position

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Large Market Opportunity: Treating Nicotine Addiction

Tobacco use is the leading cause of preventable death[1]

1B

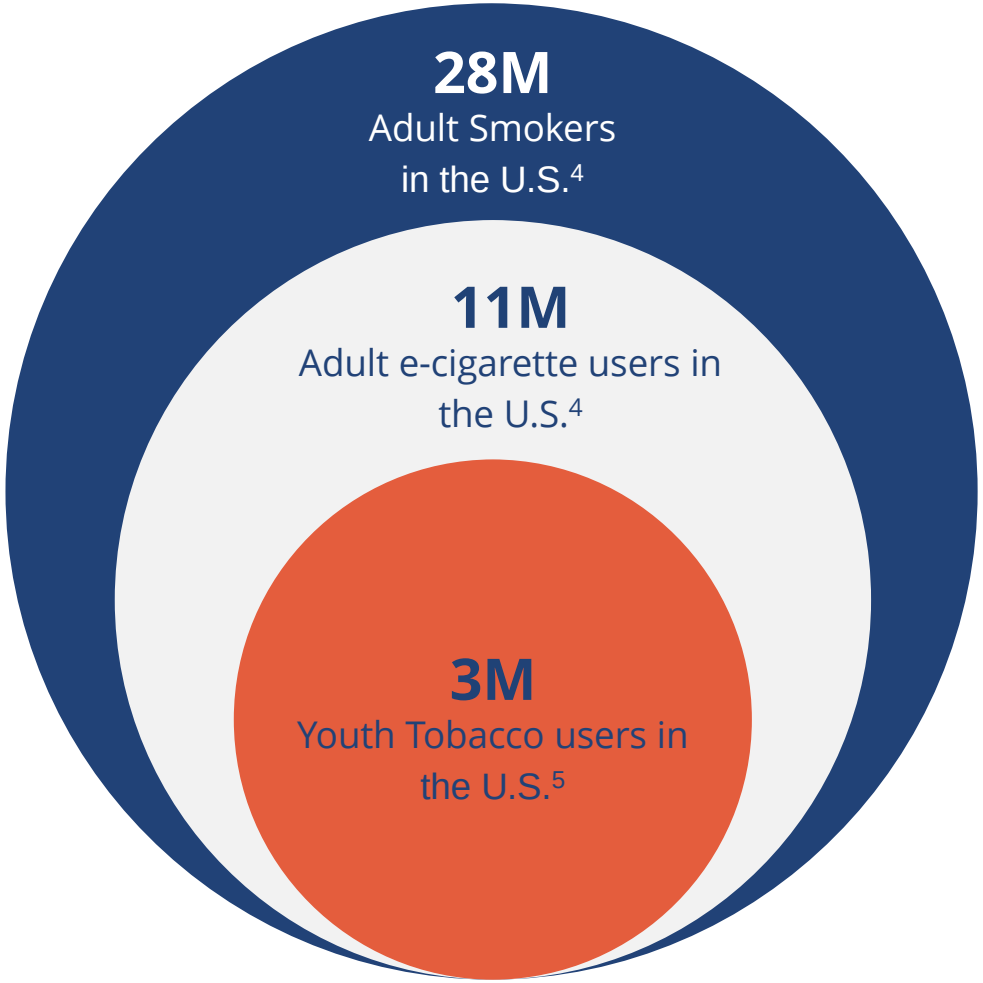
Global Tobacco Smokers[2]

~480K

Deaths in the U.S. annually[3]

$300B

Annualized healthcare costs associated with smoking costs in the U.S.[3]



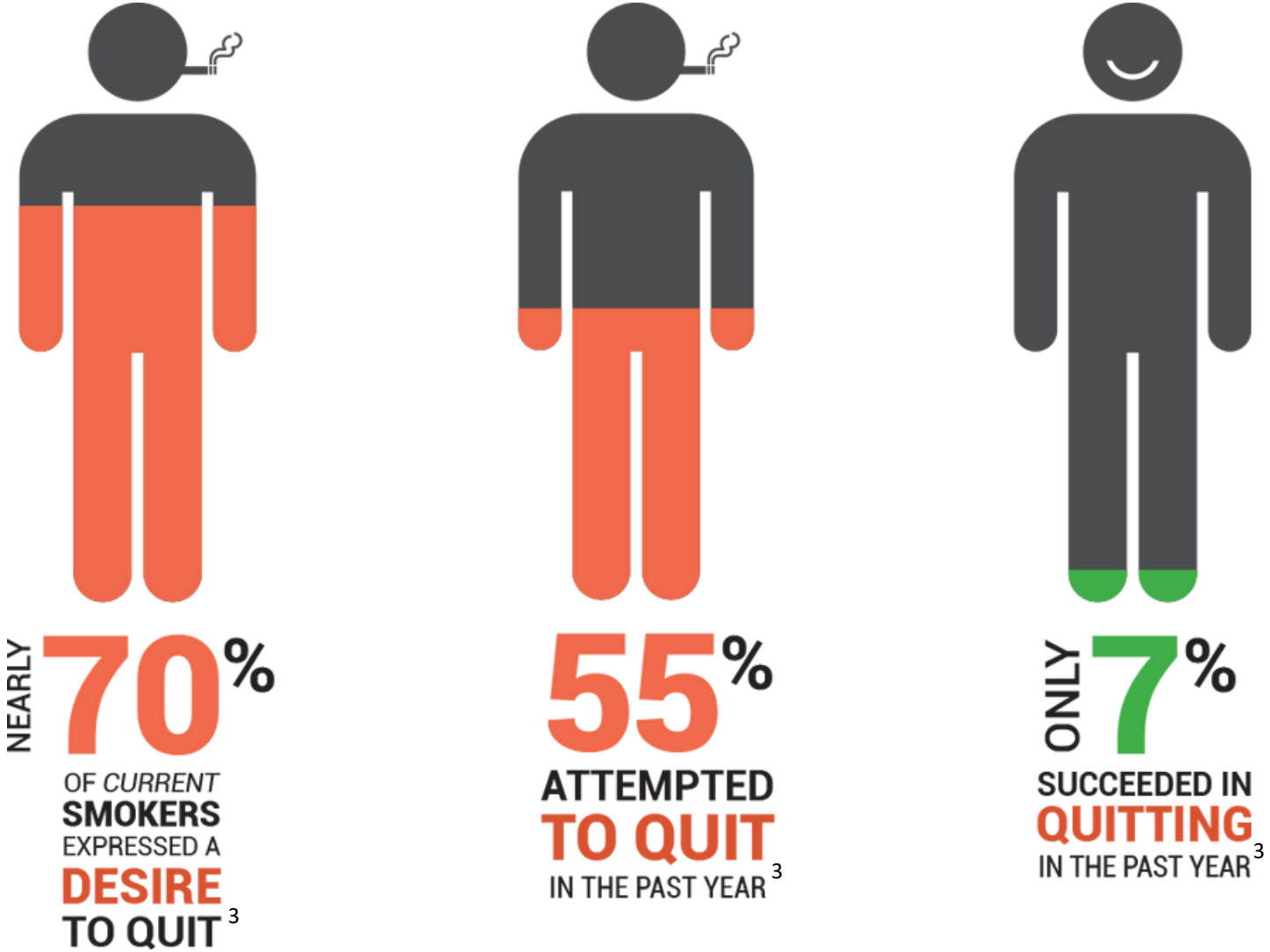
1. World Health Organization (WHO). WHO Report on the Global Tobacco Epidemic, 2019.
2. WHO global report on trends in prevalence of tobacco use 2000–2030. Geneva: World Health Organization; 2024.
3. U.S. Department of Health and Human Services, The Health Consequences of Smoking, 50 Years of Progress: A Report of the Surgeon General, 2014.
4. Cornelius ME, Loretan CG, Jamal A, et al. Tobacco Product Use Among Adults – United States, 2021. MMWR Morb Mortal Wkly Rep 2023;72:475–483.
5. Birdsey J, Cornelius M, Jamal A, et al. Tobacco Product Use Among U.S. Middle and High School Students — National Youth Tobacco Survey, 2023. MMWR Morb Mortal Wkly Rep 2023;72:1173–1182.

Lack of Innovative Treatment Options

8 to 11 estimated attempts before quitting **successfully**[1]

4 out 5 patients relapse six months post-initiation of treatment with Chantix[2]

No new FDA-approved treatments in **the last 18 years**



1. Babb S, Malarcher A, Schauer G, Asman K, Jamal A. Quitting Smoking Among Adults — United States, 2000–2015. MMWR Morb Mortal Wkly Rep 2017;65:1457–1464.
2. EAGLES: Anthenelli et al; Lancet; 2507-20, June 18, 2016.
3. https://www.cdc.gov/tobacco/data_statistics/fact_sheets/cessation/smoking-cessation-fast-facts/index.html (accessed 5.08.23)

Cytisinicline is Well Positioned…

To Meet the Cessation Needs of Smokers and Patients Battling Nicotine Addiction

Well-Tolerated
Dual-acting, differentiated, and highly selective MOA demonstrated minimal adverse events (AEs) and excellent compliance rates

Demonstrated Robust Efficacy
Robust efficacy demonstrated in multiple, large, randomized controlled trials

Short Course of Treatment
6-week treatment with option to extend to 12 weeks for extended benefit

Positive In-Market Experience
Positive patient & HCP perceptions with no product history of black-box warnings or suicidality

Naturally Derived Therapy
Sourced from plant-based material which is appealing to specific patient populations

Path to FDA Approval
Agreement reached with FDA on NDA required safety exposure data

Smoking Cessation Market Landscape

- Most successful product has been Chantix®
  - Peak global sales of $1.1B[1]
  - ~75% of sales attributed to U.S. market[1]
  - Withdrawn from market in 2021
- All FDA-approved products are **generic** with **limited promotion**
- 8M smoking cessation Rx written in U.S. market in 2023[2]
  - Generic varenicline market $300M in U.S. in 2022[3]

1. Pfizer, Inc. 2018 Annual Report
2. Source: Symphony Health Patient Source, Smoking Cessation TRx 2023
3. Endo Pharmaceuticals YE 2022 Report, March 6, 2023

A Significant Market Expansion Opportunity

ACA Coverage

Affordable Care Act (ACA) **mandates coverage** for all FDA approved drugs

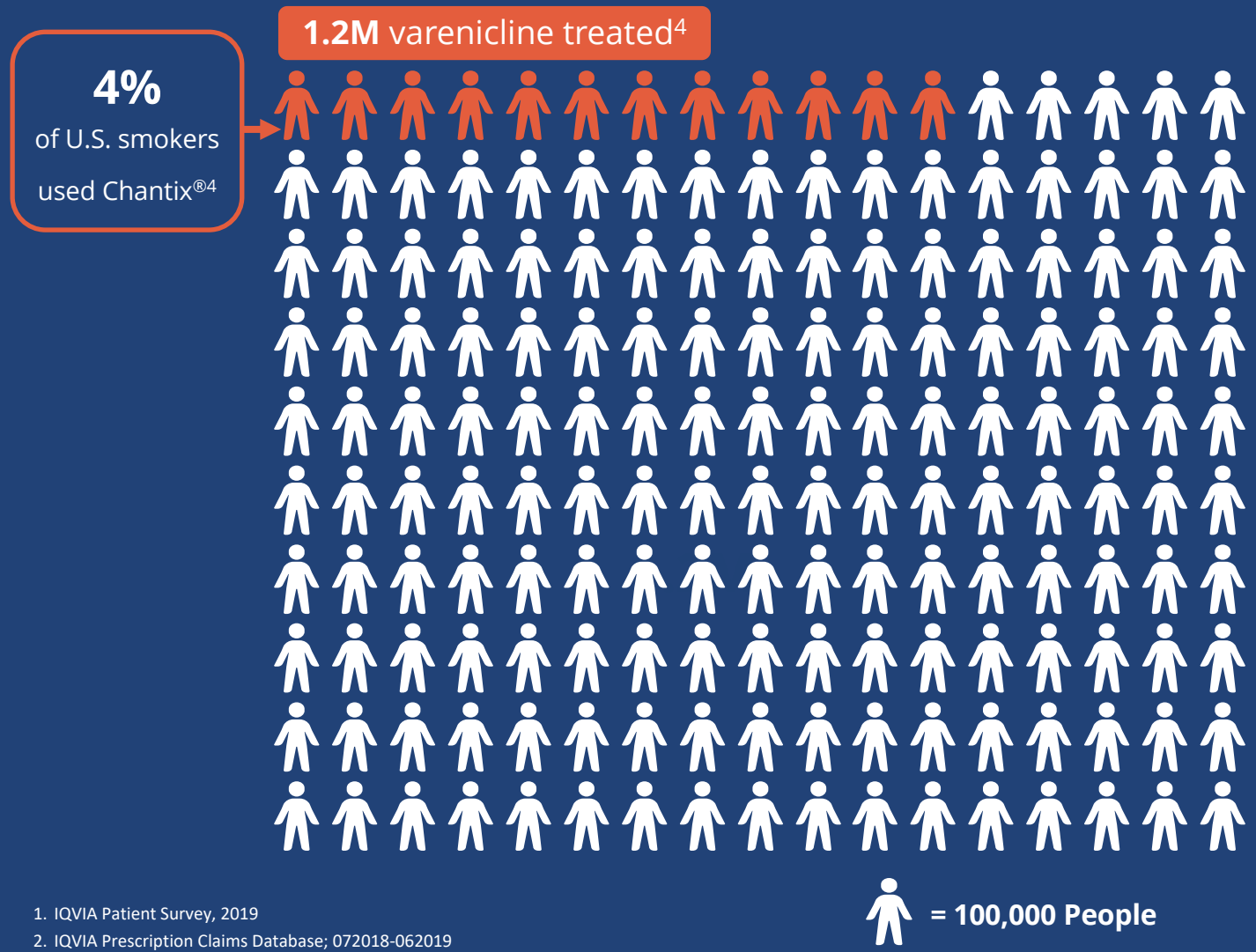
Chantix® + Zyban

patients report side effects as the top reason for **non-compliance**[1]

Poor Compliance

76% of patients do not complete the full course of Chantix®[2]

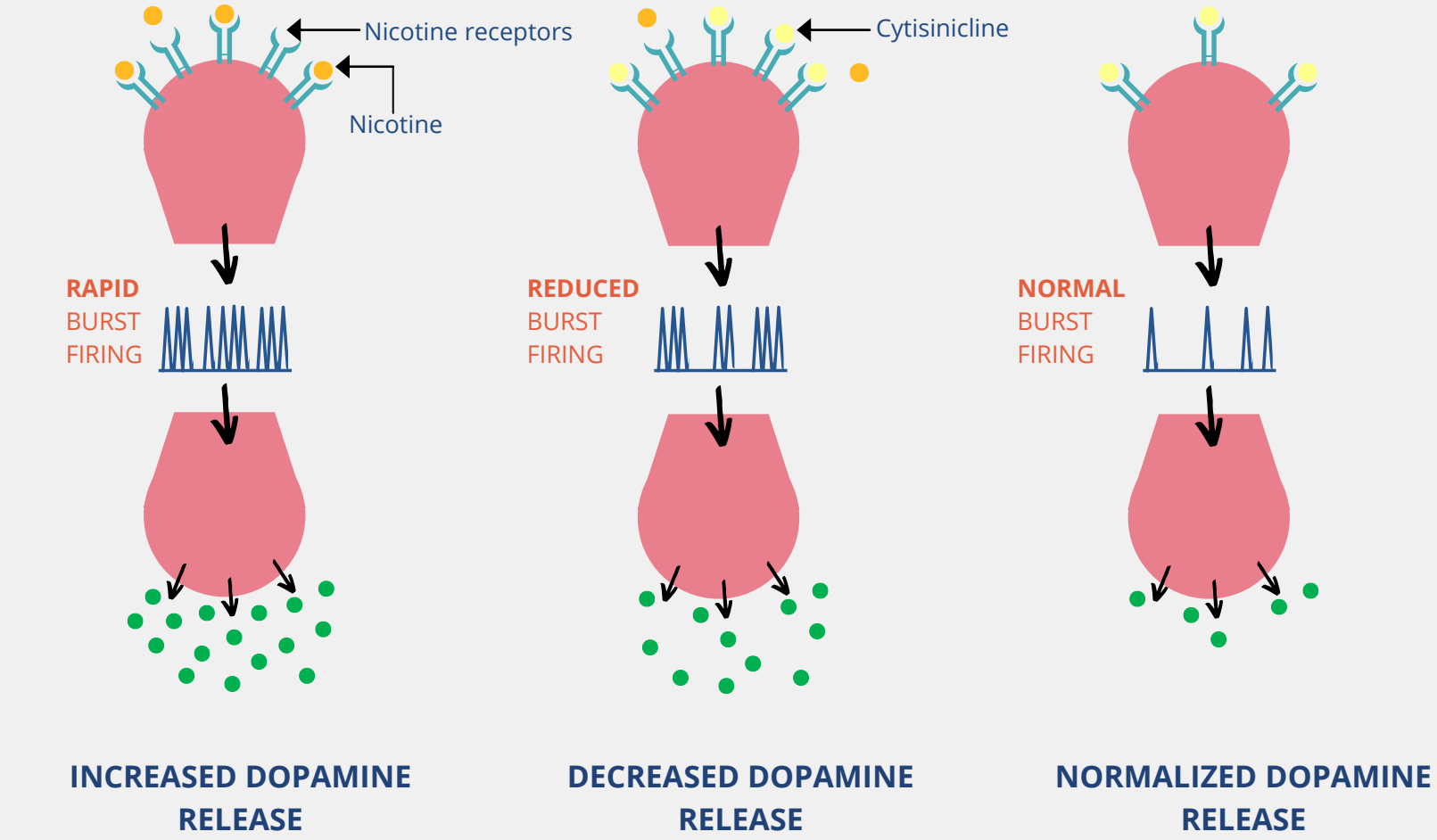
17M U.S. Smokers Make a Quit Attempt Annually [3]



1. IQVIA Patient Survey, 2019
2. IQVIA Prescription Claims Database; 072018-062019
3. Centers for Disease Control and Prevention (CDC). Quitting smoking among adults--United States, 2001-2010. MMWR Morb Mortal Wkly Rep. 2011 Nov 11;60(44):1513-9. PMID: 22071589.
4. Symphony IDV Database, accessed May 2023

Dual-Acting MOA:

Specifically Targets $\alpha^4\beta^2$ Nicotine Receptors as Partial Agonist and Antagonist



Sources: Biodo-2003, Papke-1994, Papke-2011,Parker-1998, Slater-2003, Zhang-2003

Cytisinicline… a Favorable Potential Treatment Option

Adverse Event Profile Compared to Chantix®

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%

Selective Receptor Targeting[3]

Cytisinicline[3]	Varenicline (Chantix)[2]	Adverse Events
	5-HT3	Nausea & Vomiting
	α7	Sleep Disturbances
α4β2	α4β2	Headaches, GI Upset

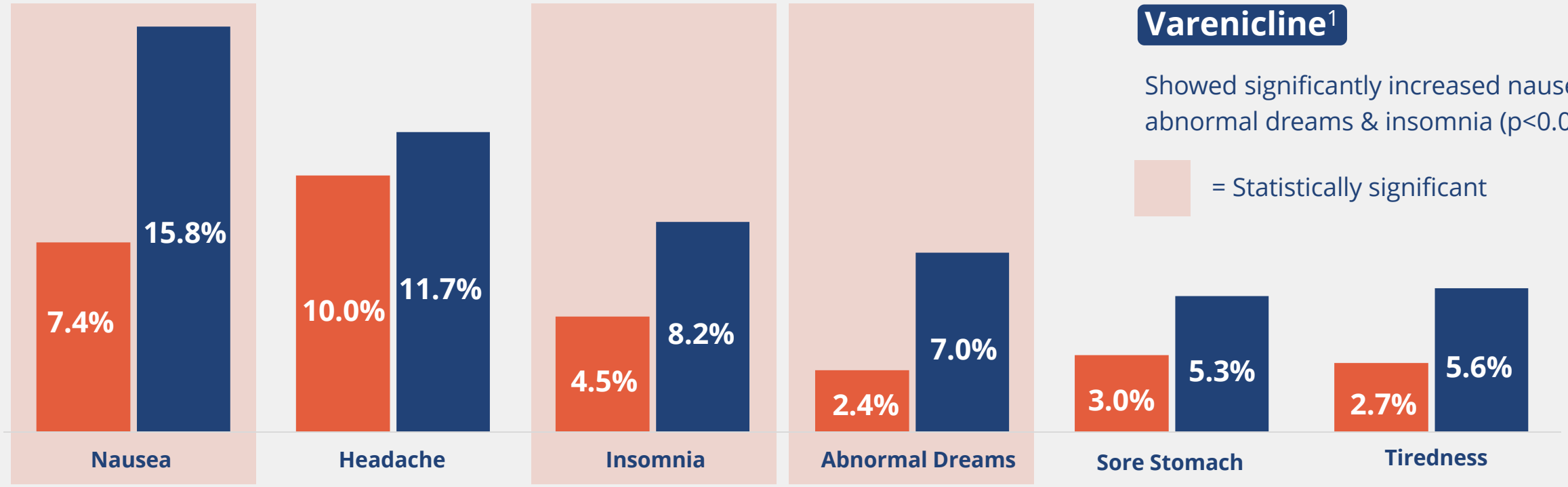
Cytisinicline is >2000 fold less potent at the human 5-HT3 receptor[4]

Chantix® is a registered trademark of Pfizer, Inc.

1. Data on file; Achieve Life Sciences ORCA-2 & ORCA-3 combined.
2. Cahill K et al; Cochrane Database of Systematic Reviews 2016, Issue 5.
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.
4. Lummis, SCR, Price,KL, Clarke A, SRNT-E 2020.

Significantly Fewer Overall Adverse Events

Adverse Events (>5% of Subjects)



Cytisinicline

Overall significantly fewer adverse events than varenicline ($p<0.001$)

Varenicline[1]

Showed significantly increased nausea, abnormal dreams & insomnia ($p<0.05$)

= Statistically significant

1. Varenicline = Chantix

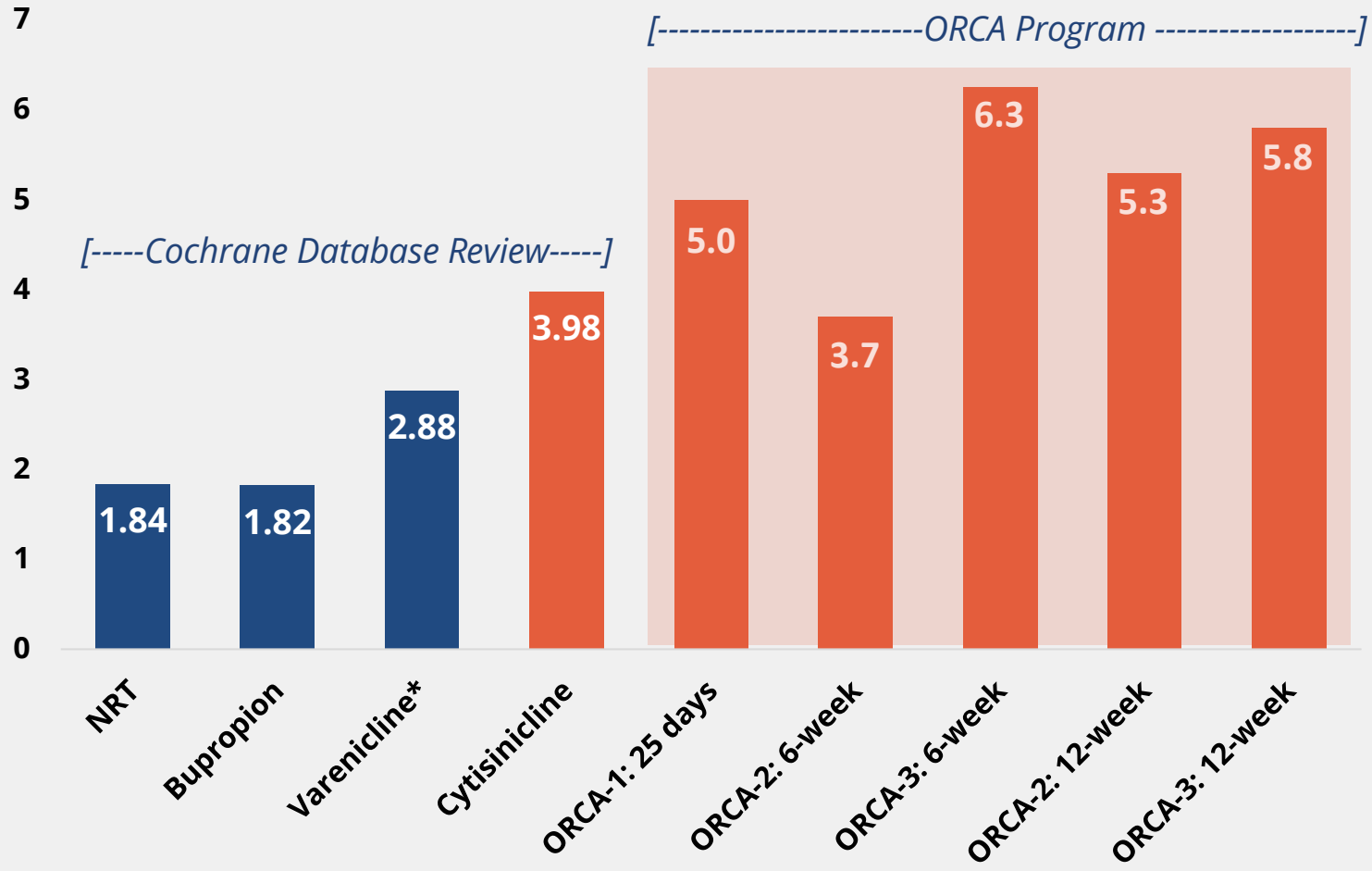
Sourced: Walker et al; Addiction; March 2021.

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) Rauora Trial.

Strong Relative Efficacy Compared to Current Treatments

- **Odds Ratio (OR) expresses the drug effect in proportion to placebo**
- **OR is the preferred outcome measure in smoking cessation trials in the literature**

Odds Ratios vs Placebo at Longest Follow-up



*Varenicline = Chantix

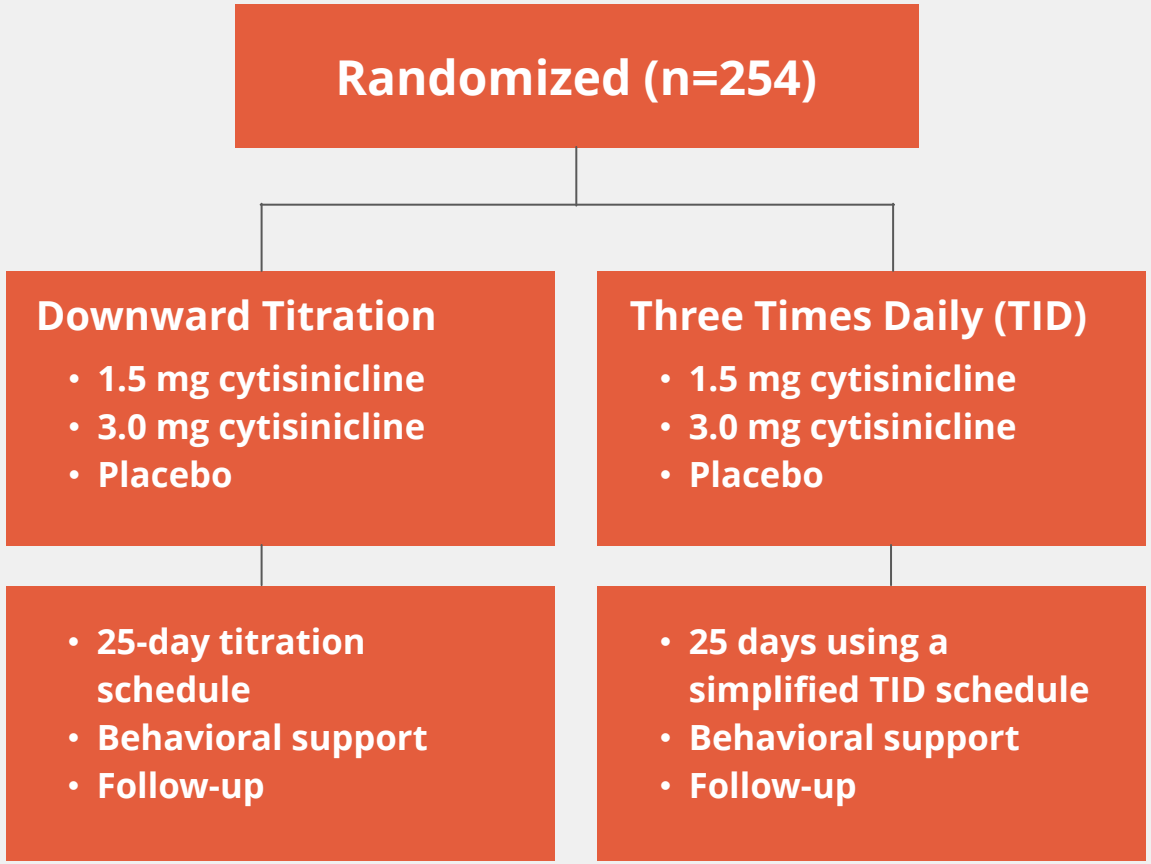
1. Cahill K et al; The Cochrane Library 2013, Issue 5 (For NRT, Bupropion and Varenicline)
2. Cahill K et al; Cochrane Database of Systematic Reviews 2016, Issue 5
3. ORCA-1 publication in NTR for 3mg TID arm weeks 5-8
4. ORCA-2 and ORCA-3 Odds Ratios at the longest follow up (weeks 9-24) for 3mg TID dosing

ORCA-1: Phase 2b Study Overview

Objective:
- Optimize Phase 3 trial planning for dosing, scheduling, compliance and efficacy rates in U.S.
- Evaluate safety and efficacy of 1.5 mg and 3 mg of cytisinicline placebo administered over 25 days
- All subjects received standardized behavioral support and followed 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

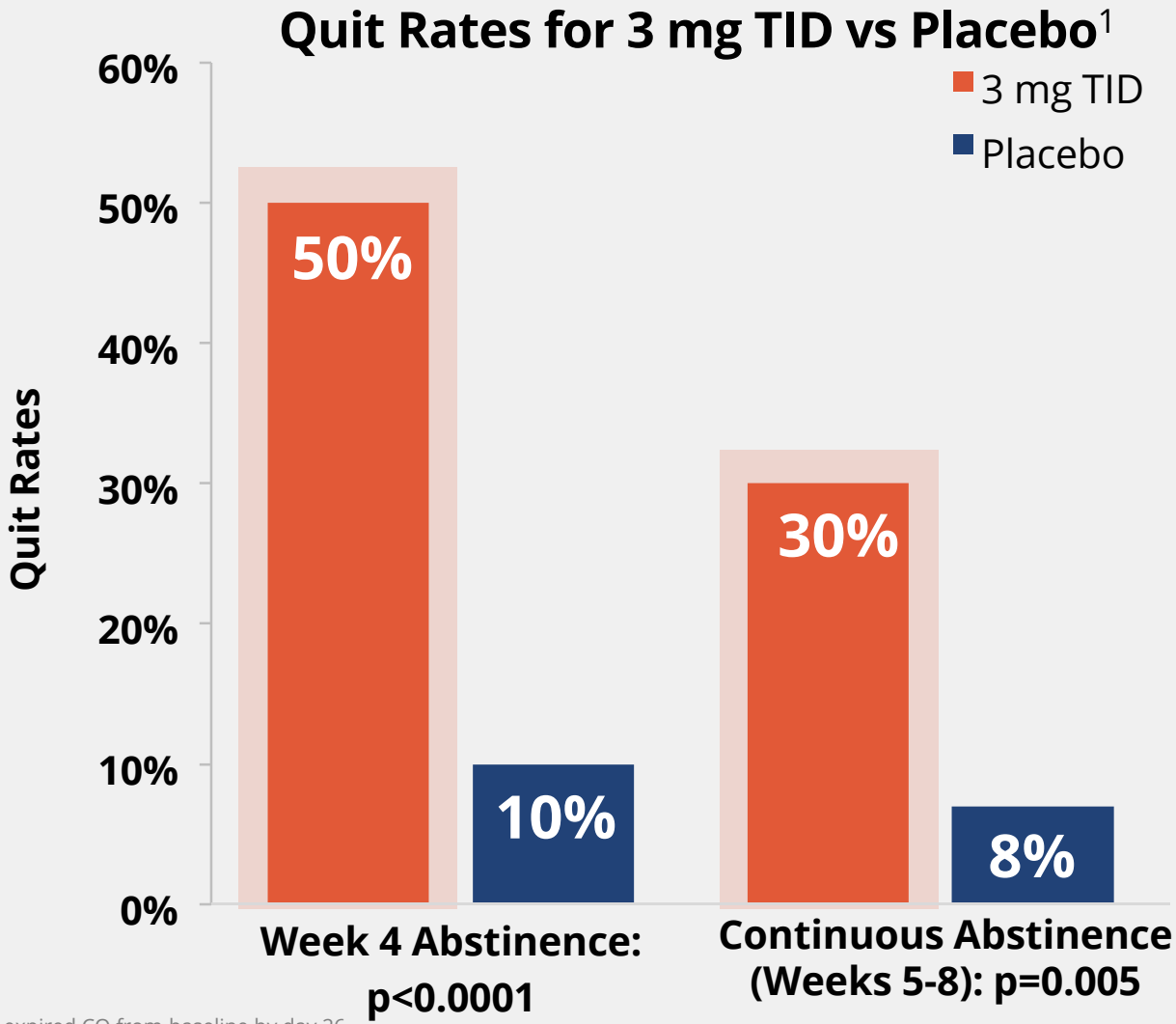


ORCA-1: Baseline Subject Demographics

	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
previous quit attempts	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						
Patch	27 (52%)	25 (50%)	23 (45%)	19 (38%)	28 (55%)	122 (48%)
All Other NRT	22 (42%)	16 (32%)	21 (41%)	12 (24%)	26 (51%)	97 (38%)
e-cigarettes	19 (37%)	13 (26%)	15 (29%)	11 (22%)	18 (35%)	76 (30%)

ORCA-1: Phase 2b Study Results

Statistically Significant Efficacy Observed for 3.0 mg TID



Odds Ratios (OR)

5.04[1]

95% CI (1.42-22.3)

Compliance

>94%[1]

across all arms

Reduction in Expired CO*

80%[2]

*Average % reduction expired CO from baseline by day 26

1. Source: Nicotine Tob Res. 2021 Aug 29;23(10):1656-1663.
2. Data on file.

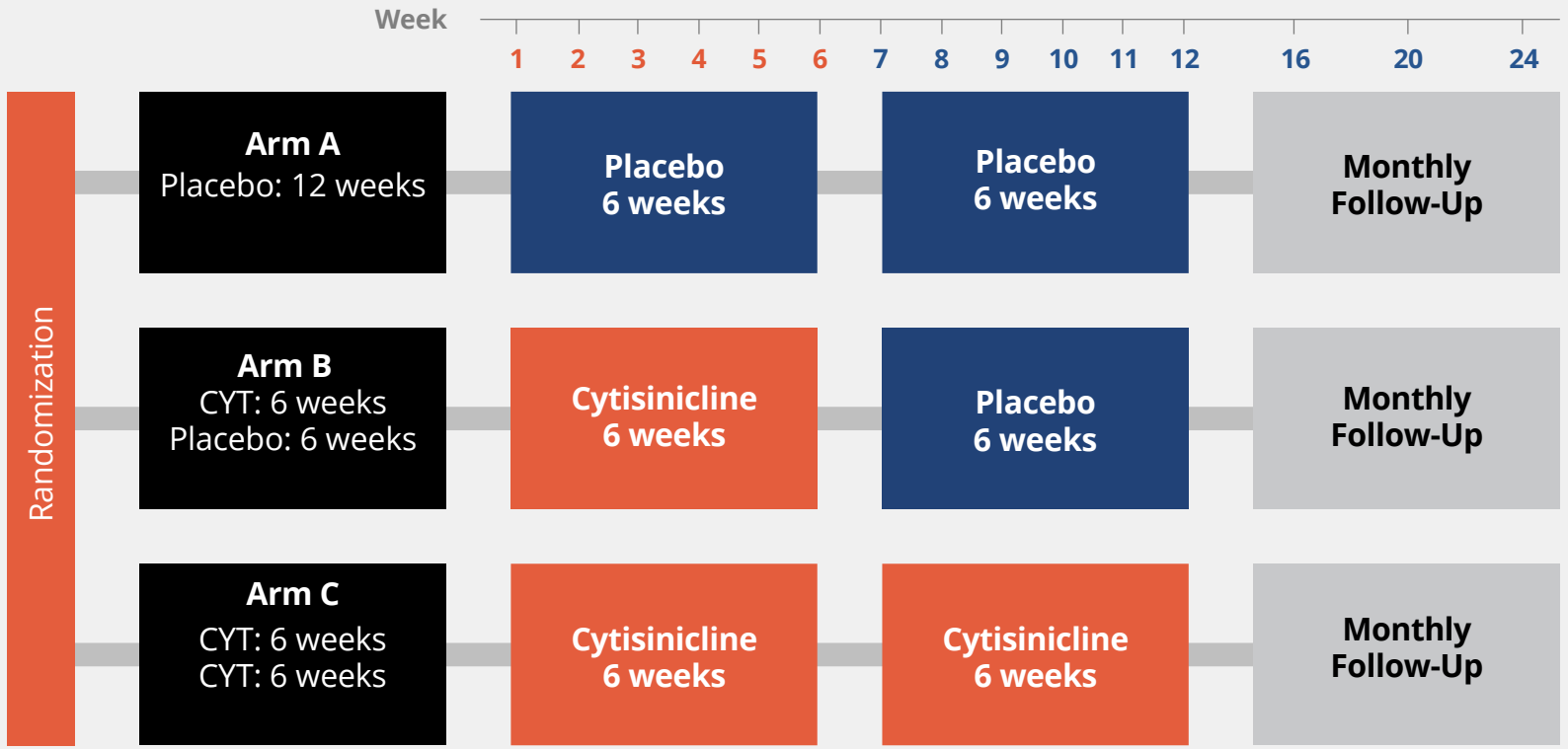
Phase 3 Study Designs: ORCA-2 & ORCA 3

Objective:

- Evaluate safety and efficacy of 3.0 mg of cytisinicline vs placebo administered 3x daily (TID) for 6 & 12 weeks
- All subjects received standard behavioral support and were followed out 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:

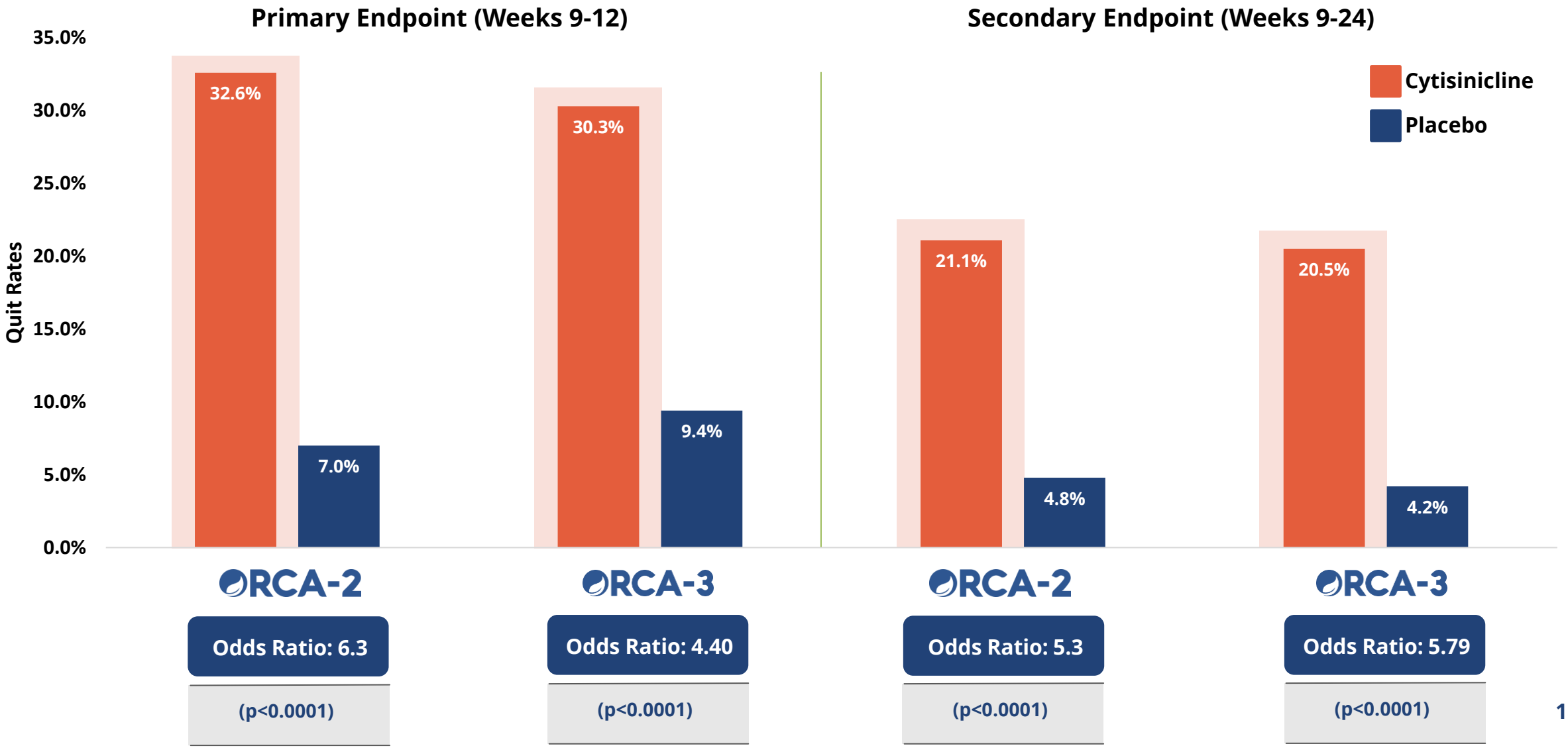
- >95% power for the 24-week comparisons

ORCA-2 and ORCA-3 Demographics and Baseline Characteristics

Characteristic	ORCA-2 Randomized (N=810)	ORCA-3 Randomized (N=792)
Sex		
Female	442 (55%)	439 (55%)
Male	368 (45%)	353 (45%)
Race		
White	659 (81%)	631 (80%)
Black or African America	130 (16%)	139 (18%)
Other	21 (3%)	21 (2%)
Age (yrs)		
Median	54	52
Average # Daily Cigarettes in last 30 days		
Median	20	20
Duration of Smoking Years		
Median	38	36
# of Previous Quit Attempts		
Median	4	4

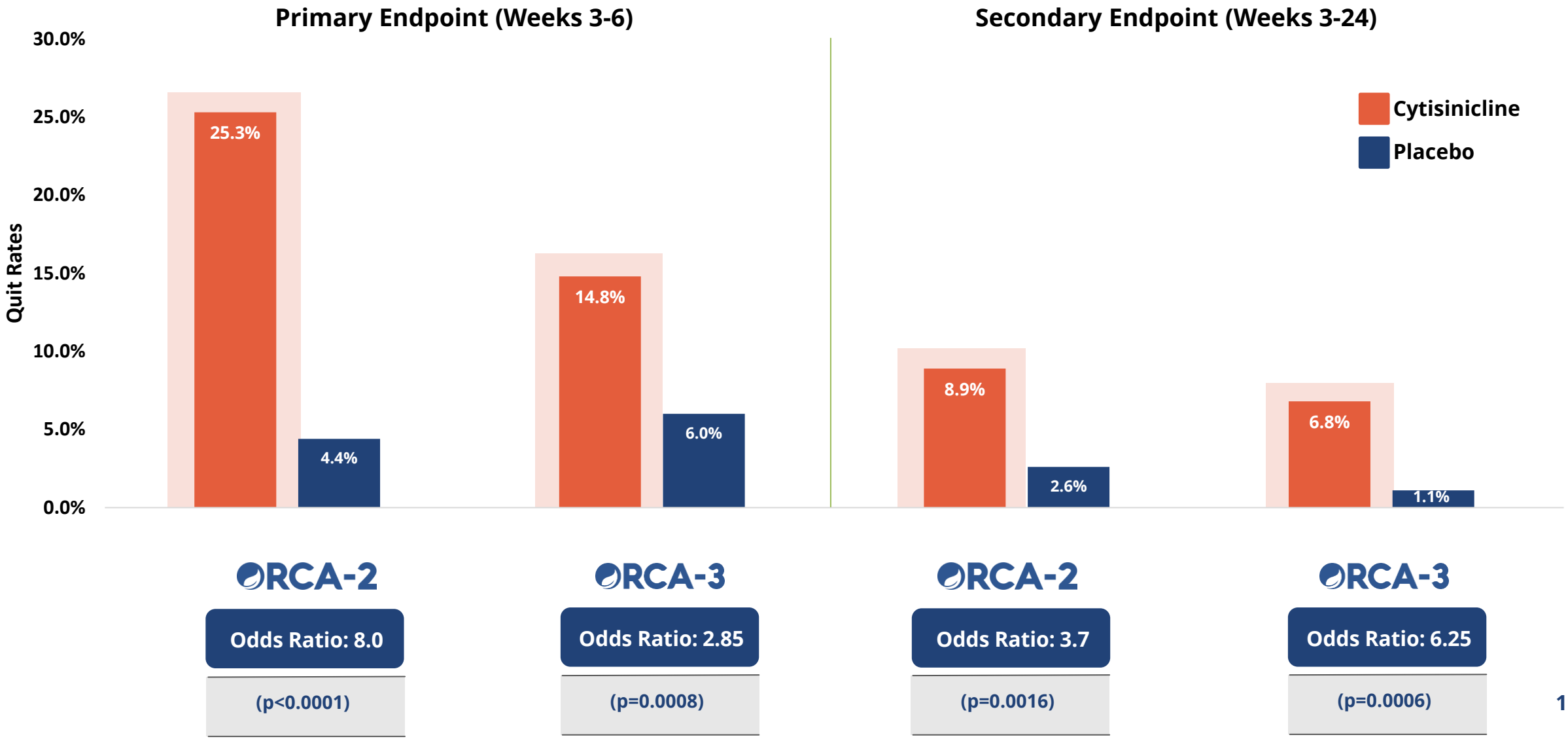
12-week Cytisinicline Treatment:

ORCA-2 and ORCA-3



6-week Cytisinicline Treatment:

ORCA-2 and ORCA-3



Safety Profile:
Well-tolerated with low rates of adverse events reported

Most commonly reported AE's (>5% Overall)[1]

Adverse Event (AE)	Placebo n=532	6-week CYT n=532	12-week CYT n=530
	ORCA-2 ORCA-3 *combined*	ORCA-2 ORCA-3 *combined*	ORCA-2 ORCA-3 *combined*
At least 1 TEAE	330 (62.0%)	342 (64.3%)	352 (66.4%)
Insomnia	33 (6.2%)	52 (9.8%)	57 (10.8%)
Abnormal Dreams	23 (4.3%)	46 (8.6%)	41 (7.7%)
Nausea	39 (7.3%)	41 (7.7%)	33 (6.2%)
Headache	38 (7.1%)	38 (7.1%)	43 (8.1%)

No treatment-related serious adverse events reported

1. Data on file; Achieve Life Sciences ORCA-2 and ORCA-3 combined

Open Label Exposure Study Design (ORCA-OL)

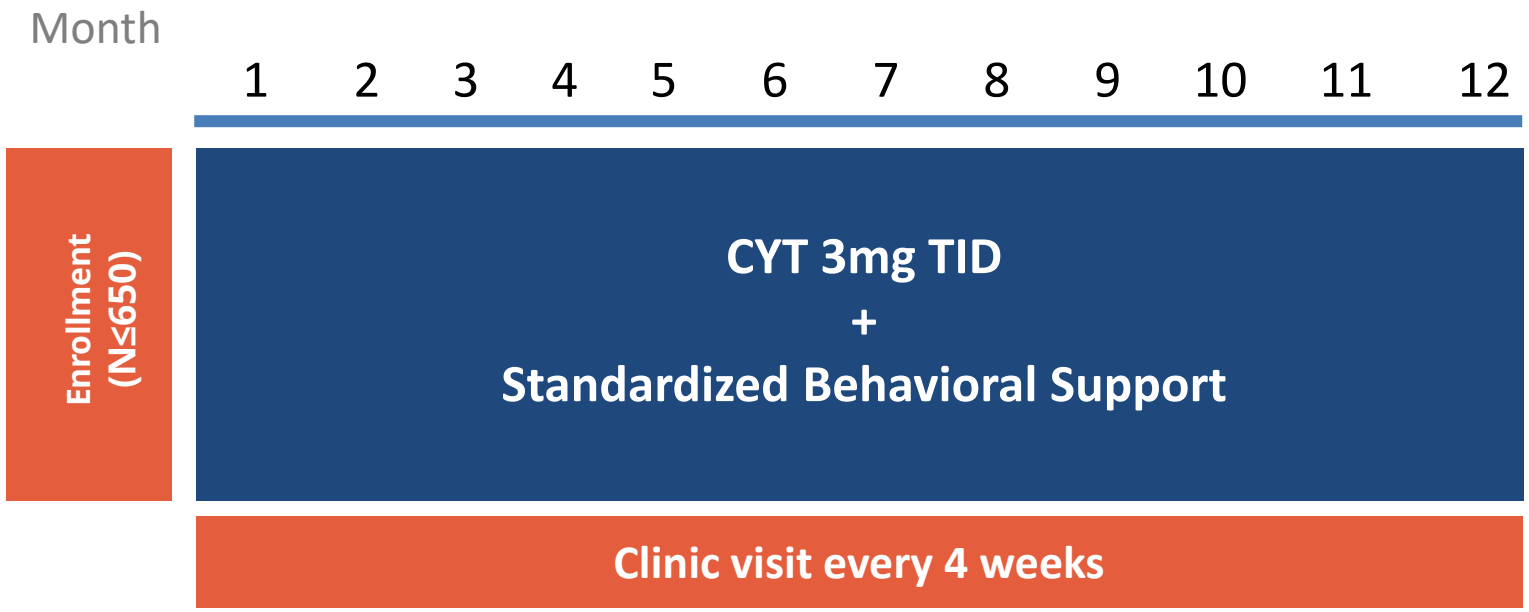
Study initiation anticipated in Q2'24

Objective:

- Evaluate safety of 3.0 mg cytisinicline TID for up to 52 weeks of treatment
- Assess efficacy with longer term treatment duration

Population:

- Relapsed cytisinicline-treated subjects from prior ORCA program trials
- Biochemically verified daily smoking or nicotine vape use



Safety Assessments:

Primary Endpoint:

- Incidence rate of serious adverse events

Secondary Endpoints:

- Reported adverse events

Efficacy Assessments:

- Smoking abstinence rates (self-reported and biochemically verified)
- Time to cessation
- Time to relapse

e-Cigarette Market

Growing Unmet Need

~11M

Adult e-cigarette users in the U.S.[1]

73%

Intend to quit vaping in the next 3-12 months[2]

65%

Of vapers would try a new, natural treatment*

No currently approved treatments specifically indicated for nicotine e-cigarette or vaping cessation

500+

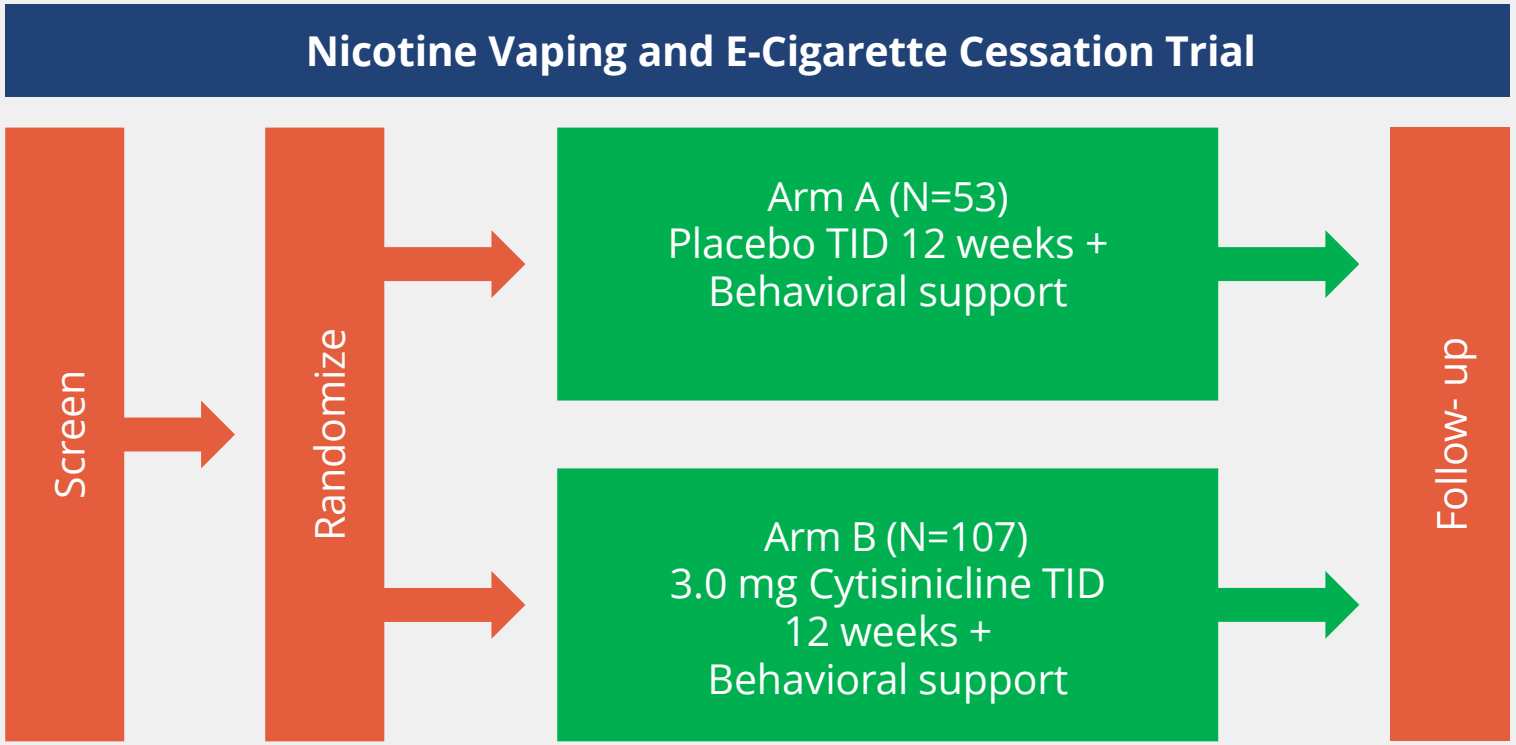
Achieve/IQVIA survey of 500+ subjects supports intention to quit[2]

*Of vapers who aim to quit in the next three months.

1. Cornelius ME, Loretan CG, Jamal A, et al. Tobacco Product Use Among Adults – United States, 2021. MMWR Morb Mortal Wkly Rep 2023;72:475–483
2. IQVIA Vaping Cessation Landscape Report, March 2020.

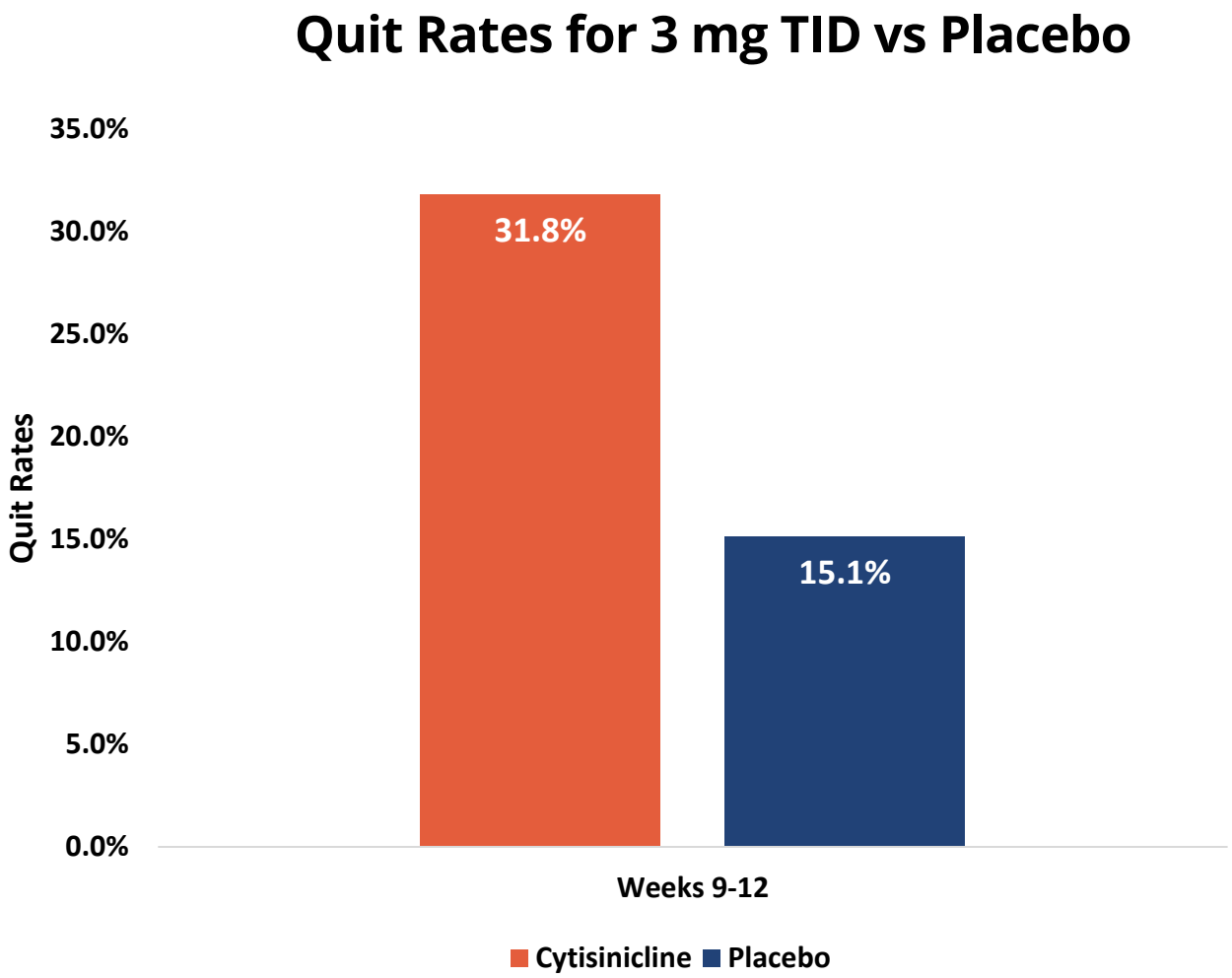
ORCA-V1: e-Cigarette Cessation

- Objective: Evaluate cytisinicline as an aid to vaping cessation in adult users of nicotine e-cigarettes who intend to quit
- Phase 2 ORCA-V1 a multi-center, double-blind, randomized, placebo-controlled, study
- NIH Grant awarded to evaluate nicotine e-cigarette cessation
  - Providing non-dilutive funding for Phase 2 ORCA-V1 trial
- Top line data announced April 2023
- End of Phase 2 meeting planned in 2024



ORCA-V1 Results:

2.6x increased likelihood of cessation at end of treatment



Primary Endpoint:
Weeks 9-12 Odds Ratio

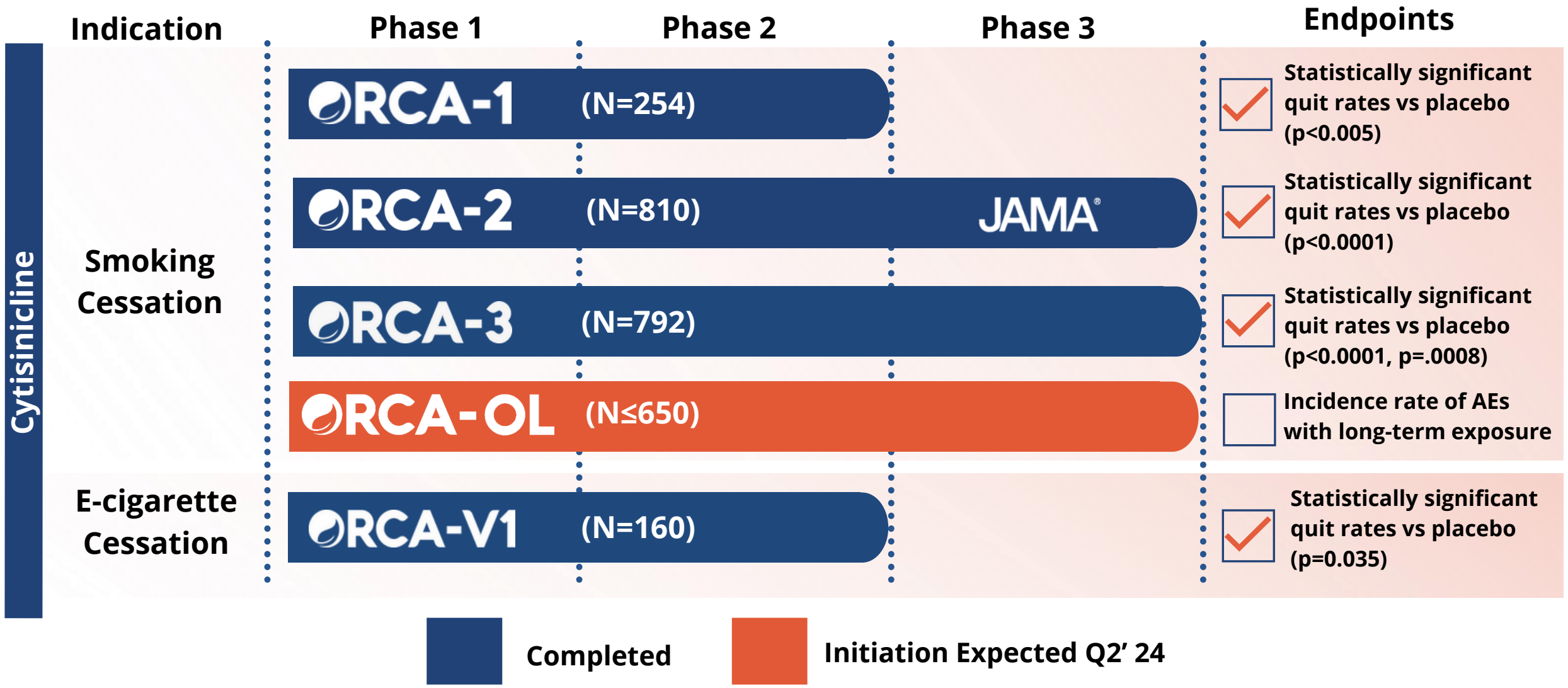
2.64 (p=0.035)

- **Primary endpoint met with statistically significant quit rates demonstrated during the last four weeks of treatment.**
- **Cytisinicline was well-tolerated with no serious adverse events reported.**

ORCA-V1

ORCA Development Program

NDA submission targeted for 1H'25 with 300 subjects from ORCA-OL treated for 6 months



Broad IP Portfolio Providing Patent Protection to 2040

PATENT PORTFOLIO

- Several patent families pursued globally including formulation, method of use, extraction
- 26 granted patents, 10 patent families; 50 pending patent applications
- Issued patents
  - 3.0 mg TID dose and administration (Q3 2040)
  - New cytisinicline salt formulations
- Ongoing discovery and other development work providing additional IP opportunities

REGULATORY EXCLUSIVITY

- U.S. – 5 years for NCE under Hatch-Waxman
- Orange Book listable patents extend U.S. regulatory exclusivity to minimum of 7.5 years
- Europe – Up to 10 years possible in countries where cytisinicline not already approved

EXCLUSIVE 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 CNS indications
- Started as a challenge project to make synthetic cytisinicline
- Research ongoing in partnership with UCLA, UCSF, Cambridge & University of Milan

Strong Cash Position

$15.6M of cash as of December 31, 2023

$60.0M of financing gross proceeds announced in February 2024

2025 Solidly funded cash runway into second half of 2025

Management Team

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

John Bencich
Chief Executive Officer

An experienced financial executive with 20 years of experience in the pharmaceutical industry having served as CFO and in senior financial positions at multiple public and private companies including OncoGenex, Integrated Diagnostics, Allozyne, and Trubion (acquired by Emergent).

Rick Stewart
Executive Chairman of the Board of Directors

Nearly 25 years of experience in the pharmaceutical industry having founded and served as CEO for private and public companies Ricanto, Renown Pharma, Brabant Pharma (sold to Zogenix), Huxley Pharma (sold to BioMarin), and Amarin Corp. Also founded and held the positions of CFO and CBO of SkyePharma.

Cindy Jacobs, Ph.D., M.D.
President & Chief Medical Officer

With over 30 years of experience in the biotechnology/pharmaceutical industry, Dr. Jacobs is an experienced executive in drug development. She served as EVP & CMO of OncoGenex, CMO & SVP of Corixa Corporation, and held VP Clinical Research positions at two other biopharmaceutical companies.

Dr. Anthony Clark
Chief Scientific Officer

Extensive experience in the biotechnology/pharmaceutical industry, Dr. Clarke is a founder and director of Ricanto, and currently serves as CSO of Renown Pharma. Dr. Clarke was CSO of Huxley Pharma, Brabant Pharma, and was VP Clinical Research and Regulatory Affairs of Amarin Corp.

Jaime Xinos
Executive VP, Commercial

More than two decades of commercial experience, including VP, Marketing and Corporate Communications at OncoGenex, and previous marketing, commercial development, sales and marketing leadership roles at Pfizer, Novartis and Abbott Labs.

Company Highlights

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