

Alpha
Cognition

Corporate Presentation

Bringing hope to people living with Neurodegenerative Diseases

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ALL CURRENCIES DENOTED ARE IN UNITED STATES DOLLARS UNLESS OTHERWISE INDICATED

NDA Accepted Biopharmaceutical Company Focused On Neurodegenerative Diseases

1

ALPHA 1062 – Best-In-Class Treatment Potential for Alzheimer’s Disease

- Large US \$5.5B, 11M Prescription (Rx) market characterized by high drug dissatisfaction and discontinuation¹
- Oral therapy uniquely designed to reduce side effects and improve long term patient outcomes
- Long Term Care (LTC) provides initial commercial opportunity (\$2B) with future expansion to Neurology (\$1.7B)

2

De-risked New Drug Application for Alzheimer’s Disease With A High Probability Of Success

- NDA submitted Sept 2023 and filing accepted by FDA Dec 2023
- Approval Targeted Q3/24; Commercialization Q1/25; Revenue generating 2025
- If approved, ALPHA-1062 will be the second Alzheimer’s Disease oral treatment approved in the last 10 years
- Patent protection granted through 2042 with additional patent filings in 2024

3

Experienced Leadership Team - History Of Multi-Billion Drug Launches

- Over 20 product launches and over 25 approvals in the USA and Europe.
- Industry leading commercial experience in Long Term Care (LTC)
- Multiple billion dollar drug launches (CELEBEX[™], CRESTOR[™], NEXIUM[™], SEROQUEL[™]) by leadership team

Alzheimer's Disease Overview

Alzheimer's Disease (AD) is a type of dementia that causes a slow decline in memory, thinking and reasoning. AD therapy represents a significant US market with high dissatisfaction, primarily due to adverse events and limited efficacy over time.

SIGNIFICANT MARKET



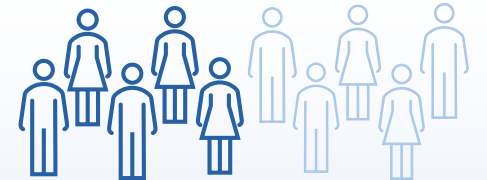
AD Impacts an estimated **6.7M** people in the U.S.
40% of life after AD spent in **Long Term Care Facility** with severe disease



11 million prescriptions written annually to treat AD and **80% of patients** prescribed **AChEI's**¹

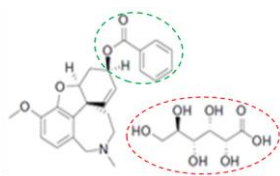


72% of MD's are **dissatisfied** with treatments mainly due to **medication side effects**

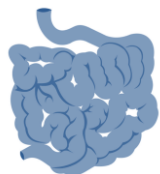


55% of patients **discontinue current medications** therapy at **12 months**^{4,5}

Potential best-in-class treatment designed to optimize efficacious dose, minimize treatment-limiting side-effects and improve long-term outcomes



The formation of the benzoyl ester eliminates AChE inhibition; the gluconate salt increases solubility



ALPHA-1062 is absorbed in the small intestine as an inactive compound with minimal or no side effects



ALPHA-1062 is subject to 1st pass effect, cleaving the benzoyl ester, resulting in the release of galantamine (active moiety)



Galantamine, the metabolite, may circulate with greater bioavailability (ability to be absorbed and used by the body)

Why Galantamine? Unique Brain Receptor Modulation And Excellent Long-Term Data

- Galantamine **affects multiple brain receptors to exert effect**
- Galantamine has **demonstrated anti-inflammation effects**²
- Galantamine has been associated with:^{3,5}
 - **Improved Memory and Attention**
 - **Significantly lower risk of death** (P-value <0.001)
 - **Strongest AChEI effect on cognitive decline**
 - **Demonstrates significant reduction in risk of developing severe dementia** (P-value 0.05) compared to donepezil (P-value 0.13) and rivastigmine (P-value 0.24)
- Use of Galantamine reduces **nursing home admission by 31% per year** of treatment⁴



Galantamine Enhances Acetylcholine Levels And Modulates Nicotinic Receptor Sensitivity



Decreased acetylcholine levels and *loss of* nicotinic acetylcholine receptors (*nAChR*) **negatively impacts learning, memory, and function**

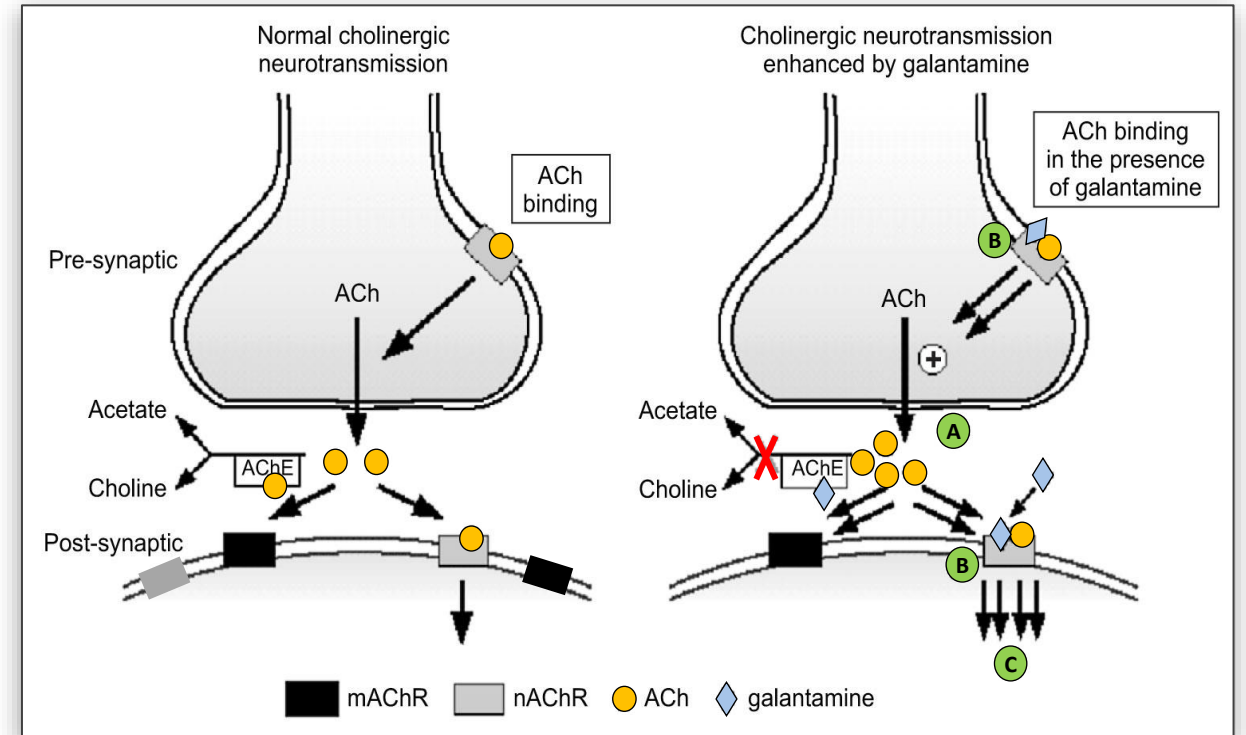


Current therapeutics¹ increase acetylcholine levels by inhibiting acetylcholinesterase (AChE)



Modulation of nAChR ($\alpha 7/\alpha 4\beta 2$)²:

- Stimulates the cholinergic pathway
- Modulates inflammation
- Buffers the effects of amyloid
- Enhances release of *other transmitters*:
Glu, DA, GABA, 5HT - resulting in enhanced:
 - Memory acquisition and retrieval
 - Attention and activity
 - Stabilization of behavior
 - Inhibition of cell death and neuroprotection



- A Galantamine raises the concentration of ACh in the synaptic cleft by inhibiting AChE
- B Galantamine modulates nAChRs, making them more sensitive to ACh
- C Raised ACh and enhanced response of nAChRs to ACh lead to improved post-synaptic response

Pivotal Trial Results Provided Data Enabling NDA Filing

Bioequivalence Study vs. Immediate Release

PK Parameter	ALPHA-1062 Delayed Release 5mg (n=36)	Gal HBr Immediate Release 4mg (n=36)	% to Reference Drug 80-125%	Sufficient Data for NDA Filing
AUC _{0-inf} (μg × h/mL) Fasted State	306.8	321.5	95%	✓
C _{max} (ng/mL) Fasted State	30.7	40.5	76%	✓
AUC _{0-inf} (μg × h/mL) Fed State	286.7	329.9	87%	✓
C _{max} (ng/mL) Fed State	27.6	30.2	91%	✓

Bioequivalence Study vs. Extended Release

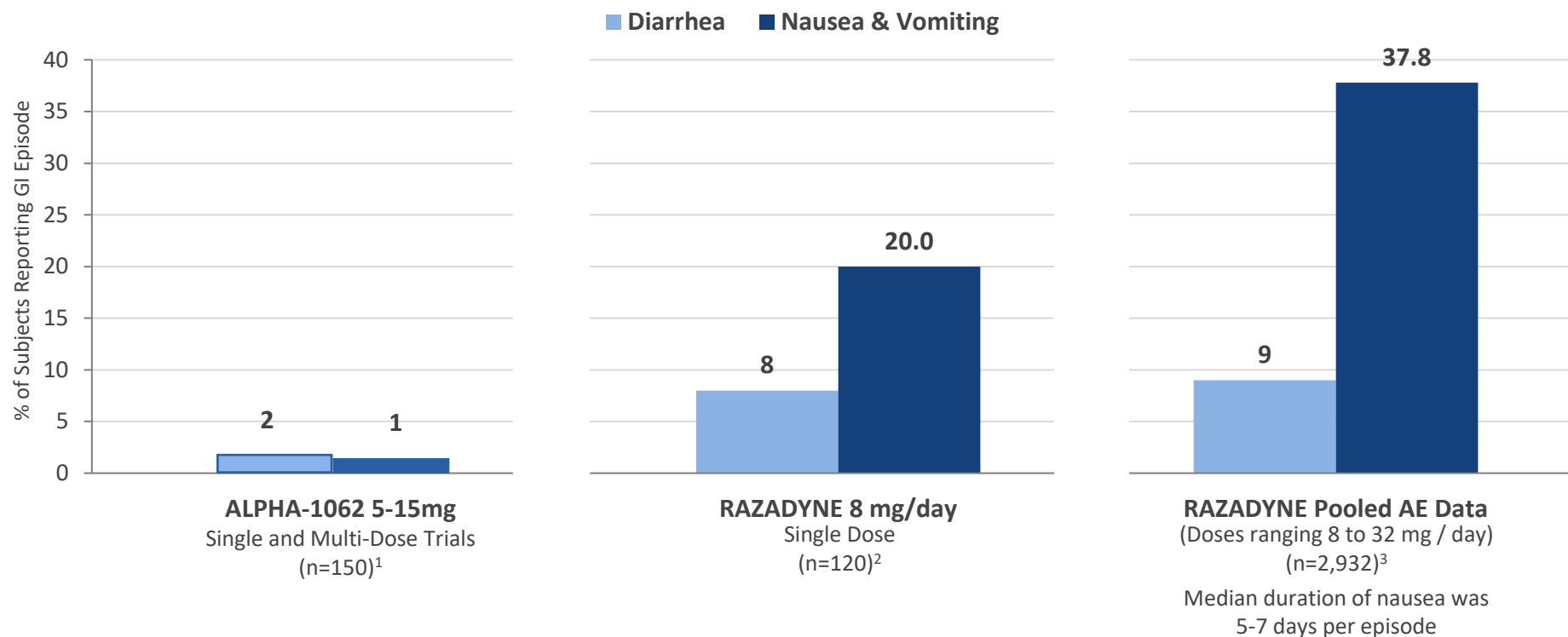
PK Parameter	ALPHA-1062 Delayed Release 5mg (n=20)	Gal HBr Extended Release 8mg (n=20)	% to Reference Drug 80-125%	Sufficient Data for NDA Filing
AUC ₀₋₂₄ (μg × h/mL) Steady State	527.5	492.1	107%	✓
C _{max} (ng/mL) Steady State	41.7	32.8	127%	✓

- Data confirmed **ALPHA-1062 AUC was bioequivalent to galantamine hydrobromide IR and ER**
- C_{max} for ALPHA-1062 is bracketed between IR and ER (lower than IR, higher than ER) providing necessary data for NDA filing (scientific bridge)
- Minimal adverse events reported in these trials
- **Enabled NDA filing** based on 505(b)(2) requirements

90% Confidence Interval (CI) acceptance criteria is 80-125% for the test/reference ratio

















Studies Have Demonstrated Improved Gastrointestinal Side Effect Profile*

**≤ 2% GI side-effects with oral formulations of ALPHA-1062
(Delayed Release and Sublingual Tablets, n=150)**

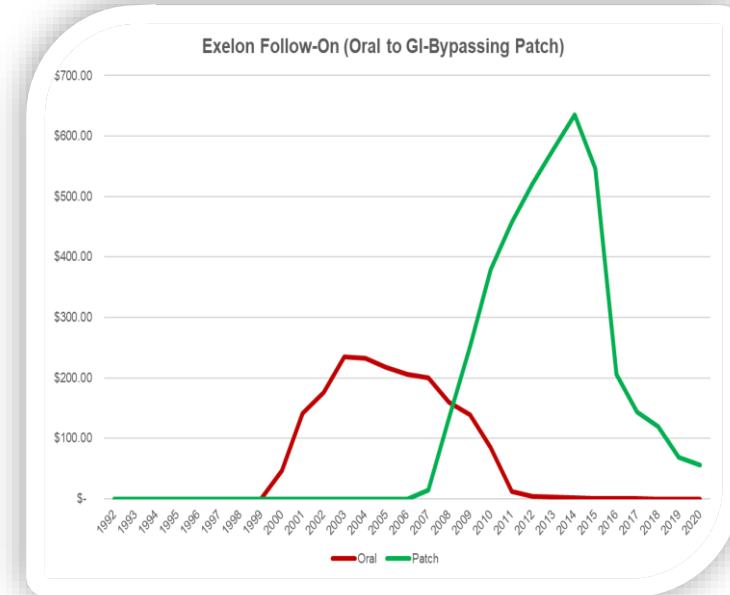
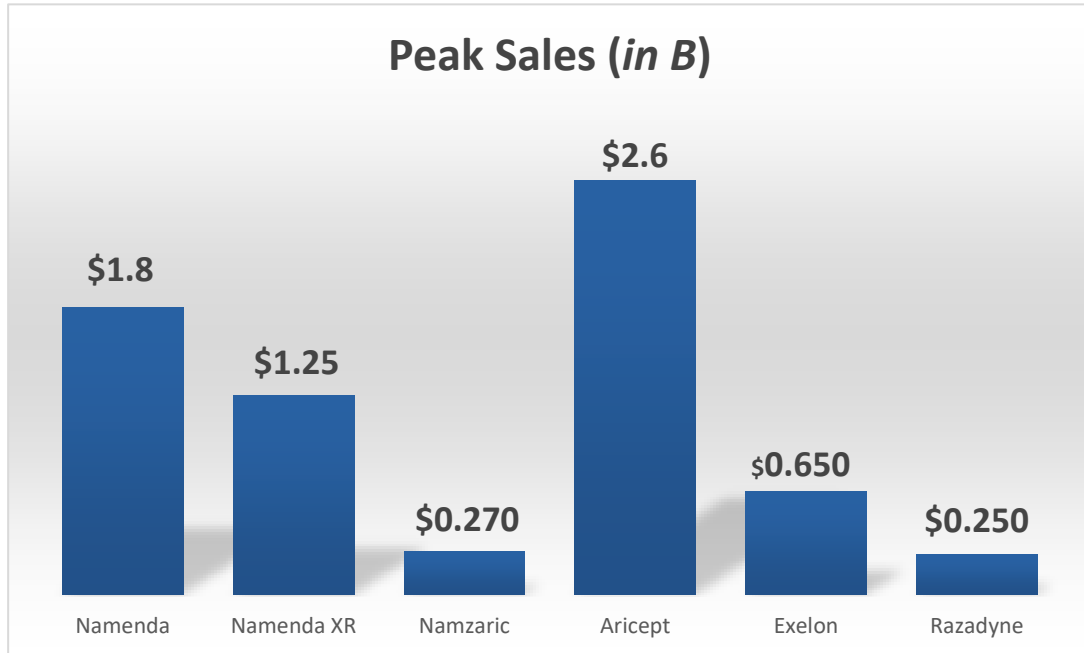


**Data from separate product monographs; comparative clinical significance has not been proven*

ALPHA-1062: Offers Potential Best-In-Class Profile Versus Approved AChEIs

		ALPHA-1062	 Aricept <i>Razadyne</i> ^{ER}	EXELON [®]
GI Safety Profile	Reduced GI side-effects (diarrhea, nausea, vomiting)			
CNS Safety Profile	No incidence of insomnia			
Long Term Outcome¹	Significant risk reduction in risk of developing severe dementia			
Cognition Effects	Demonstrated strongest effect on cognition			
Mechanism of Action	Dual mechanisms of action that potentiate acetylcholine transmission and modulate nAChR ($\alpha7/\alpha4\beta2$) ²			

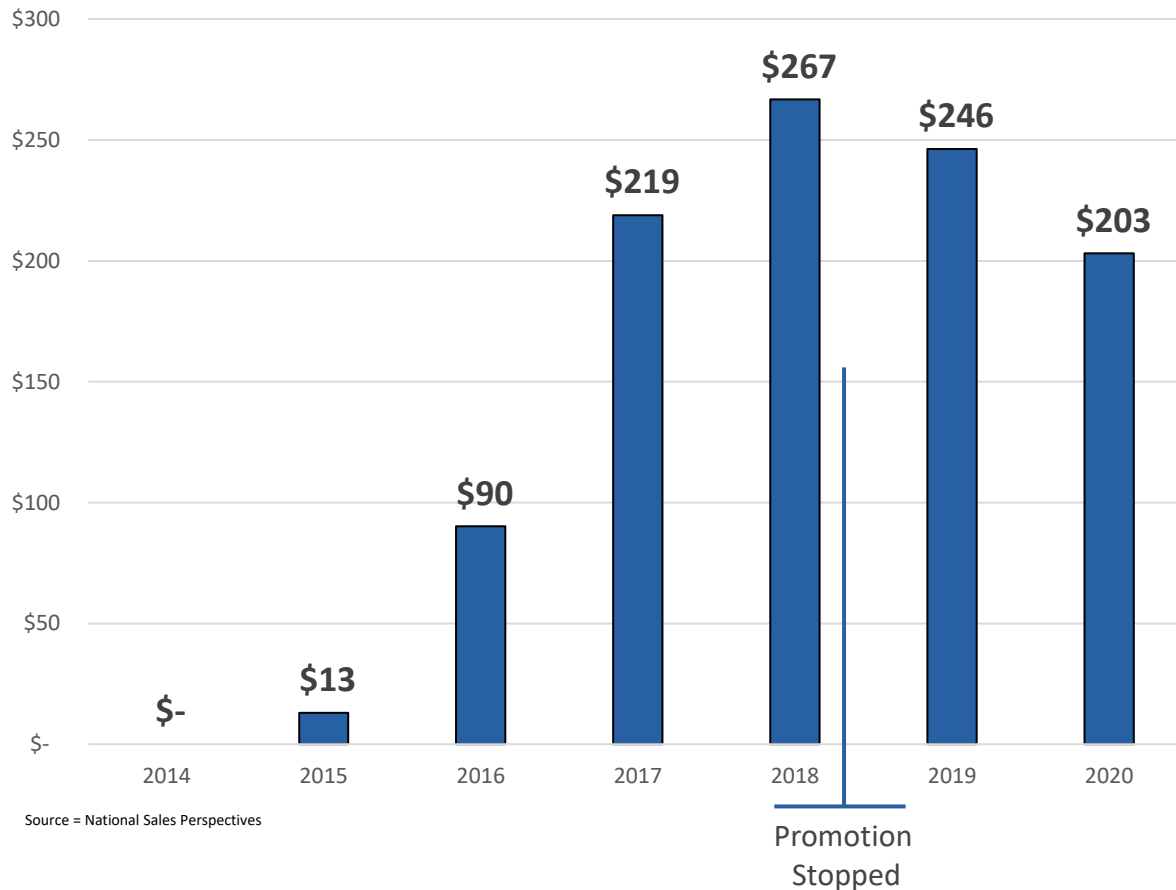
Multiple AD Launches Have Achieved Blockbuster Status



- Large US \$5.5B, 11M Rx market characterized by high drug dissatisfaction and discontinuation
- Multiple successful launches into the AD space
- **Significant brand sales despite generic competition**
- Exelon Patch (*above graph*) achieved \$650M in peak sales in fully generic market on promise of lower gastrointestinal adverse events

Despite No Differentiation Or Promotion, NAMZARIC, 505(b)(2) Treatment For Moderate-To-Severe Alzheimer’s Delivers +\$200M In Yearly Sales

NAMZARIC Sales by Year (\$M)

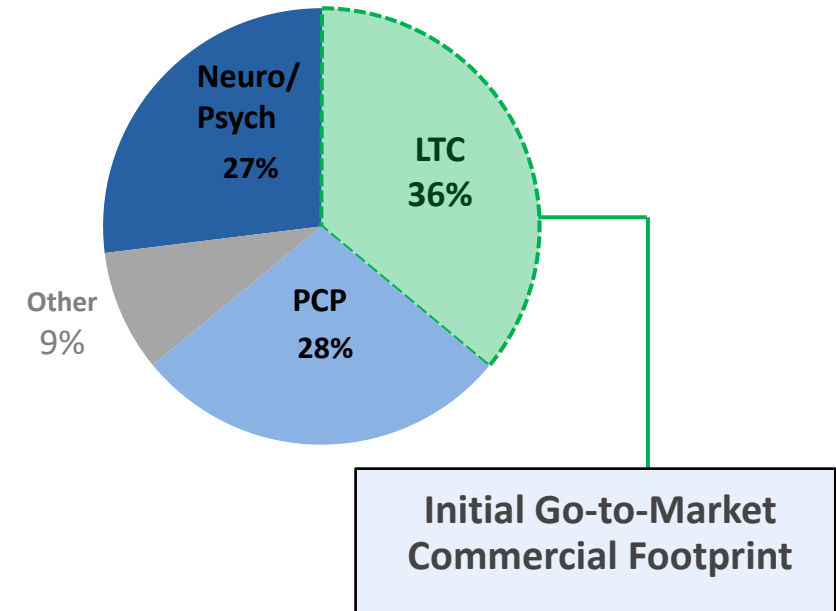


- NAMZARIC provides **base case for sales** for a new symptomatic entrant into the Alzheimer’s (AD) market
- 505(b)(2) pathway with **no differentiation versus generics**
- Moderate-to-severe AD is 33% smaller potential than mild-to-moderate AD
- Launched May 2015; **No promotion since 2018**
- ~75% of MA lives have access to NAMZARIC¹ with Average co-pay of \$50.00-\$67.50¹
- Average retail price of \$667.74¹

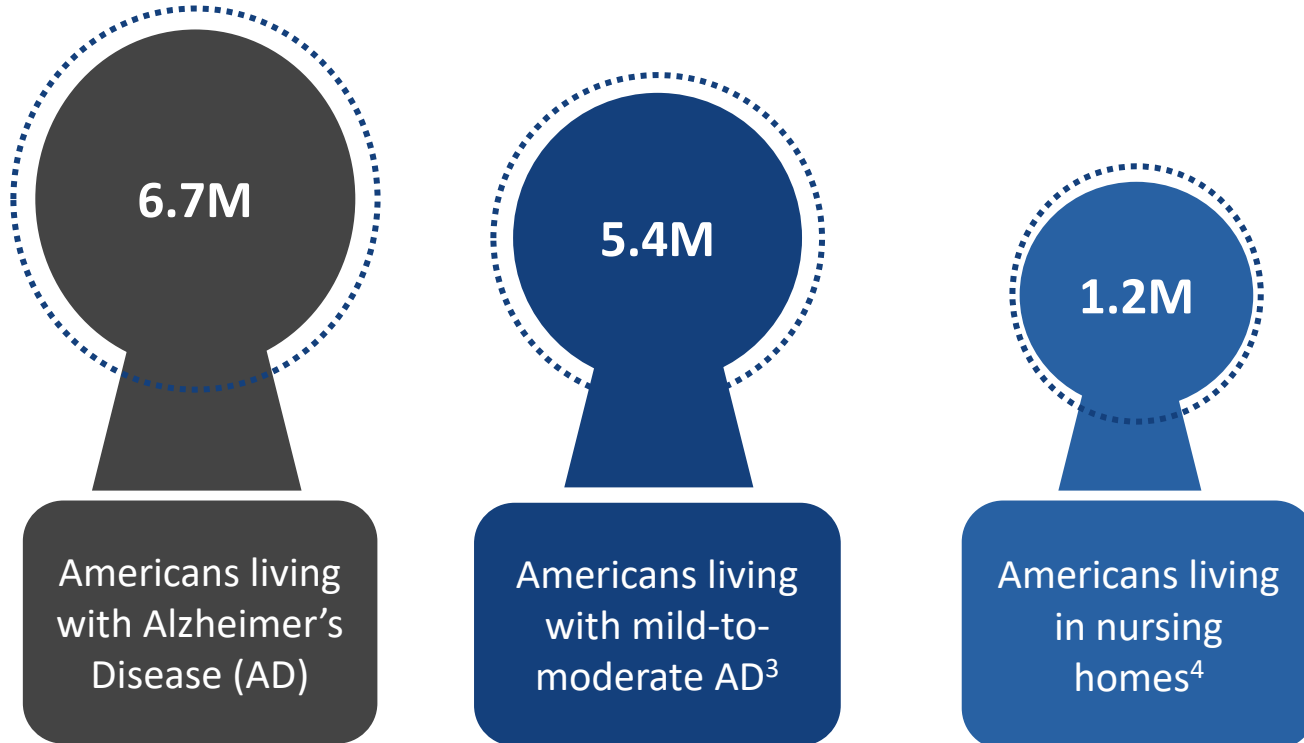
AChEIs Market Large But Dissatisfied Creating Opportunity For Improved Treatment Option, Specifically In Long Term Care (LTC)

- Large, but dissatisfied market creates significant market opportunity
 - 11M AChEI RX's dispensed each year
 - High discontinuation rates due to side-effects
- Initial go-to-market commercial footprint to focus on highest volume, most favorable market access conditions
 - LTC accounts for 36% of total market Rx's¹
 - LTC provides initial commercial opportunity (\$2B) with future expansion to Neurology (\$1.7B)
 - Branded medications used more commonly in LTC market
 - 65-70% of LTC lives have access to ALPHA-1062 with zero co-pay
 - LTC business model includes “best in class” reimbursement process

Prescriptions by Specialty



Alzheimer's Dementia Affects 70% Long Term Care (LTC) Residents And 88% LTC Doctors Likely To Prescribe



LTC represent ~13% of the AD population but delivers 36% of the market

Large, Underserved LTC Market

In Nursing Homes, Alzheimer's Dementia:

- Affects 70% residents¹
- Is the leading reason for placement¹
- Is the leading cause of death¹

Significant Dissatisfaction with Current Treatments Leads to ALPHA-1062 Opportunity

- Current treatment options cause burden for staff and risks for residents due to GI side effects and insomnia²
- 55% patients discontinue their AD medication due to side effects²
- ~88% of LTC HCPs Likely to Prescribe ALPHA-1062²

Commercialization Strategy Will Leverage Best-In-Class Profile And Focused Sales Effort At Launch

Commercial leadership intends to build
a best-in-class LTC sales force
with the following focus:



Potential key points of differentiation



Exploit key issues with existing AChEI
treatments



Franchise with potential additional indications
and new products

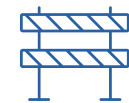
Success to be further enabled by:



Targeting largest volume nursing
homes/geriatricians specializing in Alzheimer's
Dementia



Experienced, account-based sales team with
demonstrated success in LTC



Limited payor barriers with 70% of residents



Strategic and clinical partnerships with
Consultant Pharmacists and LTC Pharmacies

Large but Dissatisfied Market

LTC represents
**largest AD
prescription volume**

**>50% discontinue
treatment at
12 months**

**88% LTC HCPs
likely to prescribe**

ALPHA-1062 Potential

**Reduced Adverse
Event Profile**

**Delayed
Progression of
Disease**

Strongest effect on
cognition

De-risked Clinical Development Program











**Positive
Bioequivalence
study results**

**FDA accepted NDA
submission.** PDUFA
date of July 2024

Near-term Milestones

**New Composition of
Matter Patent** Q1
2024

**ALPHA-1062
Expected Approval**
Q3 2024

Indication	Preclinical	Phase 1	Phase 2	Phase 3 /Pivotal	Entity Responsible
ALPHA-1062					
<i>Oral: Mild-to-Moderate Alzheimer's Disease (AD)</i>					
<i>Sublingual Formulation: Mild-to-Moderate Alzheimer's Disease (AD)</i>					
<i>Moderate-to-Severe Alzheimer's Combination with Memantine (AD)</i>					
ALPHA-1062 Intranasal (Partnered Asset)*					
<i>Cognitive Impairment with Mild Traumatic Brain Injury</i>					
ALPHA-0602, -702 -802 Progranulin Franchise					
<i>ALS and SMA; Neurodegenerative diseases</i>					

Potential Catalysts And Upcoming Events

- 2024**
- *Composition of Matter IP filing – US/Rest of World (Q1)*
 - *ALPHA-1062 anticipated FDA product approval (Q3)*
 - *IND Submission for Cognitive Impairment with mTBI – Alpha Seven Therapeutics (Q4)*
 - *DOD Sponsored Bomb-blast study results (preclinical) (Q4)*

- 2025**
- *ALPHA-1062 commercial launch (1Q)*
 - *ALPHA-1062/Memantine initiation of clinical trial (2H)*
 - *mTBI PH2 interim study results – Alpha Seven Therapeutics (Q3)*

Leadership Has Impressive Track Record For Successful New Drug Development And Commercialization



Michael McFadden
Chief Executive Officer



Denis Kay
Chief Scientific Officer



Lauren D'Angelo, MBA
Chief Operating Officer



Don Kalkofen
Chief Financial Officer

UROVANT
SCIENCES

neurodyn

UROVANT
SCIENCES

Protagonist
Therapeutics

AVANIR
pharmaceuticals

CNS|CRO
Preclinical Neurological Disease Services

AVANIR
pharmaceuticals

DEPOMED

AMYLIN

MEDIVATION

align

PHARMACIA

Genentech

Lilly

AstraZeneca

pwc

Share Structure

ACOG.CN, ACOGF		
Share Price (as of January 31, 2024)	\$0.83 CAD / \$0.65 USD	
Market Cap	\$124M CAD / \$97M USD	
January 22, 2024		
	Issued and Outstanding*	% of total
Common Shares	149,733,036	60.65%
Class B Preferred Series A Shares	7,916,380	3.21%
Performance Shares	6,821,057	2.76%
Non-Trading Warrants	61,732,886	25.01%
Stock Options	<u>20,672,207</u>	<u>8.37%</u>
TOTAL ALL SHARES	246,875,566	100%

*PROFORMA



**Alpha
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