Alpha Cognition

Corporate Presentation

October 2024

Bringing hope to people living with Neurodegenerative Diseases

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Forward-Looking Statements

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Alpha Cognition's Oral Therapy ZUNVEYL Has Received FDA Approval To Treat Alzheimer's Disease

The Second Oral Therapy Approved This Decade, ZUNVEYL's Dual MOA Was Designed to Eliminate Drug Absorption in the Gastrointestinal (GI) Tract, Potentially Addressing Certain Tolerability Issues with Leading Alzheimer's Disease (AD) Medications, Combined with a Long-Term Efficacy Profile

INDICATION: ZUNVEYL (benzgalantamine) is a cholinesterase inhibitor indicated for the treatment of mild to moderate dementia of the Alzheimer's type in adults.

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Commercial and R&D Biopharmaceutical Company Focused On Neurodegenerative Diseases

1 ZUNVEYL® – Differentiated Treatment Potential for Alzheimer's Disease

- Large US 11M annual prescription (Rx) market characterized by high drug dissatisfaction and discontinuation[1]
- Oral therapy uniquely designed to reduce side effects and improve long term patient outcomes
- Long Term Care (LTC) represents approximately 36%[2] of annual prescription and provides an estimated, potential initial commercial opportunity ($2B)[3] with future expansion to Neurology (27% of annual prescription, $1.5B)[4]

2 Pipeline to expand treatments for Alzheimer's Disease

- ZUNVEYL approved for treatment of mild-to-moderate Alzheimer's disease (AD) July 26, 2024
- ALPHA-1062 sublingual tablet to treat AD patients with aphagia in pre-clinical development
- ALPHA-1062 combination product to treat AD patients with moderate-to-severe disease in pre-clinical development
- Patent protection granted through 2044

3 Experienced Leadership Team - History Of Multi-Billion Drug Launches

- Management team has been involved over 20 product launches and over 25 approvals in the USA and Europe for other companies
- Extensive commercial experience in Long Term Care (LTC)
- Multiple billion dollar drug launches (CELEBREX™, CRESTOR™, NEXIUM™, SEROQUEL™) by leadership team

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1. Symphony METYS Retail 2019:Includes donepezil, galantamine, rivastigmine and Namzaric
2. Symphony METYS Retail 2019; Average WAC prices from Access Pointe Managed Markets Market Research
3. . Estimated based on US$11 million annual prescriptions x LTC percentage of prescriptions (36%) x average WAC price of $500
4. Estimated based on US$11 million annual prescriptions x Neurology percentage of prescriptions (27%) x average WAC price of $500
5. Prescription Drug User Free Act

Alzheimer's Disease Has Significant Treatment Challenges And High Drug Discontinuation

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

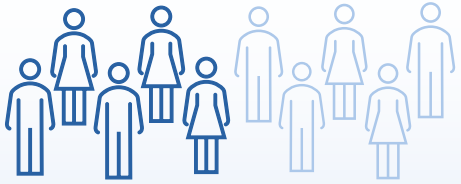
AD Impacts nearly **7M** people in the U.S.[1]

40% of life after AD spent in **Long Term Care Facility** with severe disease[1]

11 million prescriptions written annually to treat AD and **80% of patients prescribed Acetylcholinesterase Inhibitors (AChEI's)[2,3]**

UNMET MEDICAL NEED

72% of MD's are dissatisfied with treatments mainly due to **medication side effects[4]**



55% of patients discontinue current medications therapy at 12 months[3]

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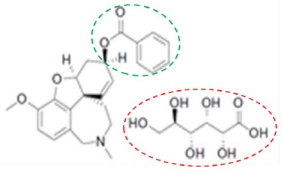
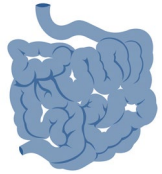
1. Alzheimer's Association 2024 Facts and Figures
2. Clarivate DRG Market Forecast Assumptions Dashboard
3. Data on File Symphony METYS Retail 2019
4. Data on File Market Research, Affinity Group July 2021

ZUNVEYL: Uniquely Designed Prodrug Of Galantamine

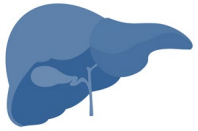
Potential treatment designed to optimize efficacious dose, minimize treatment-limiting side-effects and improve long-term outcomes



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



ZUNVEYL is absorbed in the small intestine as an inactive compound with <u>minimal or no side effects</u>



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

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

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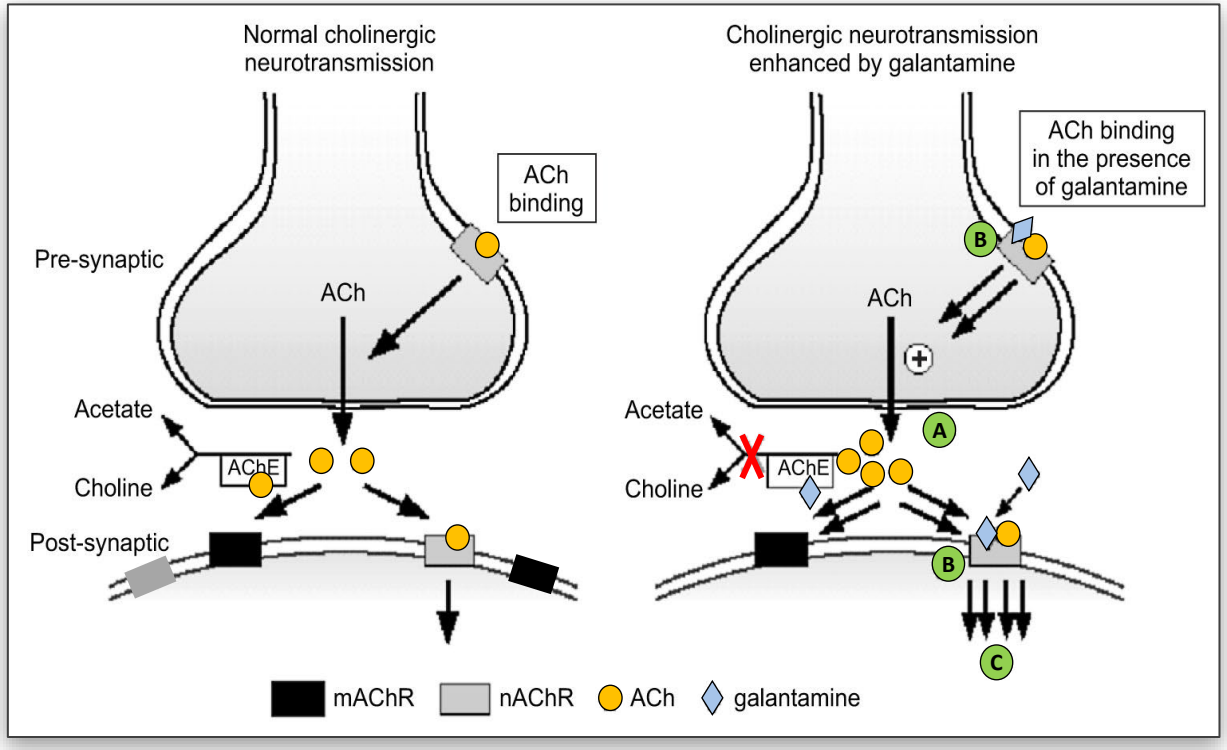
Galantamine (ZUNVEYL's Active Moiety) Enhances Acetylcholine Levels And Modulates Nicotinic Receptor Sensitivity

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

Current therapeutics[1] increase acetylcholine levels by inhibiting acetylcholinesterase (AChE)

Modulation of nAChR (α7/α4β2)[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

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1. Excluding Memantine for moderate-to-severe Alzheimer's disease
2. Lilienfeld, S. (2002) *CNS Drug Reviews,* 8(2), 159-176

Pivotal Trial Results Provided Data Enabling NDA Filing

Bioequivalence Studies vs. Immediate Release

PK Parameter	ALPHA-1062 Delayed Release 5mg (n=36)	Gal HBr Immediate Release 4mg (n=36)	% to Reference Drug 80-125%	Enabled NDA Filing
AUC0-inf (µg × h/mL) Fasted State	306.8	321.5	95%	✓
Cmax (ng/mL) Fasted State	30.7	40.5	76%	✓
AUC0-inf (µg × h/mL) Fed State	286.7	329.9	87%	✓
Cmax (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%	Enabled NDA Filing
AUC0-24 (µg × h/mL) Steady State	527.5	492.1	107%	✓
Cmax (ng/mL) Steady State	41.7	32.8	127%	✓

- Data suggests **ALPHA-1062 AUC was bioequivalent to galantamine hydrobromide IR and ER**[1]
- Cmax for ALPHA-1062 is bracketed between IR and ER (lower than IR, higher than ER) providing 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[1]

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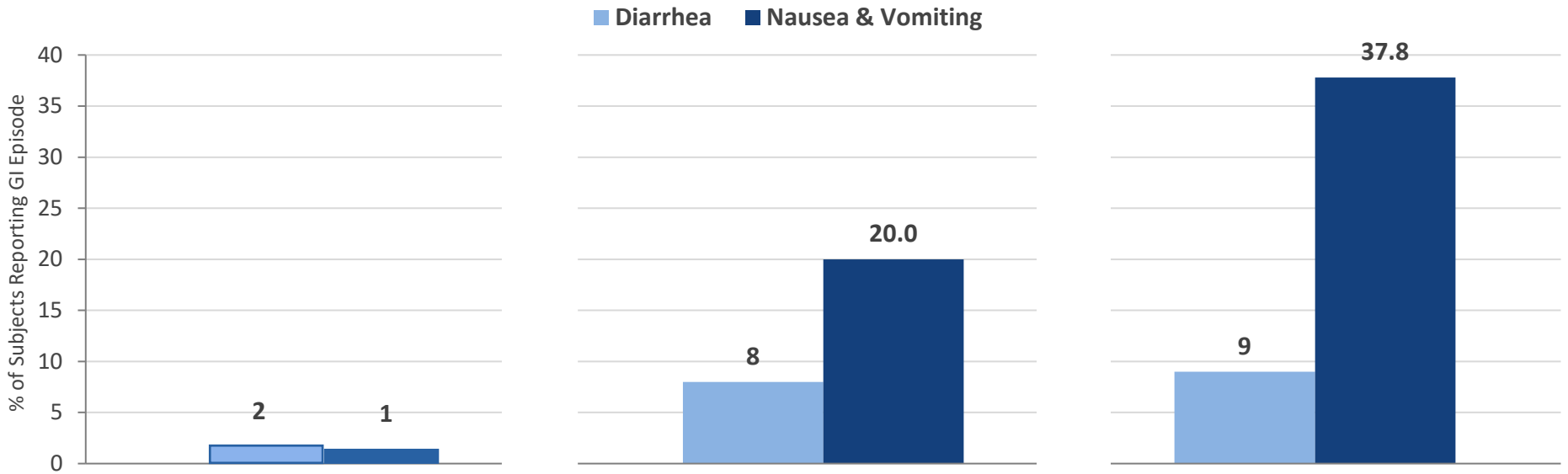
1. DA Guidance: https://www.fda.gov/files/drugs/published/Bioavailability-and-Bioequivalence-Studies-Submitted-in-NDAs-or-INDs

Studies Have Reported Improved Gastrointestinal Side Effect Profile*

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



ALPHA-1062 5-15mg
Single and Multi-Dose Trials
(n=150)[1]

RAZADYNE 8 mg/day
Single Dose
(n=120)[2]

RAZADYNE Pooled AE Data
(Doses ranging 8 to 32 mg / day)
(n=2,932)[3]

Median duration of nausea was 5-7 days per episode

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

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1. Alpha Cognition: Data on File
2. ISSO; Completed Phase 1 trials in healthy adults; J&J Reminyl NDA package submission
3. RAZADYNE Full Prescribing Information accessed: https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/RAZADYNE+ER-pi.pdf

Zunveyl's Differentiated Profile Will Make A Meaningful Difference In The Lives Of Those Affected By Alzheimer's Disease

Razadyne ER	EXELON®	Aricept
GALANTAMINE	RIVASTIGMINE	DONEPEZIL

There is a significant need for better treatment options

- Current treatment options can have significant side effects, including gastrointestinal and insomnia issues.
- Physicians report feeling dissatisfied and/or apathetic about their symptomatic treatment options.[3]
- Caregivers also expresses dissatisfaction with the currently approved treatments options.[3]

ZUNVEYL
(benzgalantamine)

GI Safety Profile	**Reduced GI side-effects** (diarrhea, nausea, vomiting)	✓
CNS Safety Profile	No incidence of insomnia	✓
Long Term Outcome[1]	**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 nACh R ($\alpha7/\alpha4\beta2$)[2]	✓

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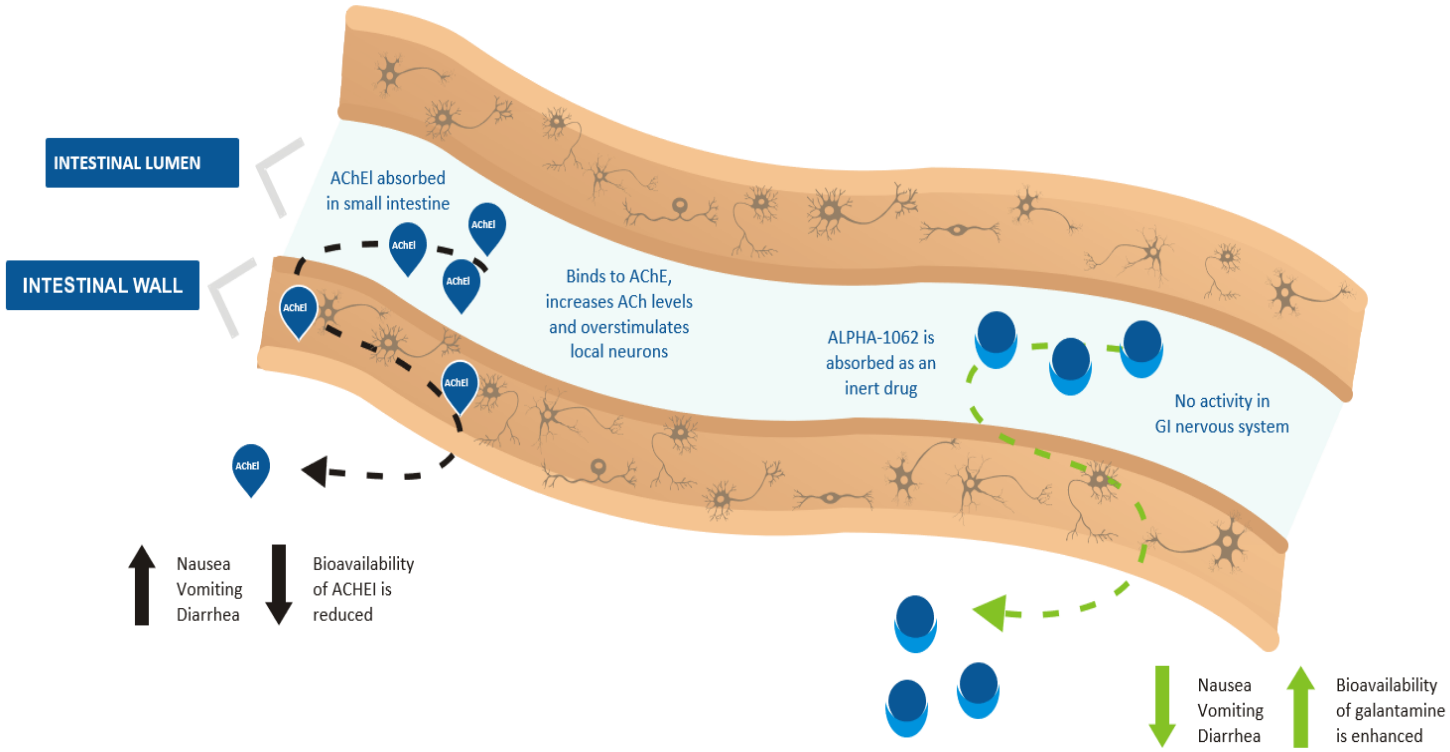
RAZADYNE is a registered trademark of Johnson & Johnson
EXELON is a registered trademark of Novartis Pharmaceuticals Corp

1. Xu et al. Neurology 96 (17) e2221 (2021)
2. Feldman et al. International Journal of Geriatric Psychiatry 2009; 24: 479–488
3. Data on File, Infinity Group, HCP and Caregiver Market Research, July 2021

**Rivastigmine is also available as a transdermal patch*

ZUNVEYL Was Designed To Eliminate Drug Absorption In The GI Tract And Has Zero Incidence Of Insomnia

ACHEIs Activity In The GI Nervous System Overstimulates Local Neurons **Resulting In Side-Effects**



0% incidence of insomnia in ZUNVEYL label

"…Accumulating evidence shows that sleep disturbance contributes to cognitive decline."[1]

"Galantamine may be the first choice of cholinesterase inhibitor in mild to moderate dementia patients in terms of improving sleep quality."[2]

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1. Lim, Gerstner, Holtzman "Neurodegenerative Dis Management. 2014; 4(5):351-362 doi:10.2217/nmt.14.30
2. Acta Neurol Belg (2015) 115:563–568 DOI 10.1007/s13760-015-0453-9

Galantamine (Zunveyl's Active Moiety) Reduces Risk Of Disease Progression And Has The Strongest Effect On Cognition

- Galantamine **affects multiple brain receptors to exert effect**
- Galantamine has **demonstrated anti-inflammation effects**[1]
- Galantamine has been associated with:[1,2]
  - **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 treatment[3]

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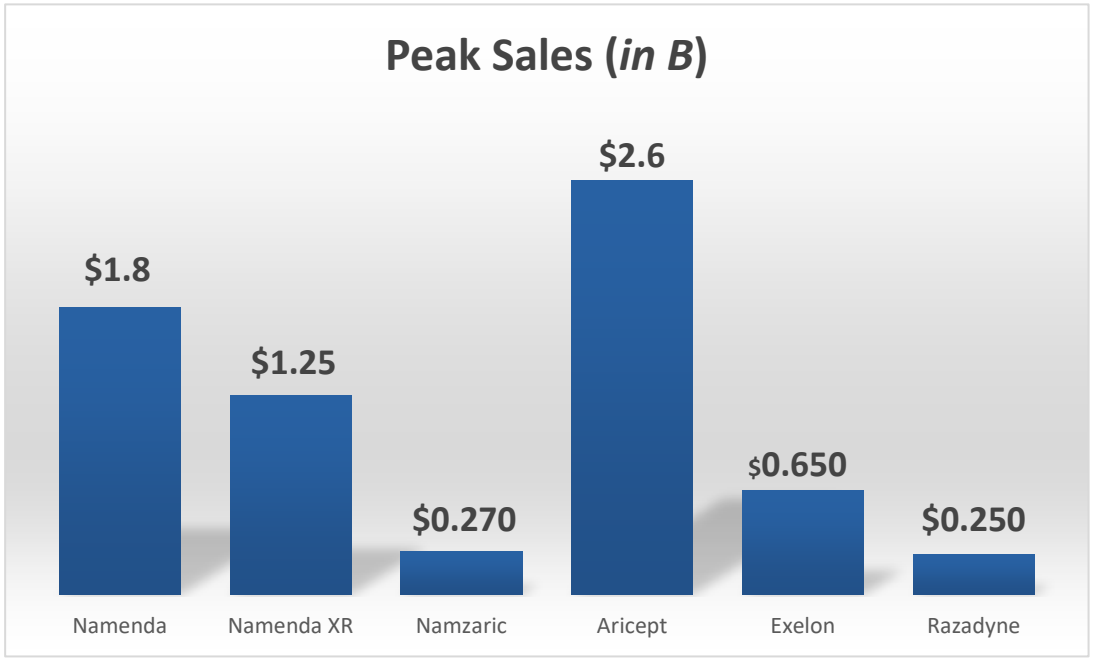
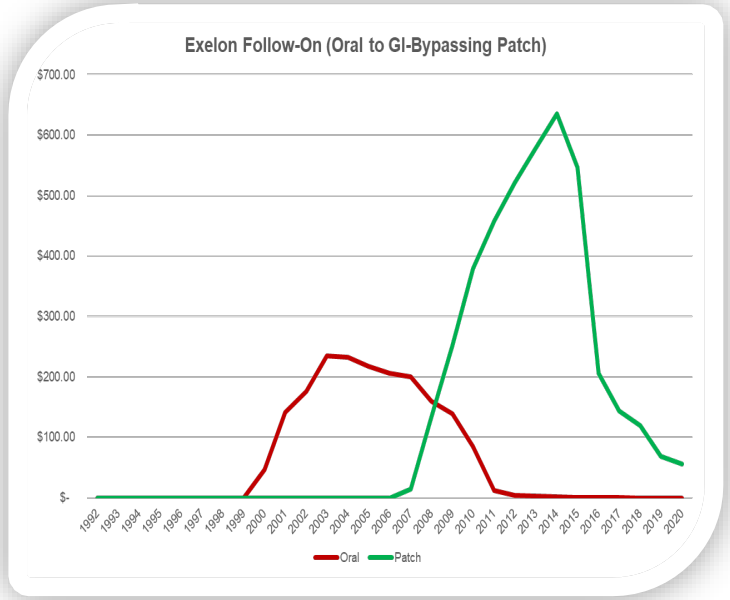
1. 2. Lilienfeld, S. (2002) *CNS Drug Reviews,* 8(2), 159-176
3. Xu et al. Neurology 96 (17) e2221 (2021)
3. Feldman et al. International Journal of Geriatric Psychiatry 2009; 24: 479–488

Multiple AD Launches Have Achieved Billion Dollar Yearly Sales





- Large US 11M annual prescription 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

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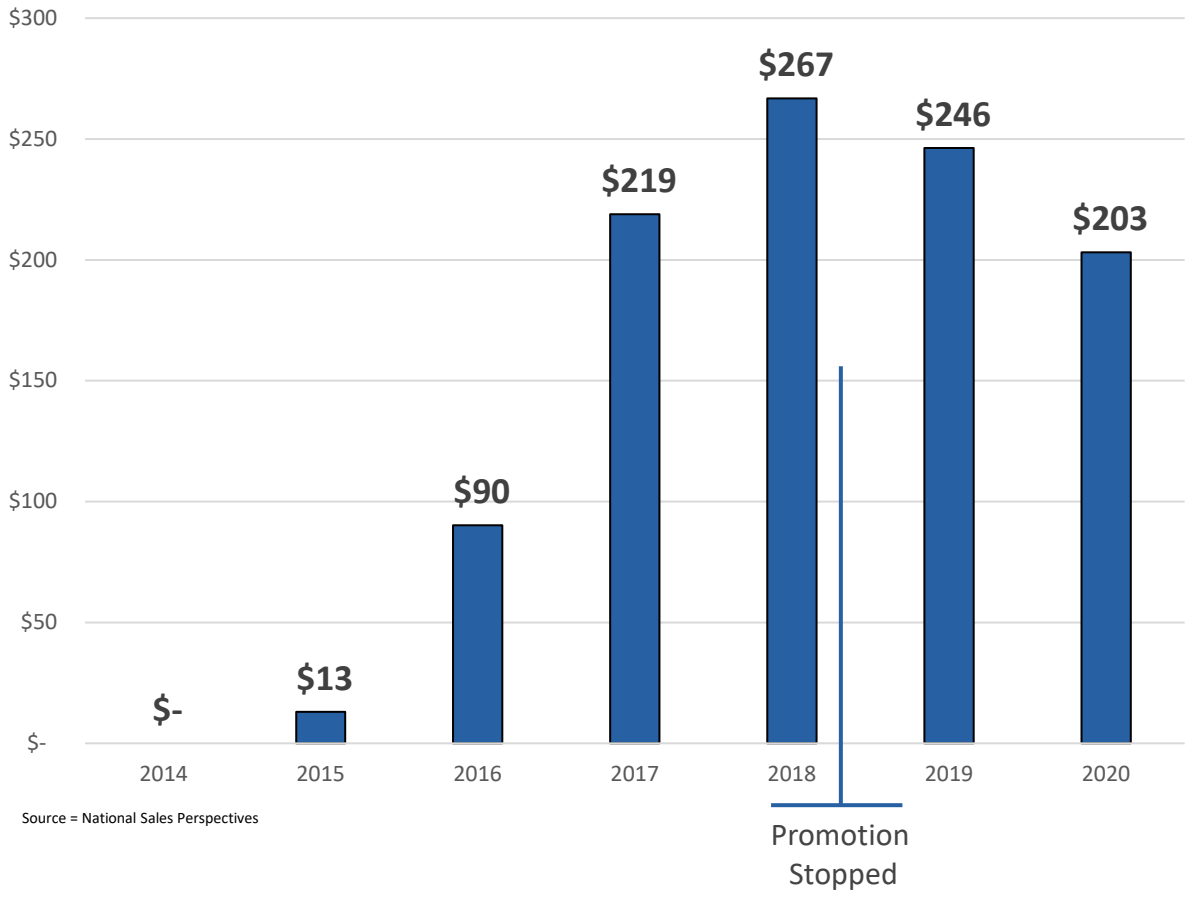
Source – IQVIA National Sales Perspectives – 1993 through 2020.

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

NAMZARIC Sales by Year ($M)



Source = National Sales Perspectives

- 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 NAMZARIC[1] with Average co-pay of $50.00-$67.50[1]
- Average retail price of $667.74[1]

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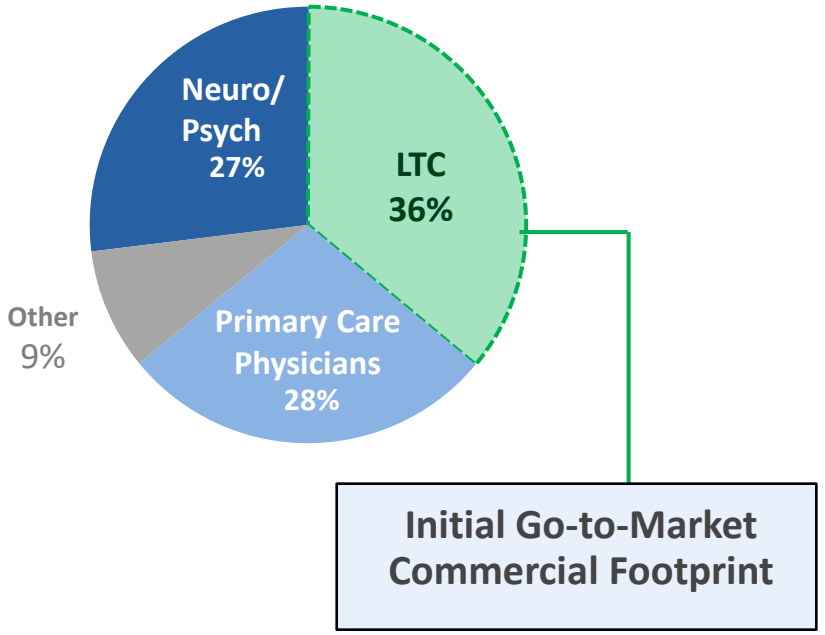
1. GoodRx 2024

AChEI's 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[1]
  - 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's[2]
  - LTC provides estimated, potential initial commercial opportunity ($2B potential)[3] with future expansion to Neurology ($1.5B potential)[4]
  - Branded medications used more commonly in LTC market
  - 65-70% of LTC lives have access to ZUNVEYL with zero co-pay

Prescriptions by Specialty [1]



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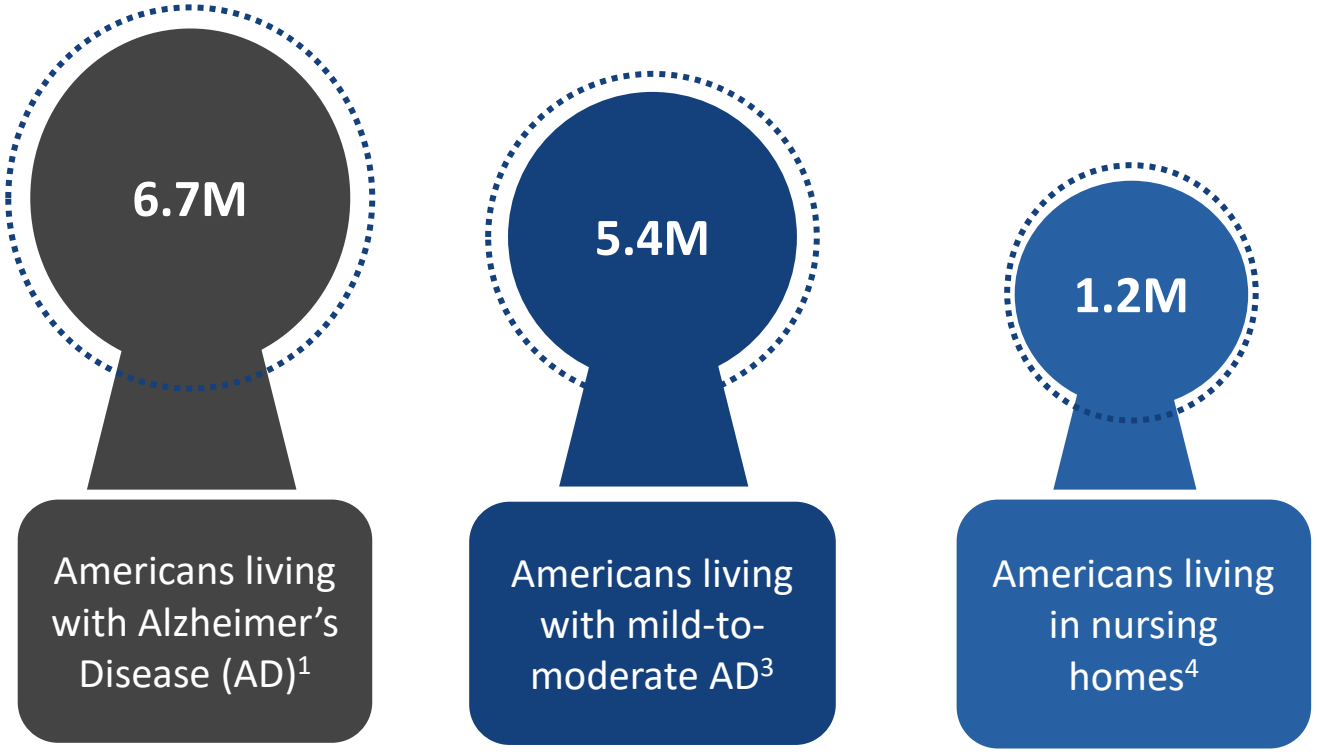
1. Symphony METYS Retail 2019:Includes donepezil, galantamine, rivastigmine and Namzaric
2. Symphony METYS Retail 2019; Average WAC prices from Access Pointe Managed Markets Market Research
3. . Estimated based on US$11 million annual prescriptions x LTC percentage of prescriptions (36%) x average WAC price of $500
4. Estimated based on US$11 million annual prescriptions x Neurology percentage of prescriptions (27%) x average WAC price of $500

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% residents[1]
- Is the leading reason for placement[1]
- Is the leading cause of death[1]

Significant Dissatisfaction with Current Treatments Leads to ZUNVEYL Opportunity

- Current treatment options cause burden for staff and risks for residents due to GI side effects and insomnia[2]
- 55% patients discontinue their AD medication due to side effects[2]
- Market research indicates ~88% of LTC HCPs Likely to prescribe ZUNVEYL[2]

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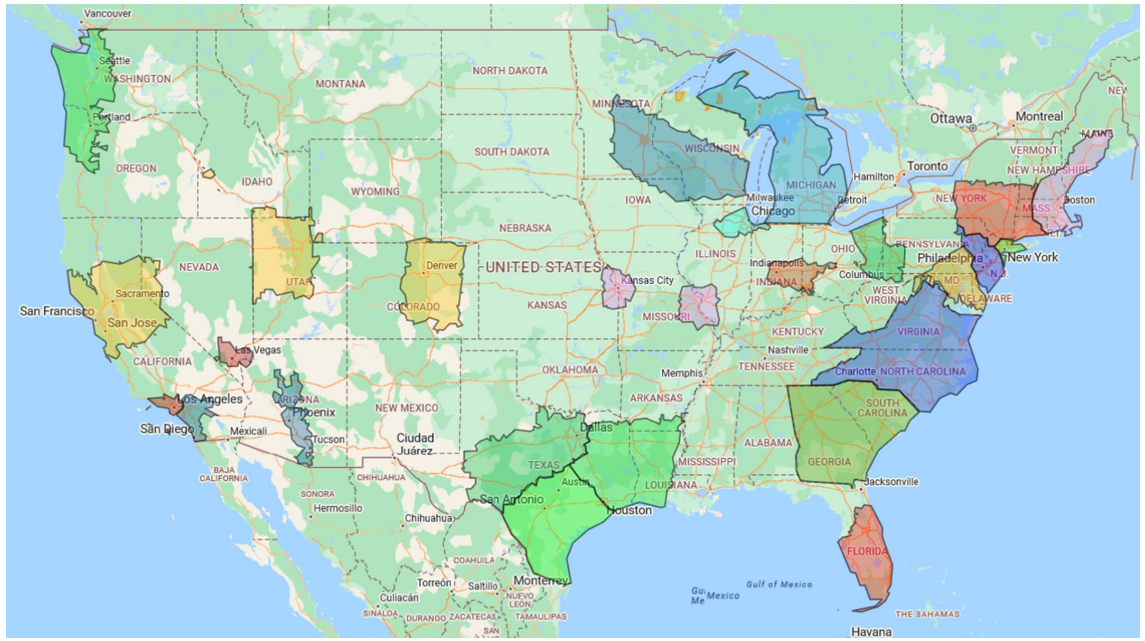
1. Alzheimer's Association Facts and Figures - 2023
2. Data on File - LTC Market Research, October 2021
3. https://www.nia.nih.gov/news/half-alzheimers-disease-cases-may-be-mild
4. https://oig.hhs.gov/reports-and-publications/featured-topics/nursing-homes/

Commercialization Strategy Will Leverage LTC Experience and Focused Sales Effort At Launch

25 Sales Reps Cover > 80% of the LTC Segment



- **Target 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**

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Commercialization Strategy Will Leverage Expected Differentiated Profile And Focused Sales Effort At Launch

Commercial leadership intends to build an excellent 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

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ZUNVEYL Alzheimer's Dementia Opportunity

Large but Dissatisfied Market

LTC represents **largest AD prescription volume**

>50% discontinue treatment at 12 months

88% LTC HCPs potentially **willing to prescribe**

ZUNVEYL Potential

Potential Reduced Adverse Event Profile

Delayed Progression of Disease

Strongest effect on cognition

Additional Clinical Development Programs

ZUNVEYL sublingual tablet pre-clinical stage

DOD Bomb-blast study results expected Q4

Near-term Milestones

ZUNVEYL Pricing Q4 2024

ZUNVEYL Commercial Launch Q1 2025

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Alpha Cognition Clinical Pipeline

Indication	Preclinical	Phase 1	Phase 2	Phase 3 /Pivotal	Approved	Entity Responsible
ZUNVEYL (ALPHA-1062)						
Oral: Mild-to-Moderate Alzheimer's Disease (AD)					★	Alpha Cognition
Sublingual Formulation: Mild-to-Moderate Alzheimer's Disease (AD)[1]	▬					Alpha Cognition
Moderate-to-Severe Alzheimer's Combination with Memantine (AD)[1]	▬					Alpha Cognition
ALPHA-1062 Intranasal (Partnered Asset)						
Cognitive Impairment with Mild Traumatic Brain Injury[1,2]	▬					ALPHA SEVEN THERAPEUTICS

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1. *Contingent on sufficient capital to be raised*
2. *Alpha Seven Therapeutics was incorporated in Delaware in July 2023. The out-license of ZUNVEYLIN technology has not yet occurred.*

Potential Catalysts And Upcoming Events

2024

- ☑ *Composition of Matter IP filing – US/Rest of World (Q1)*
- ☑ *ZUNVEYL anticipated FDA product approval (Q3)*
- ☑ *Composition of Matter IP approval – US (Q4)*
- ☐ *DOD Sponsored Bomb-blast study results (preclinical) (Q4)*

2025

- ☐ *ZUNVEYL commercial launch (1Q)*
- ☐ *IND Submission for Cognitive Impairment with mTBI – Alpha Seven*
- ☐ *Zunveyl + Memantine initiation of clinical trial (Q4)*

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

Michael McFadden
Chief Executive Officer

UROVANT SCIENCES
AVANIR pharmaceuticals
AMYLIN
PHARMACIA
Lilly

Denis Kay
Chief Scientific Officer

neurodyn
CNS|CRO Preclinical Neurological Disease Services

Lauren D'Angelo, MBA
Chief Operating Officer

UROVANT SCIENCES
AVANIR pharmaceuticals
MEDIVATION
Genentech
AstraZeneca

Henry Du, CPA
VP Finance and Accounting

AMPLIFY SURGICAL
HUYABIO INTERNATIONAL
Eledon Pharmaceuticals
AVANIR pharmaceuticals

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Share Structure

ACOG.CN, ACOGF				
Share Price (as of September 3, 2024)	$0.53 CAD / $0.40 USD			
Market Cap (as of September 3, 2024)	$79M CAD / $60M USD			
September 3, 2024	**Issued and Outstanding**	**% of total**	**Proforma Outstanding (1)**	**% of total**
Common Shares	150,855,536	56.7%	6,034,221	56.7%
Class B Preferred Series A Shares	7,916,380	2.9%	316,655	2.9%
Performance Shares	6,641,057	2.5%	265,642	2.5%
Non-Trading Warrants	69,441,236	26.1%	2,933,555	26.1%
Stock Options	20,399,367	7.7%	1,019,968	7.7%
Convertible Notes (convert to common)	10,770,133	4.05%	430,805	4.05%
TOTAL ALL SHARES	**244,483,443**	**100.0%**	**12,224,172**	**100.0%**

(1) Proforma shares are based on the contemplated 1 for 25 reverse stock split, which is contingent on the Company's Nasdaq listing.

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1. CSE and OTC markets do not always trade at currency differentiation.

Alpha Cognition

Michael McFadden
info@alphacognition.com
www.Alphacognition.com
https://x.com/alpha_cognition

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