
Trial TRAX[®]

Alzheimer's Disease

Clinical Trial Monitoring Brief

September 2007

SAMPLE

Trial TRAX® Clinical Intelligence Monitoring

Austin Research Group's Trial TRAX Clinical Intelligence Monitoring series provides detailed compilations and analysis of ongoing clinical studies within a specific therapeutic area or indication. Additionally, the Trial TRAX briefs contain synthesized background information on the profiled-disease including:

- Epidemiology
- Patient Segmentation
- Clinical endpoints

The Trial TRAX brief also contains analysis of the clinical landscape which comprises assessments including:

- % utilization of key clinical endpoints
- Number of ongoing trials (by phase of development)
- Key companies sponsoring clinical trials

Key data points from competitor clinical trials presented in the briefing include:

- Study Drug
- Mechanism of Action
- Company-Sponsor
- Phase of Development
- Number of Patients
- Study Design
- Primary Endpoints
- Study Start Date

The brief's reference-guide format is designed to provide decision makers with easy access to key intelligence on competitive clinical development programs. The information contained within the report is updated on a quarterly basis to ensure accuracy, relevancy, and timeliness of the intelligence.

Clients utilize the Trial TRAX briefing reports to:

- Monitor clinical development programs of competitors
- Evaluate depth and breadth of competitive landscape
- Identify potential patient recruitment challenges
- Benchmark competitor clinical trial designs

Table of Contents

| | |
|---|-----------|
| Section 1: Executive Summary | 4 |
| Alzheimer's Disease Overview: Background, Epidemiology | 5 |
| Alzheimer's Disease Overview: Etiology & Disease Staging | 6 |
| Treatments for Alzheimer's Disease | 7 |
| Historical Sales of Market Alzheimer's Disease Therapeutics | 8 |
| Clinical Endpoints in Alzheimer's Disease Trials | 9 |
| Overview of Clinical Landscape | 10 |
| Key Players in Rheumatoid Arthritis | 11 |
| | |
| Section 2: Ongoing Clinical Trial in Alzheimer's Disease | 12 |
| Competitive Clinical Trial Details | 13 |
| | |
| Section 3: Appendix | 24 |
| Disclaimer | 25 |
| Report Licensing | 26 |

SAMPLE

Section 1:

Executive Summary

SAMPLE

Background & Epidemiology

Background

Alzheimer's disease (AD) is a brain disorder named for German physician Alois Alzheimer, who first described it in 1906. AD is a progressive and fatal neurodegenerative disorder manifested by cognitive and memory deterioration, progressive impairment of activities of daily living, and a variety of neuropsychiatric symptoms and behavioral disturbances. The disease gradually progresses over time and destroys a person's memory and ability to learn and carry out daily activities such as talking, eating, and going to the bathroom. As the disease progresses, individuals may also experience changes in personality and behavior. Unfortunately, there are no cures for AD and there is no way to predict how fast someone will progress through the stages of the disease.

Physicians often divide the symptoms of Alzheimer's disease into "cognitive" and "behavioral and psychiatric" categories. Cognitive symptoms affect memory, language, judgment, planning, ability to pay attention and other thought processes. Behavioral and psychiatric symptoms affect the way we feel and act.

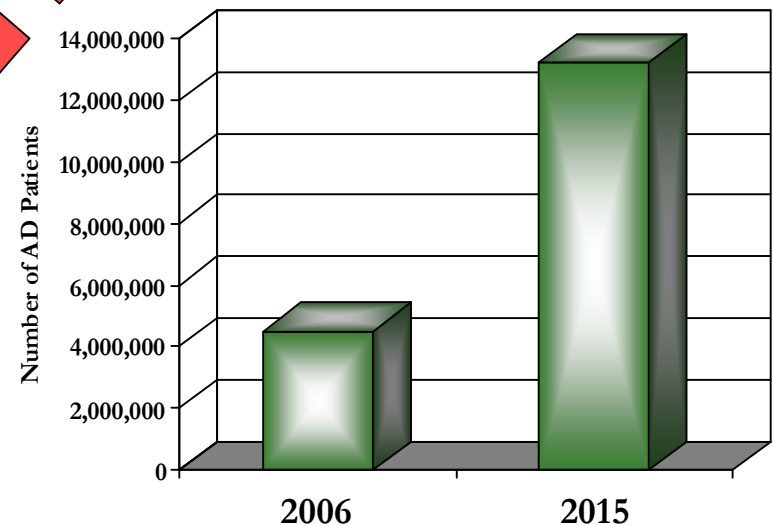
Alzheimer's Disease Fast Facts¹

AD affects approximately 5 million people in the U.S. and 15 million individuals worldwide.
(number is rising with aging population)

\$80-\$100 billion per year in total treatment costs
(\$213,000 per family treatment costs)

>50% have psychosis and/or behavioral disturbances

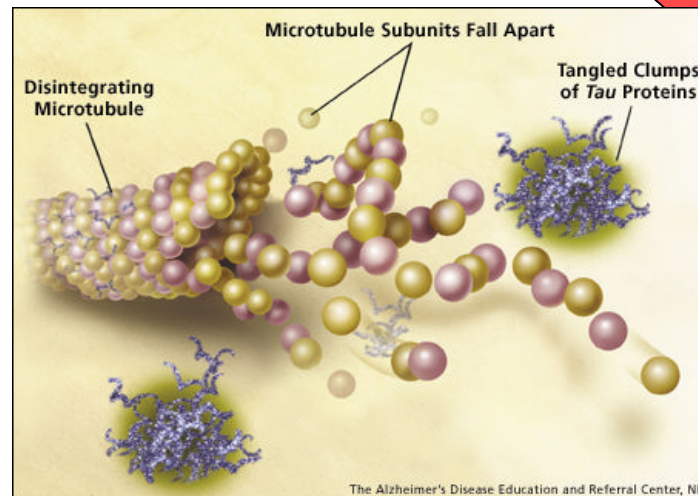
U.S. Alzheimer's Disease Prevalence Rate²



Etiology and Stages of Alzheimer's Disease

Plaques & Tangles:

Researchers aren't exactly sure what causes AD, but they do know that people with the disease have an abundance of two abnormal structures in the brain: plaques and tangles. Plaques and tangles are prime suspects in damaging and killing nerve cells. **Plaques** build up between nerve cells. They contain deposits of a protein fragment called beta-amyloid. **Tangles** are twisted fibers of another protein called tau. Tangles form inside dying cells. Though most people develop some plaques and tangles as they age, those with Alzheimer's tend to develop far more. The plaques and tangles tend to form in a predictable pattern, beginning in areas important in learning and memory and then spreading to other regions.



Stages of AD:

Stage 1: No impairment

Stage 2: Very mild decline--Individuals may feel as if they have memory lapses, especially in forgetting familiar words or names or the location of keys, eyeglasses or other everyday objects.

Stage 3: Mild decline --Problems with memory or concentration may be measurable in clinical testing or discernible during a detailed medical interview.

Stage 4: Moderate decline (mild or early stage)--Medical interview detects clear-cut deficiencies in the following areas:

Decreased knowledge of recent occasions or current events

Stage 5: Moderately severe decline (moderate or mid-stage)--Major gaps in memory and deficits in cognitive function emerge. Some assistance with day-to-day activities becomes essential.

Stage 6: Severe decline (moderately severe or mid-stage)--Memory difficulties continue to worsen, significant personality changes may emerge and affected individuals need extensive help with customary daily activities.

Stage 7: Very severe decline (severe or late stage)--This is the final stage of the disease when individuals lose the ability to respond to their environment, the ability to speak and, ultimately, the ability to control movement.

Treatments for Alzheimer's Disease (Cognitive Symptoms)

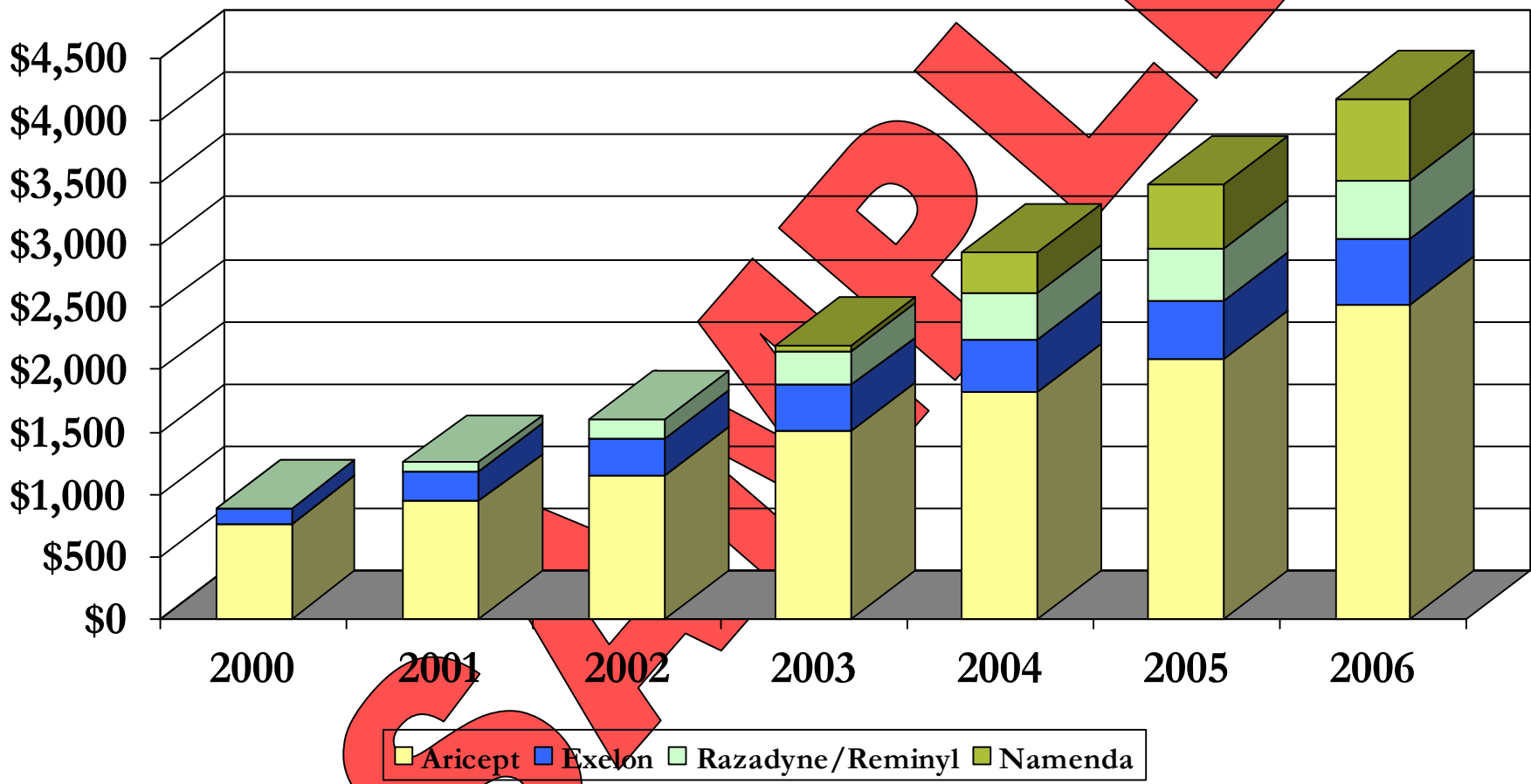
The U.S. Food and Drug Administration (FDA) has approved two types of medications to treat cognitive symptoms of Alzheimer's disease. These drugs affect the activity of two different chemicals involved in carrying messages between the brain's nerve cells.

| Class | Target/MOA | Description | Approved Products |
|---------------------------|--|---|--|
| Cholinesterase inhibitors | Prevent the breakdown of acetylcholine | <ul style="list-style-type: none">-Support communication among nerve cells by keeping acetylcholine levels high.-Are approved to treat <i>mild to moderate</i> AD.-On average, delay worsening of symptoms for 6 to 12 months for ~50% pts. treated. | Donepezil (Aricept) Rivastigmine (Exelon) Galantamine (Razadyne) |
| NMDA antagonist | Regulates the activity of glutamate | <ul style="list-style-type: none">-Approved for treatment of moderate to severe Alzheimer's disease.-Currently only one drug in class approved to treat AD.-Temporarily delays worsening of symptoms for some people.-Degree of benefit is similar to the cholinesterase inhibitors. | Memantine (Namenda) |

SAM

Historical WW Sales of Marketed AD Products

WW Sales of Alzheimer's Disease Treatments



Clinical endpoints used in AD trials

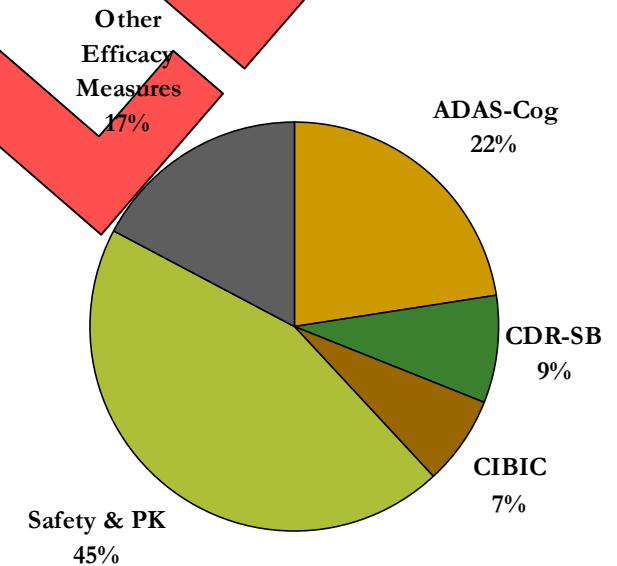
ADAS-cog* Scores are the most commonly utilized efficacy endpoint in AD clinical trials.

The endpoint is recognized by the U.S. FDA, Commission of the European Communities, and in Japan.

ADAS-cog-Definition

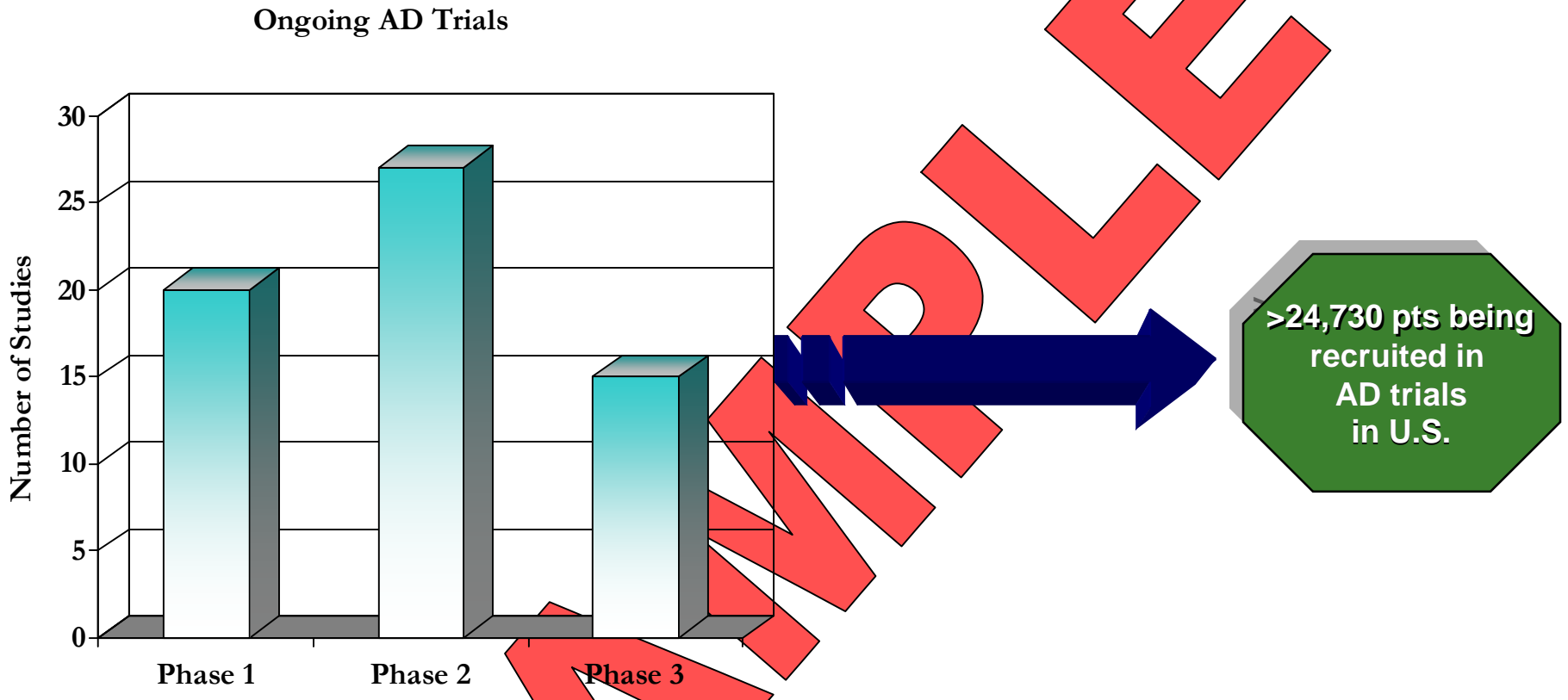
- ADAS independently measures both cognitive and non-cognitive function, but it is the cognitive items (ADAS-Cog) which have been used most widely in clinical investigations¹.
- ADAS is a 21-item performance-based scale (11 items to assess ADAS-Cog) and 10 items to assess non-cognitive function,.
- Score 0-70 is possible on the ADAS-Cog part of the scale: (0 means the patient made no errors at all and 70 means the patient is profoundly demented)

Commonly Used Clinical Endpoints in AD Trials



Another endpoint utilized is Clinical Deterioration/ Dementia Scale Sum of Boxes (CDR-SB)

Overview of Clinical Landscape

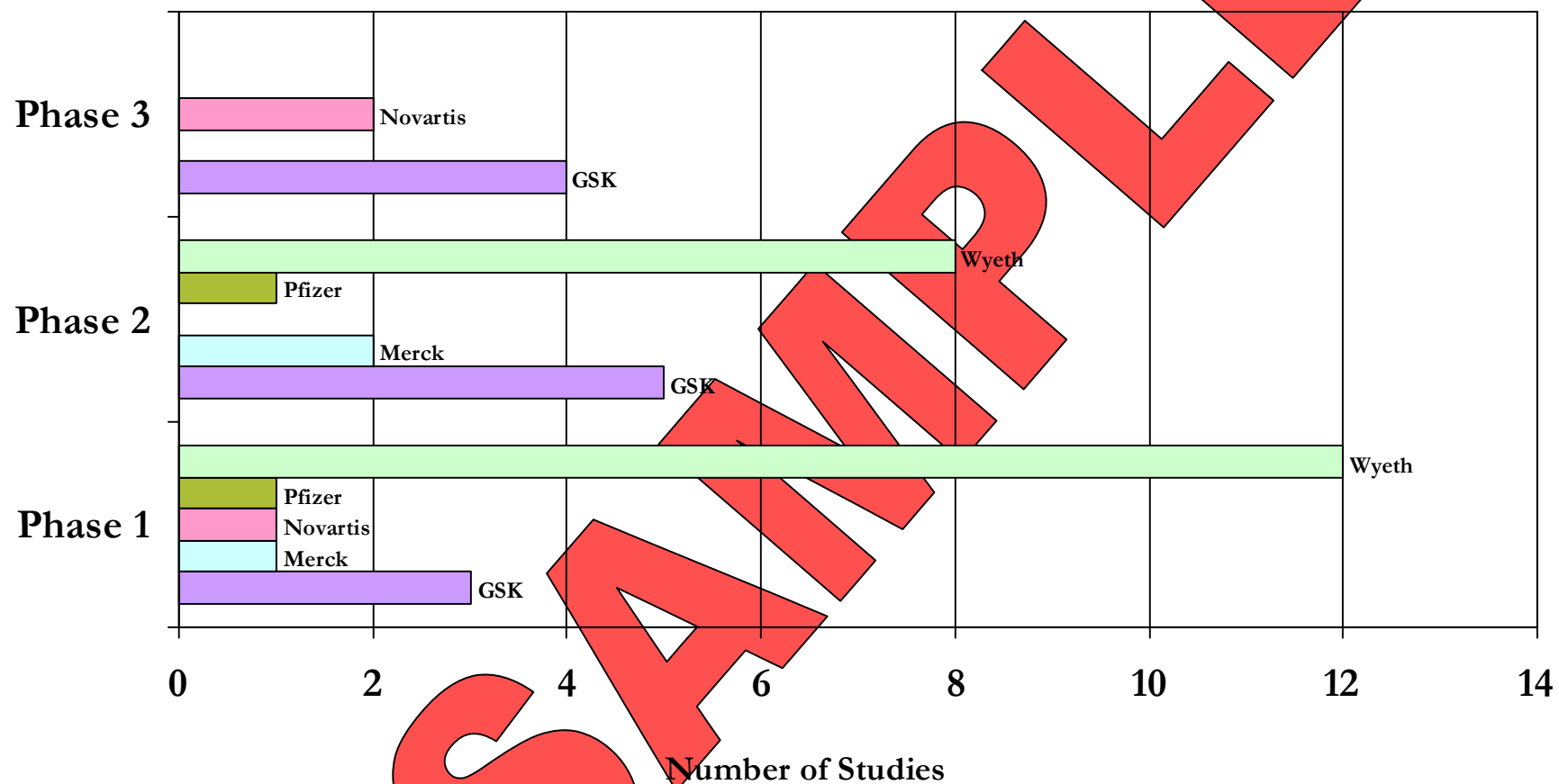


Notable phase 3 programs

- Avandia XR: 6,430 pts. in >5 trials
- Flurizan (MPC-7869): 3,400 pts. in 3 trials
- Alzhemed: 2,530 pts. in 3 trials

Executive Summary:

Key Industry Players in Alzheimer's Disease Clinical Research



Section 2:

Clinical Trials in Alzheimer's Disease

SAMPLE

| Ongoing Clinical Trials: Alzheimer's Disease | | | | | | | | |
|--|--|-----------------|---|-------|-------|---|---|---------------------|
| Drug | Mechanism | Company | Study Title | Phase | # Pts | Study Design | Primary Endpoint | Start/End Dates |
| Affitope AD01 | N/A | Affiris GmbH | Randomized, Controlled, Parallel Group, Patient-Blinded, Single-Center Phase I Pilot Study to Assess Tolerability and Safety of Repeated s.c. Administration of a Single-Dose of Affitope AD01 Applied With or Without Adjuvant to Patients With Mild to Moderate Alzheimer's Disease | 1 | 24 | Randomized, Single Blind, Active Control, Parallel Assignment, Safety Study | Tolerability | July 2007-July 2008 |
| GSK933776A | Nootropic agent | GlaxoSmithKline | Randomised, Single-Blind, Placebo-Controlled Study to Investigate the Safety, Tolerability, Immunogenicity, Pharmacokinetics and Pharmacodynamics of Intravenous Infusion of GSK933776A in Patients With Alzheimer's Disease. | 1 | 122 | Randomized, Single Blind, Placebo Control, Single Group Assignment, Safety Study | Adverse events from dosing to week 52. Changes suggesting potential adverse events detected in the physical & neurological examination, brain MRI, cognitive status, laboratory parameters, ECG & vital signs from dosing to week 52. | Mar-07 |
| Avandia XR (Rosiglitazone XR) | PPAR-gamma receptor agonist | GlaxoSmithKline | Open-Label, Randomized, Two-Period Crossover Study to Demonstrate the Bioequivalence of a Tablet Formulation of Rosiglitazone XR (BRL-049653) 8mg Manufactured at Two Different Sites in Healthy Volunteers in Fasting Conditions | 1 | 50 | Randomized, Open Label, Uncontrolled, Crossover Assignment, Bio-equivalence Study | PK samples [Time Frame: at Pre-dose,0.5, 1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 16, 24, 32] | Feb-07 |
| Avandia XR 2 formulations mfg. at 2 different sites (Rosiglitazone XR) | PPAR-gamma receptor agonist | GlaxoSmithKline | Open-Label, Randomized, Two-Period Crossover Study to Demonstrate the Bioequivalence of a Tablet Formulation of Rosiglitazone XR (BRL-049653) 8mg Manufactured at Two Different Sites in Healthy Volunteers in Fasting Conditions | 1 | 50 | Randomized, Open Label, Uncontrolled, Crossover Assignment, Bio-equivalence Study | PK samples [Time Frame: at Pre-dose,0.5, 1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 16, 24, 32] | Feb-07 |
| V950 | Anti-amyloid beta (A-beta) vaccine | Merck | N/A | 1 | N/A | Randomized, Double-Blind, Placebo Control, Parallel Assignment, Safety Study | N/A | Apr-07 |
| CAD106 | Beta amyloid-modulating (antibody) therapeutic vaccine | Novartis | 52-Week, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Time-Lagged, Parallel Group Study in Patients With Mild to Moderate Alzheimer's Disease (AD) to Investigate the Safety, Tolerability and Aβ-Specific Antibody Response Following Three Subcutaneous Injections of CAD106 | 1 | 60 | Randomized, Double-Blind, Placebo Control, Parallel Assignment, Safety Study | Safety/tolerability assessments: at multiple timepoints including but not limited to screening, baseline, and through the end of the study to Week 52. Antibody titer assessments: at multiple timepoints including but not limited to baseline and through the end of the study to Week 52 | Jun-05 |
| PF-04360365 | Humanized monoclonal antibody against amyloid beta | Pfizer | Phase I, Randomized, Placebo Controlled, Double Blind Dose Escalation Study of the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Immunogenicity of a Single Intravenous Dose of PF-04360365 in Adults With Mild to Moderate Alzheimer's Disease | 1 | 36 | Randomized, Double-Blind, Placebo Control, Parallel Assignment, Pharmacokinetics/Dynamics Study | Safety, tolerability, and pharmacokinetics of a single dose of PF-04360365 in subjects with mild to moderate AD for one year following dosing. | Mar-07 |

Section 3:

APPENDIX

SAMPLE

Disclaimer

Although the information contained within this report is rigorously assessed and scrutinized for accuracy Austin Research Group is not liable for the any incorrect or erroneous information contained in this report. Additionally, Austin Research Group is not liable for actions taken or decisions made on the basis of this information.

SAMPLE

Report Licensing

No part of this publication should be reproduced or redistributed in any form or by any means including but not limited to graphic, electronic or mechanical, including photocopying, recording, taping or storage in information retrieval systems without the express written permission of the Austin Research Group.

© Copyright 2006-2007 Austin Research Group

All rights reserved.

SAMPLE