

---

**Trial TRAX<sup>®</sup>**

***Multiple Sclerosis  
Clinical Trial Monitoring Brief***

---

**October 2007**



**Sample**

# Trial TRAX<sup>®</sup> 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

<b>Section 1: Executive Summary</b>	<b>4</b>
Multiple Sclerosis Disease Overview: Background	5
Clinical Courses of Multiple Sclerosis	6
Clinical Endpoints in Multiple Sclerosis Trials	7
Overview of Clinical Landscape	8
Key Players in Multiple Sclerosis R&D	9
Competitor Clinical Trial MAP- <i>The Orals</i>	10
Competitor Clinical Trial MAP- <i>Biologics</i>	11
<b>Section 2: Ongoing Clinical Trial in Rheumatoid Arthritis</b>	<b>12</b>
Phase I & Phase II: Competitive Clinical Trial Details	13
Phase III: Competitive Clinical Trial Details	15
Phase IV: Competitive Clinical Trial Details	18
<b>Section 3: Appendix</b>	<b>19</b>
Disclaimer	20
Report Licensing	21`

---

Section 1:

Executive Summary

---

Sample

# Multiple Sclerosis Disease Overview: Background & Epidemiology

## Background

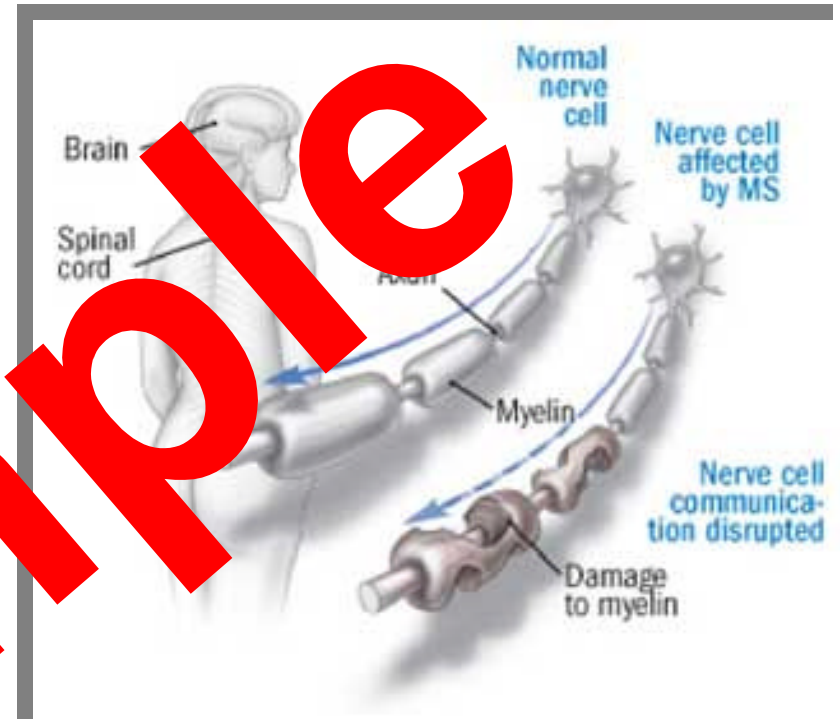
Multiple sclerosis (MS) is an inflammatory disease of the central nervous system (CNS), in which the body's immune system attacks the protective sheath surrounding nerve fibers. White blood cells infiltrate CNS by crossing the blood-brain barrier, leading to inflammatory damage of the neural structures, including myelin and axons.

MS presents with sudden loss of neurological function, typically affecting vision, walking, bladder and sensation. Disorders affecting information processing, memory and personality are also common. Attacks of MS symptoms are caused by inflammatory lesions in the central nervous system, including the brain or spinal cord.

Symptoms of these attacks are usually caused by local swelling within brain or spinal cord tissue, and disappear when swelling resolves.

Underlying damage accumulates so that after ten years of disease, most patients experience a slow, progressive decline. This phase of disease, termed secondary progression, affects about two-thirds of MS patients. At disease onset, it is not possible to predict which patients will develop secondary progression, and a small minority of patients will not be severely affected by MS at all.

Many of the prescribed medications in the treatment of MS address its symptoms or shorten the duration of symptomatic attacks. These medications are useful for managing the disease but do not affect the underlying cause of the condition because they do not address the inflammatory response responsible for the damage.



# Clinical Courses of MS

## Multiple Sclerosis Disease Background: Clinical Courses of MS

People with MS can expect 1-of-4 clinical courses of disease, each of which might be mild, moderate, or severe.

### ■ **Relapsing-Remitting (RRMS)**

Characteristics: Pts. experience clearly defined flare-ups (a.k.a. relapses, attacks, or exacerbations)—which are episodes of acute worsening of neurologic function, followed by partial or complete remission periods free of disease progression.

### ■ **Primary-Progressive (PPMS)**

Characteristics: People with this type of MS experience a slow but nearly continuous worsening of their disease from the onset, with no distinct relapses or remissions. However, there are variations in rates of progression over time, occasional plateaus, and temporary minor improvements.

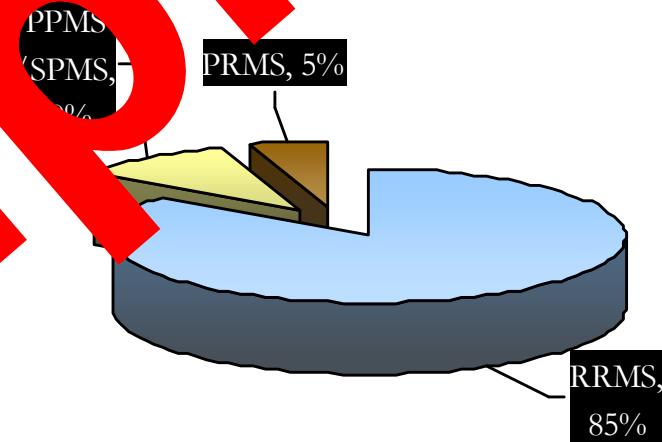
### ■ **Secondary-Progressive (SPMS)**

Characteristics: Pts. experience initial period of RRMS, followed by steadily worsening disease course with/without acute flare-ups, remissions, or plateaus. Prior to the introduction of disease modifying drugs, 50% of RRMS pts. develop this form of disease within 10 years of initial diagnosis, but the introduction of the "disease-modifying" drugs. Long-term data are not available to demonstrate if this is significantly delayed by treatment.

### ■ **Progressive-Relapsing (PRMS)**

Characteristics: Pts. experience steadily worsening disease from onset and have clear acute flare-ups (attacks or exacerbations), with or without recovery. Periods between relapses are characterized by continuing disease progression.

**MS: Clinical Courses of Disease**  
% of MS Patients



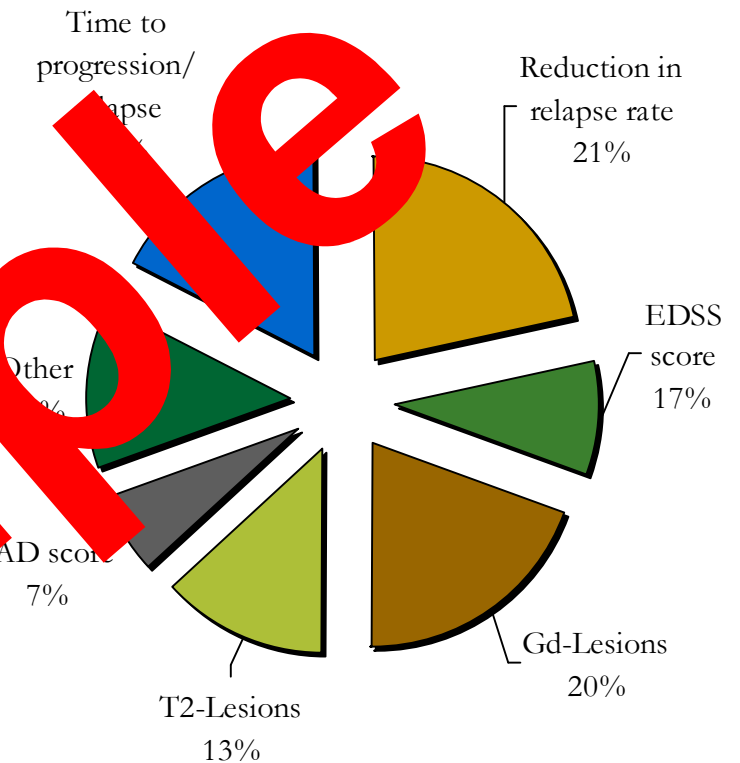
# Clinical endpoints used in Multiple Sclerosis trials

- Reduction in relapse rate is the most commonly utilized efficacy endpoint in pivotal MS clinical trials.
- Relapse rate is mainly used as an endpoint in phase III trials; while measures of Gd-lesions are more common in phase II proof-of-concept studies.

## Relapse-Definition

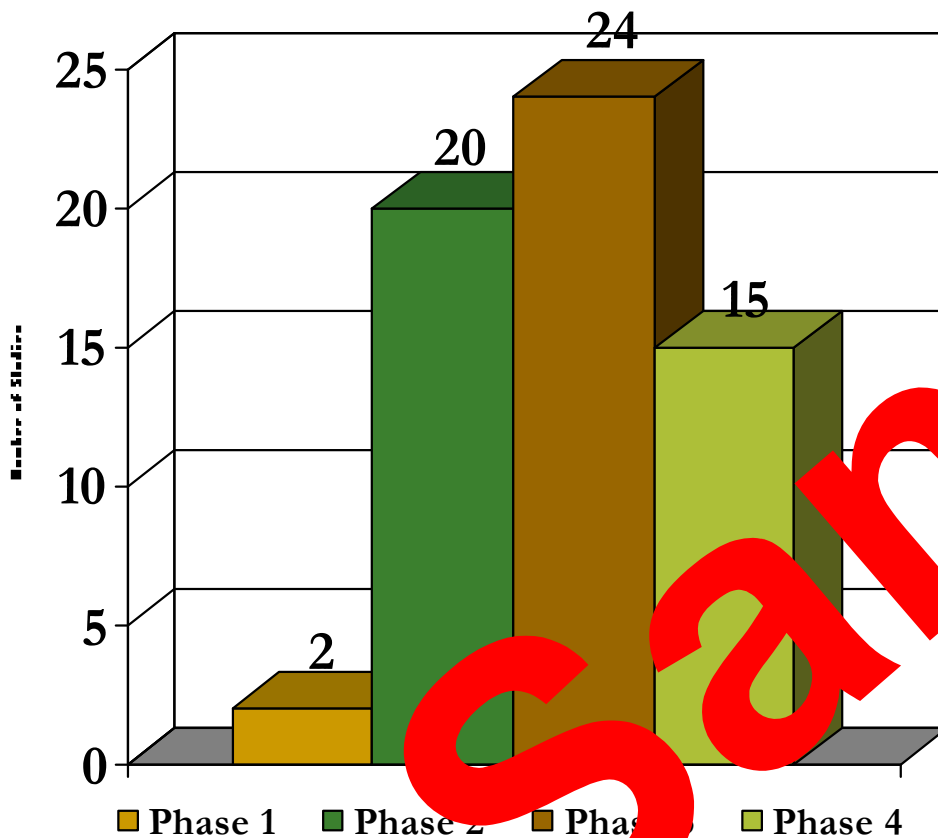
“New or recurrent neurological symptoms, not associated with fever or infection, lasting for at least 24 hours, and accompanied by new objective neurological findings upon examination by the Examining Neurologist”

## Primary Endpoints in MS Trials



# Overview of Clinical Landscape

Breakdown of Industry Sponsored Multiple Sclerosis Clinical Trials



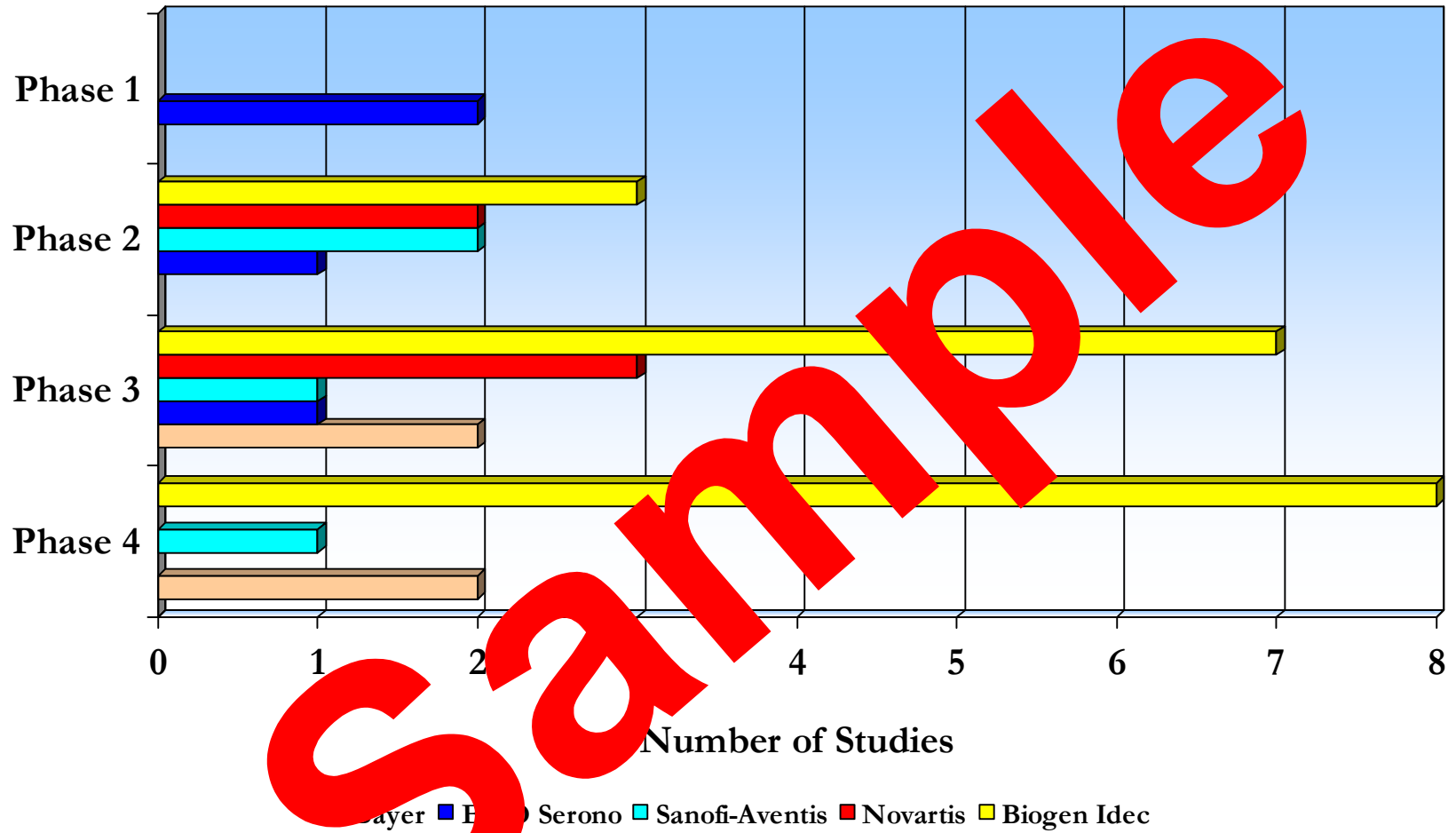
## Notable Programs

- Campath: 525 pts. in 1 trial\*
- FTY-720: 1,000 pts. in 5 trials
- Triflunomide: 1,320 pts. in 3 trials
- Copaxone: 1,550 pts. in 2 trials
- Tysabri: 11,000 pts. in 8 trials

>33,000 pts. enrolled or are being recruited in MS trials

# Key Players in Multiple Sclerosis Research & Development

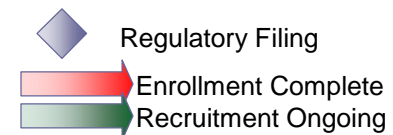
Key Players Conducting MS Trials



# Clinical Trial MAP-Oral Competitors



*Assumptions: Enrollment for pivotal trials takes 18 months for Biologics and 12 months for orally formulated products*






# Clinical Trial MAP-Biologic Competitors



Sample

Assumptions: Enrollment for pivotal trials takes 18 months for Biologics and 12 months for orally formulated products

 Regulatory Filing  
 Enrollment Complete  
 Recruitment Ongoing

---

## Section 2:

# Ongoing Clinical Trial in Multiple Sclerosis

---

Industry-Sponsored Clinical Trials: Multiple Sclerosis								
Drug	Mechanism	Company	Study Title	Phase	# Pts	Study Design	Primary Endpoint	Start Date/End Dates
BHT-3009	Myelin basic protein modulator	Bayhill Therapeutics	Phase I Trial of Immunotherapy With BHT-3009 Alone or Combined With Atorvastatin in Patients With Multiple Sclerosis	1	30	Randomized, Double-Blind, Active Control, Crossover	Safety	July 2004-March 2007
RTL1000	T-lymphocyte inhibitor	Artielle ImmunoTherapeutics	Phase 1 Safety Study of RTL1000 (Recombinant T Cell Receptor Ligand) in Subjects With Multiple Sclerosis	1	30	Randomized, Double-Blind, Placebo Control, Single Group Assignment, Safety	Safety	Dec-06
ABT-874	Fully human anti-IL-12/IL-23 monoclonal antibody	Abbott	24-Week, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Dose Finding, Safety, Tolerability, and Efficacy Study of the Human Anti-IL-12 Antibody ABT-874 in Subjects With Multiple Sclerosis With a 24-Week Double-Blind, Active Extension Phase	2	215	Randomized, Double-Blind, Placebo Control, Parallel Assignment, Safety/Efficacy	Gd enhanced (T1 weighted) lesions [24 weeks]	May-04
BHT-3009	Myelin basic protein modulator	Bayhill Therapeutics	BHT-3009 Immunotherapy in Relapsing Remitting Multiple Sclerosis	2	252	Randomized, Double-Blind, Placebo Control, Parallel Assignment, Safety/Efficacy	New Gd-enhancing MRI lesions in relapsing remitting MS	February 2006-June 2007
BHT-3009	Myelin basic protein modulator	Bayhill Therapeutics	BHT-3009 Immunotherapy in Relapsing Remitting Multiple Sclerosis	2	252	Randomized, Double-Blind, Placebo Control, Parallel Assignment, Safety/Efficacy	New Gd-enhancing MRI lesions	February 2006-June 2007
Campath	Humanized anti-CD52 monoclonal antibody	Genzyme/Bayer	Phase II, Randomized, Open-Label, Three-Arm Study Comparing Low- and High Dose CAMPATH (MABCAMPATH) and High-Dose Rebif in Patients With Early, Active Relapsing-Remitting Multiple Sclerosis	2	334	Randomized, Open-Label, Parallel Assignment, Safety/Efficacy--Number of relapses in study	Time to Sustained Accumulation of Disability (SAD) [3 years] Relapse Rate [3 years]	December 2002-December 2009
CDP323	Oral VLA-4 integrin antagonist	UCB/Biogen	Double-Blind, Placebo-Controlled, Randomized, Parallel-Group Phase II Study in Subjects With Relapsing Remitting Multiple Sclerosis to Evaluate Safety, Tolerability, and Effects of CDP323	2	279	Randomized, Double-Blind, Placebo Control, Parallel Assignment, Safety/Efficacy--Number of arms in study: 3	MRI lesion parameters [24 weeks]	May 2007-December 2008
Cladribine+Rebif	Oral adenosine deaminase inhibitor	EMD Serono	Phase II, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Safety, Tolerability, and Efficacy Study of Add-on Cladribine to Rebif in Relapsing-Remitting Multiple Sclerosis Subjects With Active Disease	2	260	Randomized, Double-Blind, Placebo Control, Parallel Assignment, Safety/Efficacy	Mean change in the number of T1 gadolinium-enhanced lesions per subject per scan from baseline to 96 weeks	December 2006-February 2010
CNTO-1275	Fully human anti-IL-12 and IL-23 monoclonal antibody	Celgene	Phase II, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Ranging Study of Intramuscular Subcutaneous Injections of Human Monoclonal Antibody to IL-12p40(CNTO1275) in Subjects With Relapsing-Remitting Multiple Sclerosis	2	250	Randomized, Double-Blind, Placebo Control, Parallel Assignment, Safety/Efficacy	New Gd-enhancing T1-weighted lesions[Week 23]	Jul-04

Source: National Institutes of Health

---

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.

---

## 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.