

A Datamonitor report

Pipeline Insight: Orphan Diseases in CNS – Part II: Amyotrophic Lateral Sclerosis – Companies Need to go Back to the Lab to Strengthen Weak Pipeline

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Use this report to...

Access the lucrative potential of this underdeveloped neurodegenerative disease therapeutic market

Providing you with:

- **Analysis** and forecasts of the commercial potential of the ALS market to 2016
- **Analysis** of patient potential, marketing factors, commercial attractiveness and clinical attractiveness of key late-stage pipeline drugs
- **Recommendations** for maximizing the potential of drugs in this niche orphan disease market
- **Indication** of specific sales forecasts of marketed and key pipeline drugs to 2016

Introduction

The ALS market was worth \$148m in 2006 across the seven major markets. With the only approved treatment for ALS, Sanofi-Aventis's Rilutek (riluzole), facing generic incursion in 2012–13, future growth in this market is dependent on the success of pipeline drugs.

Given the rapid progression of neurodegeneration observed in this condition, the ability to use survival as a viable endpoint, and the increasing incorporation of translational medicine into drug development, Datamonitor suggests that new market entrants use ALS as a model disease for developing anti-neurodegenerative drugs. With the underlying features of neurodegeneration similar across disease states, the patient potential for such drugs could be large, with Alzheimer's disease and Parkinson's disease possible targets.

Key findings and highlights

- A lack of new entrants, and the possibility of polytherapy, results in Sanofi-Aventis's Rilutek (riluzole) dominating the market until patent expiry in 2012-13 in Datamonitor's base scenario.
- Orphan drug status, rapid uptake following launch, limited risk to the company's share price if drugs fail, and possible indication expansions make long-term investment in ALS a commercially viable option.
- A scenario forecast based on the clinical success of rhIGF-1 (recombinant human insulin-like growth factor I) related therapies reveals a potentially lucrative market. However, with a high attrition rate of ALS Phase III clinical trials, and mixed efficacy data in Phase II, the results of currently underway studies will be pivotal.

Reasons to buy

- **Access** the lucrative potential of this underdeveloped neurodegenerative disease therapeutic market
- **Benchmark** key late-stage compounds against the current leading therapy Sanofi-Aventis's Rilutek (riluzole)
- **Understand** the opportunities in this market based on the comments of interviewed key opinion leaders

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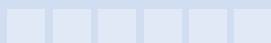
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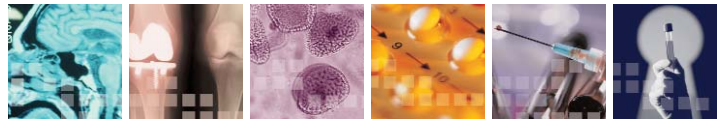
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Sample pages from the report

Market Overview DATAMONITOR

Figure 7 illustrates Datamonitor's identified key unmet needs in ALS treatment. These have been identified by Datamonitor's secondary research, and confirmed by key opinion leaders.

Figure 7: Key unmet needs in ALS treatment

Source: Datamonitor

Given the delay in diagnosis (see Table 2), drugs to recover lost function are required for an effective treatment. If such drugs cannot be developed, then drugs to slow disease progression longer than Rilutek, or that...

"First of all we have to slow down therapy, the drug..."

The delay in diagnosis is a high priority. The general theory is that the earlier the effect it will have on disease progression destroyed before the disease becomes irreversible.

"You are not going to get better neuron function, you are late, you have to..."

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Pipeline Overview and Dynamics DATAMONITOR

Figure 12 shows the novelty of key late-stage pipeline drugs, 2007.

Figure 12: Origin of ALS key late-stage pipeline drugs, 2007

Source: Datamonitor; MedTRACK, October 2007, Copyright Thomson Scientific

Advantages of developing drugs for orphan diseases

Given the small patient potential, developing drugs for orphan diseases may not see enough of an incentive of recouping money spent in developing the development of drugs for ALS and advantages over alternative treatments.

NINDS funding of clinical trials

Many of the drugs under development by the National Institute of Neurological Disorders and Stroke (NINDS) are in the late stage pipeline (e.g. rhIGF-I and Ceftriaxone) and ALS is comparatively cheap.

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Late-stage Drug Analysis & Forecasts DATAMONITOR

As can be seen in Table 6, this would set rhIGF-I at \$12,417 per patient per year in the US, \$9,783 per patient per year in the EU and \$11,765 per patient per year in Japan. The Rilutek and Avonex estimates in Table 6 are based on 2006 IMS MIDAS sales data. The rhIGF-I estimate is for year of launch.

Table 6: Estimated cost of Rilutek, Avonex and rhIGF-I, 2006

	US (\$)	SEU (\$)	Japan (\$)
Rilutek			
IMS sales/Standard Units			
Price per IMS Standard Unit	12.1	6.5	12.43
Cost per day (twice-daily)	24.3	13.0	24.86
Cost per year	8,809.5	4,745.0	9,073.9
Avonex			
IMS sales/Standard Units			
Price per IMS Standard Unit/weekly dose	307	265	270
Cost per year	15,954	14,820	14,456
rhIGF-I			
Estimated cost per year per patient	12,417	9,783	11,765

Source: Datamonitor, Thomson Reuters 2007 edition and IMS MIDAS Sales Data, IMS Health, August 2007, Copyright ©, printed with permission. DATAMONITOR

Patient potential

The patient potential of rhIGF-I is clearly dependent on a successful outcome of the ongoing Phase III clinical trial. Under Datamonitor's IGF-1/PLEX successful clinical development scenario, clinical efficacy will be proven in this trial.

In the first Phase II clinical trial investigating the efficacy of rhIGF-I, progression of functional impairment in patients receiving high-dose (0.10mg/kg/day) rhIGF-I was 26% slower than in patients receiving placebo (p=0.01) (Lai et al., 1997). If this prolongation of function were translated to survival, this would appear to be a drug that is not inferior to Rilutek.

Even a modest increase in the lifespan of ALS patients will offer enough efficacy to warrant significant uptake in the ALS patient population. This can be seen with the marketed drug Rilutek (see Table 2). From consultation with key opinion leaders,

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"...It's naive to pull drugs off the shelf which have mild effects on inflammation or excitotoxicity and try them in patients with ALS..."

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LATE-STAGE DRUG ANALYSIS & FORECASTS

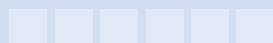
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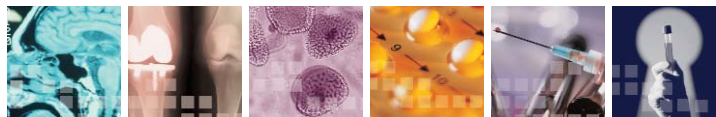
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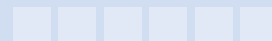
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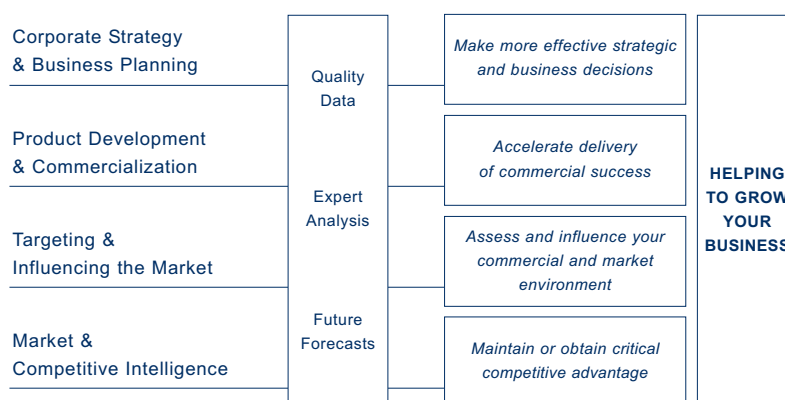
"...ALS is a very interesting paradigm for neuronal cell degeneration..."



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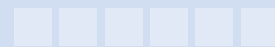
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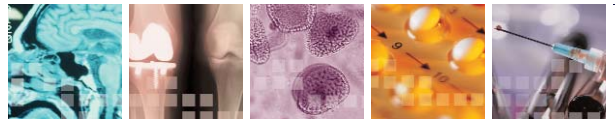


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- Antidepressants
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- Neurology

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Pipeline Insight: Orphan Diseases in CNS – Part I: Huntington's Disease

Analysis of the future amyotrophic lateral sclerosis (ALS) market with scenario based revenue forecasts of marketed and late-stage pipeline drugs to 2016. Conclusions are supported by key opinion leader comments.

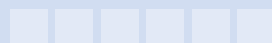
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