

**FORM 6-K**

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

**Report of Foreign Private Issuer  
Pursuant to Rule 13a-16 or 15d-16  
under the Securities Exchange Act of 1934**

For the month of March, 2006

Commission File Number 0-21392

AMARIN CORPORATION PLC

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(Translation of registrant's name into English)

7 Curzon Street, London W1J 5HG, England

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(Address of principal executive offices)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

Form 20-F  x

Form 40-F  o

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Yes  o

No  x

Note: Regulation S-T Rule 101(b)(1) only permits the submission in paper of a Form 6-K if submitted solely to provide an attached annual report to security holders.

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

Yes  o

No  x

Note: Regulation S-T Rule 101(b)(7) only permits the submission in paper of a Form 6-K if submitted to furnish a report or other document that the registrant foreign private issuer must furnish and make public under the laws of the jurisdiction in which the registrant

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is incorporated, domiciled or legally organized (the registrant's "home country"), or under the rules of the home country exchange on which the registrant's securities are traded, as long as the report or other document is not a press release, is not required to be and has not been distributed to the registrant's security holders, and, if discussing a material event, has already been the subject of a Form 6-K submission or other Commission filing on EDGAR.

Indicate by check mark whether by furnishing the information contained in this Form, the registrant is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes

No

If "Yes" is marked, indicate below the file number assigned to the registrant in connection with Rule 12g3-2(b):

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This report on Form 6-K is hereby incorporated by reference in (a) the registration statement on Form F-3 (Registration No. 333-104748) of Amarin Corporation plc and in the prospectus contained therein, (b) the registration statement on Form F-3 (Registration No. 333-13200) of Amarin Corporation plc and in the prospectus contained therein, (c) the registration statement on Form F-3 (Registration No. 333-12642) of Amarin Corporation plc and in the prospectus contained therein, (d) the registration statement on Form F-3 (Registration No. 333-121431) of Amarin Corporation plc and in the prospectus contained therein and (e) the registration statement on Form F-3 (Registration No. 333-121760) of Amarin Corporation plc and in the prospectus contained therein, and this report on Form 6-K shall be deemed a part of each such registration statement from the date on which this report is filed, to the extent not superseded by documents or reports subsequently filed or furnished by Amarin Corporation plc under the Securities Act of 1933 or the Securities Exchange Act of 1934.

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**EXHIBIT LIST**

<u>Exhibit</u>	<u>Description</u>
99.1	Press release dated March 2, 2006 titled: Quarterly Update: Year-End 2005 Financial Results Reported.

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## SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

AMARIN CORPORATION PLC

By: /s/ Richard A. B. Stewart  
Richard A. B. Stewart  
Chief Executive Officer

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Date: March 6, 2006

# QUARTERLY UPDATE

## Year-End 2005 Financial Results Reported

### Snapshot

□ 60;

March 2, 2006

Amarin Corporation plc is a neuroscience company focused on the research, development, and commercialization of novel drugs to treat central nervous system disorders, with a particular emphasis on neurological diseases and disorders. The Company's most advanced product, Miraxion™, is in Phase III development for Huntington's disease (HD), in Phase II development for depressive disorders, and in pre-clinical development for Parkinson's disease. The Company is using a proprietary technology platform based on an understanding of the chemical nature of the brain. Amarin's lipophilic drugs are predominantly fat-soluble and thus can easily cross the blood-brain barrier into the brain, conferring many advantages over traditional treatments. HD is a lethal, autosomal dominant, genetic disease characterized by severe movement disorder, dementia, and psychiatric disturbance. There is currently no approved treatment for this disease in the U.S. Miraxion™ has been granted Fast Track designation by the U.S. Food and Drug Administration (FDA) for HD and has received Orphan Drug Status in the U.S. and Europe. The Company estimates the global market for HD to be in excess of \$500 million. Depression is one of the most common mental illnesses, affecting more than 19 million people in the U.S. and representing a \$14 billion market dominated by selective serotonin reuptake inhibitors (SSRIs). Miraxion™ has been shown in Phase II clinical trials to benefit those individuals with melancholic depression, a potential market worth \$2-3 billion in the U.S. alone.



### **Amarin Corporation plc**

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England

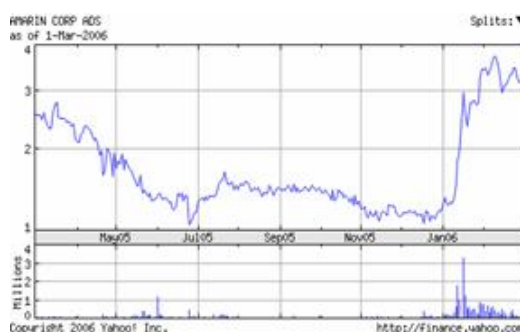
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### Recent Financial Data

Ticker (Exchange)	AMRN (NASDAQ)
Recent Price (03/01/06)	\$3.26
52-Week Range	\$1.03-3.92
Shares Outstanding	78.4 million
Market Cap.	\$255.6 million
Average 3-month volume	370,525
Insider +5% Owners	34%
Institutional Owners	40%
EPADS (qtr. ended 12/31/05)	(\$0.10)
Employees	25



### Key Points

§ For the quarter ending December 31, 2005, Amarin reported a net loss of \$5.2 million or (\$0.10) per ADS, compared with a net loss of \$4.8 million or (\$0.13) per ADS for the quarter ended December 31, 2004. For the year ended December 31, 2005, Amarin reported a net loss of \$18.7 million or (\$0.40) per ADS, compared with net income of \$4.7 million or \$0.21 per ADS for the year-ago period.

§ Research and development (R&D) expenses for the quarter were \$2.4 million, up from \$981,000 for the same period last year. R&D expenses increased by approximately \$1.4 million primarily due to costs associated with the Phase III trials with Miraxion™ in Huntington's disease (HD).

§ At December 31, 2005, Amarin had cash of \$33.9 million, compared to \$11.0 million at December 31, 2004. The increase is primarily due to the \$46.3 million in proceeds raised from financings over the year and a license fee received in December 2005.

§ On January 23, 2006, Amarin announced that it entered into a definitive purchase agreement with Dr. Tony Ryan for a private equity placement resulting in the proceeds of \$2.0 million.

§ Amarin has no debt other than working capital liabilities, and the Company forecasts to have sufficient cash to fund operations into the second half of 2007 and, with possible revenue from partnering activities, potentially beyond.

§ On January 3, 2006, Amarin announced that it has licensed to Multicell Technologies Inc. (MTEC.OB-OTC.BB) the exclusive, worldwide rights of LAX-202 for the treatment of fatigue in patients suffering from multiple sclerosis in return for a series of development-based milestones and a royalty on net sales.

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## **Business and Financial Update**

### **Fourth Quarter Results**

Amarin Corporation plc reported fourth quarter financial results on February 9, 2006. Revenues for the fourth quarter were \$500,000, representing an initial access fee received from Multicell Technologies Inc. on the licensing of exclusive, worldwide rights to LAX-202 for the treatment of fatigue in patients suffering from multiple sclerosis. Research and development (R&D) expenses for the fourth quarter were \$2.4 million, up \$1.4 million compared with \$980,000 for the year ago period. R&D expenses reflect costs of staff, third party research contracts, preclinical studies, clinical supplies, and the costs of conducting the Phase III trials in HD, including those associated with the two contract research organizations (CROs) performing the HD trials, the Huntington's Study Group ("HSG") and Icon, plc. Selling, general, and administrative expenses (SG&A) for the fourth quarter 2005 were \$3.4 million versus \$4.3 million for the same period last year. These costs primarily represent Amarin's general and administrative expenses, business and corporate development expenditures, the cost of maintaining and renewing Amarin's portfolio of intellectual property, and group restructuring spending of \$652,000. The Company reported a net loss of \$5.2 million or (\$0.10) per ADS for the fourth quarter, compared with a net loss of \$4.8 million (\$0.13) per ADS for the same period last year.

### **Year End Financial Results**

For the year end 2005, revenues were \$500,000 (representing an initial access fee received from Multicell Technologies received in the fourth quarter) versus \$1.0 million in 2004. R&D expenses for the year ended 2005 were \$8.3 million versus \$3.5 million for the year ended December 31, 2004. SG&A expenses for the year ended December 31, 2005 were \$11.1 million, compared to \$10.5 million for the same period last year. For the year ended December 31, 2005, Amarin reported a net loss of \$18.7 million or (\$0.40) per ADS, as compared to net income of \$4.7 million or \$0.21 per ADS for the year ended December 31, 2004. As of December 31, 2005, the Company had a cash position of \$33.9 million versus \$11.0 million at December 31, 2004.

### **Recent Events**

§ *Amarin Announced a \$2.0 Million Equity Investment by Dr. Tony Ryan.* On January 23, 2006, Amarin announced that it entered into a definitive purchase agreement with Dr. Tony Ryan for a private equity placement resulting in proceeds of \$2.0 million. Dr. Ryan is an existing investor, as well as a director of Ryanair Holdings, and was a founder and former chairman of GPA Group plc, an operating lessor of commercial aircraft. Dr. Ryan also served as executive chairman of GE Capital Aviation Services, Ltd.

§ *Amarin Reported Preliminary Results from Parkinson's Disease Pre-Clinical Program Using Miraxion™.* On January 10, 2006, Amarin announced results from two studies in its pre-clinical program investigating Miraxion™. The first study showed Miraxion™'s neuroprotective effects in cell lines associated with Parkinson's disease by interacting with brain-derived neurotrophic factor, leading to improved cell viability and the slowing of neuronal apoptosis (cell death) associated with the symptoms of Parkinson's disease. The second study demonstrated that Miraxion™ modulated cellular function in MPP+ treated SH-SY5Y cells in an *in vitro* Parkinson's disease model and behavior in an MPTP-induced PD model. MPTP is a neurotoxin commonly used to investigate PD in pre-clinical models. MPP+ is a metabolite of MPTP. In this study, treatment with Miraxion™ enhanced learning performance, improved motor function, and reduced bradykinesia in such preclinical models.

§ *Amarin Licensed Phase IIB/III Drug for the Treatment of Fatigue in Multiple Sclerosis to Multicell Technologies.* On January, 3, 2006, Amarin announced that it had licensed to Multicell Technologies the exclusive, worldwide rights of LAX-202 for the treatment of fatigue in patients suffering from multiple sclerosis (MS). Multicell renamed LAX-202 to MCT-125, and is expected to further evaluate MCT-125 in a pivotal Phase IIB/III clinical trial.

- o MCT-125 has demonstrated efficacy in significantly reducing the levels of fatigue in MS patients who enrolled in a 138 patient, multi-center, double-blind, placebo-controlled Phase IIb clinical trial conducted in the UK. The drug proved to be effective in both moderately and severely affected MS patients. Multicell Technologies intends to proceed with the Phase IIb/III trial of MCT-125 using the data generated by Amarin following discussions with the FDA.
- o Multicell's discussions later this year with the FDA could help to determine whether they will go directly into Phase III or conduct a Phase IIb trial. Under the terms of the agreement, Amarin received an upfront fee of \$500,000 million upon signing and is expected to receive a second equivalent amount in May/June of this year. Amarin is expected to receive milestones on regulatory filing, approval, and 12 months following approval for each of the U.S. and EMEA markets. The royalty rate on worldwide sales is high-single-digit.

§ *Amarin Announced a \$26.4 Million Private Placement.* On December 22, 2005, Amarin announced that it had completed a private equity placement resulting in proceeds of \$26.4 million in American Depository Shares (ADSs) and warrants. As a result of this financing, the Company's cash position at year end was estimated at \$33 million, and the Company now forecasts having sufficient cash to fund operations into mid-2007 and, with possible revenue from partnership activities in 2006, potentially beyond. Investors in the private placement included Southpoint Capital Advisors LP, Biotechnology Value Fund LP, Fort Mason Capital LP, Domain Public Equity Partners LP, and other new and existing institutional and accredited investors, including certain directors and executive officers of Amarin.

§ *Amarin Announced Commencement of European Pivotal Phase III Clinical Trial for Miraxion™ in Huntington's Disease (HD).* On December 15, 2005, Amarin announced that the European Phase III clinical trial of Miraxion™ in HD had commenced. The European trial is a multi-center, randomized, double-blind, placebo-controlled study of Miraxion™ in 240 patients at up to 33 sites over a six month period. The U.S. Phase III clinical trial of Miraxion™ in HD commenced dosing in September 2005.

§ *Neuroprotective Effects of Miraxion™ Demonstrated.* On November 16, 2005, the Company announced important results in two specific areas of research on Miraxion™. Amarin, along with the Institute of Neuroscience at Trinity College, Dublin, has progressed in determining the effect of Miraxion™ on modulation of neuron-inflammation and the impact of Miraxion™ on the reduction of microglial activation. Miraxion™ has demonstrated effects that protect the brain from inflammation (which is often associated with a number of neurodegenerative diseases, including Alzheimer's, Parkinson's, and HD), as well as a decrease in the age-related learning and memory decline accompanied by the inflammatory changes associated with neuro-degenerative diseases. This reduction of "bad" cytokines and increase in "good" cytokines also applies to the response seen in Amarin's Phase III trial in HD and the Phase IIa trials in depressive disorders. The impact of Miraxion™ effectively acts on the aging process in the brain, which causes inflammation leading to various neurodegenerative diseases and depression.

§ *Miraxion™ Trial for HD Up and Running in U.S.* On September 12, 2005, Amarin announced that it had reached an agreement with the U.S. FDA under the special protocol assessment (SPA) procedure for the design of two pivotal Phase III clinical trials of Miraxion™ in HD. The SPA is a process under which the FDA provides evaluation and guidance on clinical trial protocols for Phase III trials. On September 21, 2005, Amarin announced that patient enrollment and first dosing had commenced in the U.S. Phase III clinical trial of Miraxion™ in HD by the HSG. Significant resources and commitment have been dedicated to the successful commencement of this trial.

§ *Addition to Management Team.* On November 2, 2005, the Company announced the appointment of Mr. Tom Maher as general counsel, effective February 2006. Mr. Maher has acted as adviser to domestic and international pharmaceutical, biotechnology, and medical technology companies and led innovative life sciences transactions while being a partner and head of the Life Sciences Group at Matheson Ormsby Prentice, a leading Dublin law firm. Mr. Maher has experience in structuring and negotiating international and domestic transactions in the pharmaceutical and biotechnology industry and general corporate and commercial law.

**Company Background**

Amarin Corporation plc is a neuroscience company focused on the research, development, and commercialization of novel drugs for the treatment of central nervous system (CNS) disorders using a proprietary technology platform based on an understanding of the chemical composition of the brain. Unlike most organs in the body, the brain is 60% fat (phospholipid) and 30% protein. Similar to the way in which oil and water do not mix, most drugs that easily dissolve in water do not readily penetrate the brain.

Amarin’s lipophilic drugs are predominantly fat-soluble and therefore easily cross the blood-brain barrier. The majority of pharmaceuticals marketed to treat neurological and psychiatric disorders have mechanisms of action that target receptors (surface proteins embedded in the phospholipid membrane) or neurotransmitters in the brain. Amarin’s novel proprietary technology targets the biochemical imbalances in the phospholipids themselves. Amarin’s first lipophilic product to use this technology is Miraxion™, in Phase III development for Huntington’s disease (HD), in Phase II development for depressive disorders, and in pre-clinical development for Parkinson’s disease . Table 1 summarizes the status of the Company’s product development pipeline, including product, indication, status, and partnerships in place (as information has been made publicly available by the Company). Below, is an introduction to these products. More comprehensive details are provided in our Executive Informational Overview® (EIO®), dated October 11, 2005.

Table 1  
Amarin Corporation plc  
PRODUCT PIPELINE

PROGRAM	INDICATION	DEVELOPMENT				Status/Partner
		P/C	I	II	III	
Amarin Commercialization						
Miraxion	Huntington's disease (US)					PIII trials on-going
Miraxion	Parkinson's disease					Planned to enter clinical trials
Comb. Lipid	Neurodegeneration					Lead Candidate selection 2006
Out -licensing/Partnering						
Miraxion	Huntington's disease (EU)					Partnered in key E.U. countries; Scil Biomedicals, Juste S.A.Q.F., Link
Miraxion	Depressive disorders					Japan-partner not disclosed U.S and EU partner discussions on-going
LAX-201	Major Depression in women					Phase II complete-seeking partner
MCT-125	Multiple Sclerosis Fatigue (EU)					Multicell Technologies-worldwide partner
IP	CNS indications					Partner discussions on-going

Current development stage

Source: Amarin Corporation plc.

**Miraxion™**

Miraxion™ is a semi-synthetic, highly purified (>97%) derivative of (all-cis)-5,8,11,14,17-eicosapentaenoic acid (ethyl-EPA). It is a long chain of highly unsaturated fatty acid. A similar product, Epadel, has been sold in Japan for approximately 15 years and has been used by more than two million patients for the treatment of hyperlipidemia and arteriosclerosis obliterans. No significant side effects, other than mild and transient gastrointestinal disturbances, have been reported, which accords with Amarin’s own experience with Miraxion™.

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### *Huntington's disease (HD)*

HD is a lethal, autosomal dominant, genetic disease, characterized by severe movement disorder, dementia, and psychiatric disturbance. It is believed to be caused by a genetic mutation of cytosine, adenosine, and guanine (CAG) polymorphic trinucleotide repeat, with a direct link between CAG repeat length and age of onset, disease progression, and the clinical symptoms. CAG repeat length can be measured by a genetic blood test.

In the U.S., there are approximately 30,000 individuals diagnosed with HD and approximately 200,000 considered 'at-risk' for developing the disease (with similar numbers in Europe). Currently, there are no approved treatments in the U.S. for HD. It is estimated that the total annual cost of caring for patients with symptoms of HD is approximately \$2.5 billion (Source: U.S. HD Economics. Babson College 2001). As such, the Company believes that the market for an effective treatment could be in excess of \$250 million in the U.S. and \$500 million worldwide.

### Miraxion™ for HD

The mechanism of action for Miraxion™ in HD is believed to involve stabilization of neuronal cell membranes and mitochondrial integrity of suffering neurons, which degenerate as the disease progresses, thereby preventing or slowing progression from neuronal dysfunction to apoptosis. Slowing or preventing neuronal cell death leads to an improvement of signal transduction resulting in significant enhancements in motor dysfunction in HD patients. Interference with the apoptotic cascade is a unique characteristic of Miraxion™.

In aging brains, Miraxion™ has been found to demonstrate neuro anti-inflammatory effects, consequently protecting the brain from inflammation which is often associated with a number of neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's disease (HD). Age-related learning and memory decline in the brain has also been shown to be accompanied by inflammatory changes, typified by microglial activation. These changes are also accompanied and possibly triggered by an increase in pro-inflammatory cytokines and a decrease in protective cytokines. Miraxion™ has been granted Fast Track designation by the U.S. Food and Drug Administration (FDA) for HD and has received Orphan Drug Status in the U.S and Europe.

Following positive results with Miraxion™ for HD in earlier Phase II studies, a 135-patient 12-month Phase III double-blind, placebo-controlled trial was conducted. In February 2003, Amarin announced the results of this study outlining that although statistical significance was not achieved in the "Intent to Treat" group, primarily due to a high number of severely ill HD patients who did not comply with the protocol, those patients that complied with the protocol ("Per Protocol") showed a strong trend towards statistical significance.

The Company had additionally pre-specified in the protocol of the initial Phase III clinical trial that it would examine the response of HD patients to Miraxion™ based on their genetic makeup. Analysis of the clinical data from the initial Phase III study identified a group of HD patients with a specific gene variant that responded to Miraxion™ with statistical significance. This group had a CAG repeat length of less than or equal to 44. It is estimated that patients with such a repeat length represent approximately 70% of all HD patients.

The trial was conducted across six centers. An analysis of the data on a center by center basis illustrated that Miraxion's effectiveness in the group of patients with a CAG repeat length less than or equal to 44 was consistent across centers, i.e. Miraxion™ worked better in patients with a CAG repeat length less than or equal to 44 than in patients with a CAG repeat length greater than 44, and that Miraxion™ worked better than placebo in patients with CAG repeat length less than or equal to 44. Based upon this data in the genetic sub-group, Amarin planned further Phase III clinical trials in the U.S. and Europe and these have now commenced.

On June 9, 2005, the Company announced that U.S. investigators had completed a meeting for the upcoming U.S. Phase III clinical trial for the treatment of HD; and on June 14, announced that the Huntington's Study Group (HSG), an organization of the leading researchers and neurologists in the U.S.,

had commenced recruitment for the U.S. Phase III clinical trial of Miraxion™ in HD. The HSG is to be conducting a clinical study (TREND-HD) of Miraxion™ in persons 35 years of age or older who have mild to moderate HD. The involvement of the HSG is expected to accelerate recruitment to the trial and ensure accurate rating of patients. A second Phase III clinical trial of Miraxion™ in HD is expected to be conducted in Europe in collaboration with Icon, plc and EURO-HD.

On September 12, 2005, Amarin announced that it had reached an agreement with the U.S. FDA under the Special Protocol Assessment (SPA) procedure for the design of two pivotal Phase III clinical trials of Miraxion™ in HD. The SPA is a process under which the FDA provides evaluation and guidance on clinical trial protocols for Phase III trials. The U.S. and European trials are expected to be multi-center, randomized, double-blind, placebo-controlled studies of Miraxion™ at 43 sites in the U.S. and up to 28 sites in Europe. The trials are expected to involve a total of up to 540 HD patients, with approximately 300 in the U.S. Phase III trial and approximately 240 in the European Phase III trial over a 6 month period. Both U.S. and European trials have now commenced.

## *Depressive Disorders*

A depressive disorder is an illness that involves the body, mood, and thoughts. It affects the way a person eats and sleeps, the way one feels about oneself, and the way one thinks about things. A depressive disorder is not the same as a passing blue mood. Approximately 19 million Americans (9.5% of the adult population) suffer from depressive illnesses every year. U.S. sales of antidepressants approximate \$14 billion annually—dominated by selective serotonin reuptake inhibitors (SSRIs) such as Prozac, Celexa, Zoloft, and Paxil. However, about one-third of patients with depression fail to respond to standard drugs and another third show only partial response. More than half of Americans affected by a depressive disorder suffer from major depressive disorder (MDD), with the remainder suffering from dysthymic disorder (chronic mild depression).

Melancholic depression represents one of two subtypes of MDD recognized by the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*, the main diagnostic reference of mental health professionals in the U.S. (published by the American Psychiatric Association, Washington D.C.). While considered one of the most severe forms of the disease, it is by no means uncommon and is a widely-accepted diagnosis. In fact, nearly one-quarter of patients with MDD exhibit melancholic features. Melancholic depression is currently treated similarly to MDD.

## Miraxion™ for Depressive Disorders

Miraxion™ for melancholic depression could become a significant product for Amarin as the potential treatable population in the U.S. is estimated at 1.3 million of the 2.7 million patients currently treated for depression, representing a market opportunity of \$2 billion to \$3 billion. In addition, an upside opportunity exists to capture another 1.1 million of the 2.2 million patients diagnosed with major depression but not treated. Should this occur, it would almost double the market potential.

Six Phase IIa placebo-controlled studies have been conducted with Miraxion™ in depressive disorders, with each showing a benefit in favor of Miraxion™. Three of the studies were investigator-lead with each showing a statistically significant benefit for Miraxion™ in the primary outcome. A further program of data analysis was carried out on the three Laxdale Limited (“Laxdale”) led studies. Laxdale is Amarin’s former research and development partner that was acquired by Amarin in October 2004. The data analysis indicated that Miraxion™ showed a significant clinical benefit in each of the three studies for those depression patients with melancholic characteristics. This sub-group of melancholic depression patients was defined by using select criteria from DSM-IV. As a result of these data, Amarin intends to further evaluate the clinical benefits of Miraxion™ in depression and intends to seek a development and marketing partner to accelerate this program.

There is currently no approved treatment specifically for melancholic depression and nothing as far advanced in clinical studies as Miraxion™, so far as the Company is aware. Thus, should Miraxion™ receive approval, it could become the first and only treatment for melancholic depression. Given its favorable safety profile and potential efficacy in the most severe patient population, Miraxion™ may also see extensive use outside the melancholic subset in the broader MDD population.

## Miraxion™ for Parkinson's Disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting approximately 1 million patients in the U.S. where the market for PD drug treatments in 2004 was approximately \$600 million. The main pathological characteristic of PD is the loss of pigmented dopamine-containing neurons of the substantia nigra associated with the presence of cytoplasmic a-synuclein-positive inclusions, the so-called Lewy bodies. Therapeutics that slow or stop the neurodegenerative processes of PD are expected to have a major impact for the treatment of PD.

Recently announced preliminary results from pre-clinical studies show that Miraxion™ has neuroprotective effects in PD. The first study showed Miraxion's neuroprotective effects in cell lines associated with PD. SH-SY5Y cells, derived from human neuroblastoma, with many properties similar to dopaminergic neurons, are widely utilized as an *in vitro* model to study effects and mode of action of drugs on PD.

Brain-derived neurotrophic factor (BDNF) and its receptor transmembrane tyrosine-specific protein kinase (TrkB) are linked to the etiology of neurodegenerative and mood disorders. The study of fully differentiated SH-SY5Y cells revealed that Miraxion™ increased the activation of TrkB and truncated TrkB messenger RNA (mRNA) expressions, which are critical functions for increasing dopamine (DA) levels in PD patients. The data showed that Miraxion™ demonstrated neuroprotective effects by interacting with BDNF, leading to improved cell viability and the slowing of the neuronal apoptosis (cell death) associated with the symptoms of PD.

The second study demonstrated that Miraxion™ modulated cellular function in MPP+ treated SH-SY5Y cells in an *in vitro* PD model and behavior in an MPTP-induced PD model. MPTP is a neurotoxin commonly used to investigate PD in pre-clinical models. MPP+ is a metabolite of MPTP. In this study, treatment with Miraxion™ enhanced learning performance, improved motor function and reduced bradykinesia in such animal models. Amarin is currently continuing preclinical studies in PD and plan to commence human studies in 2006.

## **Other Pipeline Products**

### *LAX-201*

LAX-201 is a patent-protected combination of folic acid and either of two leading classes of anti-depressant drugs (i.e. SSRIs and Serotonin Norepinephrine Reuptake Inhibitors [SNRIs]). A Phase II study showed LAX-201 increased the response rate in depressed women from 50%-60% to approximately 90%. Amarin is currently seeking a development partner for this product.

### *MCT-125 (formerly LAX- 202)*

MCT-125 is a patent-protected combination of an atypical antidepressant and an amino acid. In a 138-patient, multi-center, double-blind placebo-controlled Phase IIb trial, MCT-125 was effective in significantly reducing the levels of fatigue in multiple sclerosis patients. Amarin has licensed worldwide rights to MCT-125 to Multicell in return for a series of development-based milestones and a royalty on net sales. Multicell renamed LAX-202 to MCT-125.

### *Combinatorial Lipid Platform*

Combinatorial lipid chemistry offers a new and unique approach to improving the therapeutic effects and delivery characteristics of both known and novel compounds. Amarin has studied the use of different types of chemical linkage to attach a range of bioactive lipids either to other lipids or other drugs. The results are novel single chemical entities with predictable properties. This could offer substantial and clinically relevant advantages over either compound alone. Amarin intends to select at least one candidate from this program for further pre-clinical testing in 2006.

## **Key Points to Consider**

### **Corporate and General**

- § On January 23, 2006, Amarin announced that it had entered into a definitive purchase agreement with Dr. Tony Ryan for a private equity placement resulting in the proceeds of \$2.0 million. Dr. Ryan is an existing investor, as well as a director of Ryanair Holdings, and was a founder and former chairman of GPA Group plc, an operating lessor of commercial aircraft. Dr. Ryan also served as executive chairman of GE Capital Aviation Services, Ltd.
- § On January 10, 2006, Amarin announced results from two studies in its pre-clinical program investigating Miraxion™. Preliminary results from these studies showed that Miraxion™ has neuroprotective effects and modulated cellular function and behavior in preclinical models of Parkinson's disease.
- § On January 3, 2006, Amarin announced that it has licensed to Multicell Technologies Inc. the exclusive, worldwide rights of LAX-202 for the treatment of fatigue in patients suffering from multiple sclerosis.
- § On December 22, 2005, Amarin announced that it had completed a private equity placement resulting in proceeds of \$26.4 million in ADSs and warrants. Net proceeds to Amarin after commissions, fees, and expenses of the offering are estimated to be \$24.5 million. As a result of this financing, the Company's cash position at year end is estimated at \$33 million, and the Company now forecasts having sufficient cash into mid 2007 and, with possible revenue from partnership activities in 2006, potentially beyond.
- § On December 15, 2005, Amarin announced the European Phase III, 240 patient clinical trial of Miraxion™ commenced.
- § On November 16, 2005, Amarin announced that its ongoing pre-clinical research programs with the Institute of Neuroscience at Trinity College, Dublin have achieved important results in two specific areas of research—both concerning the mechanism of action and properties of Miraxion™.
- § Amarin made three senior management and board appointments, strengthening the Company's management team. Dr. Anthony Clarke as vice president of clinical development; Dr. Prem Lachman as non-executive director; and Tom Maher as general counsel effective as of February 2006.
- § Amarin has significant "insider" holdings, with the Board and insiders currently greater than 30% of the Company, including an 11% interest held by Amarin chairman, Mr. Thomas Lynch.

### **Huntington's Disease (HD)**

- § Huntington's disease (HD) is a genetic neurodegenerative disease characterized by movement disorder, dementia, and psychiatric disturbance. It has been diagnosed in approximately 30,000 patients in the U.S. and a similar number in Europe. Additionally, over 200,000 people in the U.S. are genetically "at risk" to developing the disease. Onset of symptoms is typically between 30 and 50 years of age with a typical life expectancy from diagnosis of 10 to 25 years. Patients with late stage disease require continuous nursing care, often in nursing homes, with an estimated annual cost to the U.S. economy of up to \$2.5 billion.
- § There is no effective treatment or cure for HD. The potential HD market in the U.S. is estimated to be in excess of \$250 million; worldwide, this market is believed to be greater than \$500 million.
- § The mechanism of action of Amarin's Miraxion™ is believed to involve stabilizing mitochondrial integrity of suffering neurons by acting on specific signal transduction pathways and a change in cellular energy metabolism. This may prevent or slow progression from neuronal dysfunction to apoptosis. In aging brains, Miraxion™ has been found to demonstrate neuro anti-inflammatory

effects, consequently protecting the brain from inflammation, which is often associated with a number of neurodegenerative diseases such as Alzheimer's, Parkinson's, and HD. Age-related learning and memory decline in the brain has also been shown to be accompanied by inflammatory changes, typified by microglial activation. These changes are also accompanied and possibly triggered by an increase in pro-inflammatory cytokines and a decrease in protective cytokines.

- § Miraxion™ for HD has been granted Fast Track designation by the U.S. FDA for HD, and has received Orphan Drug designation in the U.S. and Europe. Fast track designation means that the FDA can take actions to expedite the development and review of this potential New Drug Application (NDA). Orphan drugs are those that treat rare diseases or conditions, and, if approved, receive marketing exclusivity for seven years in the U.S. and up to 10 years in Europe. In addition to Orphan Drug marketing exclusivity, pending patents for Miraxion™ in HD will, if granted, provide protection through at least 2023.
- § Ethyl-EPA-based compounds have been approved for use in triglyceride-lowering drugs in Japan (i.e., Mochida's cardiovascular drug Epadel) and in the U.S. (Reliant's Omacor). Epadel's history illustrates the excellent safety profile of EPA-based compounds. Omacor's approval is important to Amarin since it identifies a regulatory pathway at the FDA for ethyl-EPA based compounds.
- § Following positive results with Miraxion™ for HD in Phase II studies, a 135-patient Phase III double-blind placebo-controlled study was initiated in 2001. In February 2003, Amarin announced the results of this study outlining that statistical significance was not achieved in the entire study patient population. However, in those patients that complied with the protocol, a trend to statistical significance was observed.
- § Further analysis of the clinical data from the Phase III study also identified a group of HD patients that responded to Miraxion™ with statistical significance. HD is believed to be caused by a genetic mutation of the cytosine, adenosine, and guanine (CAG) polymorphic trinucleotide repeat. It has been demonstrated that there is a direct link between CAG repeat length and age of onset, disease progression, and clinical symptoms.
- § Based on the strength of the response in the genetic sub-group, Amarin planned and recently commenced further Phase III clinical trials in the U.S. and Europe. These further trials have been designed utilizing the valuable findings from the initial Phase III trial, feedback from the FDA and EMEA, and target the sub-group of patients that responded to Miraxion™.
- § In September 2005, Amarin reached an agreement with the U.S. Food and Drug Administration (FDA) under the Special Protocol Assessment (SPA) procedure for the design of the Phase III clinical trials in HD with Miraxion™; (a SPA is the process under which the FDA provides evaluation and guidance on clinical trial protocols).
- § Miraxion™ has demonstrated a strong safety profile, with only one patient of 135 dropping out of the study over a year because of a treatment-related side effect, and all but one patient who completed a year opted to continue in an open label study for a second year.

### **Melancholic Depression**

- § Clinical depression is one of the most common mental illnesses, affecting more than 19 million people in the U.S. each year and 120 million worldwide. U.S. sales of anti-depressants are approximately \$14 billion annually, largely dominated by SSRIs. However, about one-third of patients with depression still fail to respond to standard drugs and another third show only partial response. Melancholic depression is related to non-response to standard antidepressants and psychotherapy.
- § Melancholic depression is a relevant subtype of depression characterized by specific somatic ("endogenous") symptoms. It is related to a dysfunction of the stress hormone regulation. This dysfunction, in particular, is the target of the action of Miraxion™.
- § Six Phase IIa placebo-controlled studies have been conducted with Miraxion™ in depressive disorders, with each showing benefit in favor of Miraxion™. Post-hoc analysis from three of the trials

demonstrated significant clinical benefits using Miraxion™ in depressed patients with melancholic features—a market estimated at \$2 billion to \$3 billion in the U.S. alone.

- § As a result of these clinical trial results, Amarin intends to further evaluate the clinical benefits of Miraxion™ in depression and has stated its intent to seek a development and marketing partner to accelerate this program.
- § Miraxion™ is protected by a broad portfolio of intellectual property. The use of Miraxion™ for depression is protected by a widely-granted patent until 2017. Other patents for Miraxion™ pending, if granted, would provide protection through at least 2023 for both HD and depression (and certain of its indications). Amarin’s broad intellectual property estate also contains patents for second-generation Miraxion™ and novel technology platforms.

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## **Risks**

Some of the information in this Quarterly Update relates to future events or future business and financial performance. Such statements can be only predictions and the actual events or results may differ from those discussed due to, among other things, the risks described in Amarin's reports on Forms 20-F and 6-K. The content of this Quarterly Update with respect to Amarin has been compiled primarily from information available to the public released by Amarin, through news releases, and through SEC filings. Amarin is solely responsible for the accuracy of that information. Information as to other companies has been prepared from publicly available information and has not been independently verified by Amarin. Certain summaries of scientific activities and outcomes have been condensed to aid the reader in gaining a general understanding. For more complete information about Amarin, please refer to the Company's website at [www.amarincorp.com](http://www.amarincorp.com). Additionally, please refer to our base report, the Executive Informational Overview<sup>®</sup> (EIO<sup>®</sup>) and Amarin's SEC filings for more comprehensive detail of Risk Factors ([www.crystalra.com](http://www.crystalra.com)).



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