Current Agreements

Dealdoc

Collaborative R&D, licensing and co-promotion agreement for mGluR4 positive allosteric modulators (terminated)

Addex Pharmaceuticals
Merck and Co

Dec 03 2007
Collaborative R&D, licensing and co-promotion agreement for mGluR4 positive allosteric modulators (terminated)

- **Companies:**
  - Addex Pharmaceuticals
  - Merck and Co

- **Announcement date:** Dec 03 2007
- **Deal value, US$m:** 172.3 : sum of upfront and milestone payments

### Details

- **Termination date:** Sep 02 2011
- **Industry sectors:** Bigpharma, Pharmaceutical, Biotech
- **Therapy areas:** Central Nervous System, Central Nervous System » Parkinson's disease
- **Technology types:** Drug delivery, Small molecules, Co-promotion, Collaborative R&D, Development
- **Deal components:** Licensing, Option, Termination, Discovery
- **Stages of development:** Preclinical, Formulation
- **Geographic focus:** Worldwide

### Financials

- **Deal value, US$m:** 172.3 : sum of upfront and milestone payments
- **Upfront, US$m:** 3.0 : upfront payment
- **Milestones, US$m:**
  - 0.25 : for achieving the first preclinical milestone
  - 0.5 : for achieving the second preclinical milestone
  - 105.75 : research, development and regulatory milestones for the first product developed for multiple indications
  - 61.0 : if a second and third product is developed
- **Quids, US$m:** n/d : Addex has an option to co-promote in certain European Union countries and will participate in the joint oversight committee for clinical development.
- **Funding, US$m:** 1.8 : receive research funding from Merck

### Termsheet

2 September 2011
Addex Pharmaceuticals will regain all rights to its metabotropic glutamate receptor 4 (mGluR4) positive allosteric modulator (PAM) program from Merck, known as MSD outside the United States and Canada, due to further pipeline prioritization.

Addex will regain rights to intellectual property and know-how and can pursue the program independently.

3 December 2007

Exclusive collaboration and license agreement with Merck & Co. with the goal of developing a new class of orally available drugs, initially as candidates for the treatment of Parkinson's disease and potentially other undisclosed indications.

The partners will discover and develop positive allosteric modulators (PAMs) targeting the metabotropic glutamate receptor 4 (mGluR4).

The deal includes lead mGluR4 PAMs discovered by Addex.

Addex will receive $3 million upfront and is eligible for up to $106.5 million in research, development and regulatory milestones for the first product developed for multiple indications.

Additional milestones of up to $61 million would be payable if a second and third product is developed.

Addex is eligible to receive undisclosed royalties on sales of any products resulting from this collaboration.

Addex and Merck will collaborate on preclinical development.

Merck will be responsible for clinical development.

Addex has an option to co-promote in certain European Union countries and will participate in the joint oversight committee for clinical development.

Extended agreement - Dec 2009

Addex will receive research funding from Merck in addition to the original financial terms, which include milestones and royalties.

Press Release

2 September 2011

Addex Regains Rights to Parkinson's Drug Candidates from Merck

Geneva, Switzerland, 2 September 2011 - Addex Pharmaceuticals (SIX:ADXN), a leading biopharmaceutical company pioneering allosteric modulation-based drug discovery and development, announced today that it will regain all rights to its metabotropic glutamate receptor 4 (mGluR4) positive allosteric modulator (PAM) program from Merck, known as MSD outside the United States and Canada, due to further pipeline prioritization.

"We continue to strongly believe that mGluR4 is a highly attractive target for treating Parkinson's and other serious diseases," said Bharatt Chowriya, CEO of Addex. "We recognize the substantial challenges for the pharmaceutical industry today and we thank our partner for this collaboration and the significant advances we made together in targeting this important receptor. We remain committed to pursuing mGluR4 PAM for Parkinson's and other diseases."

Under the agreement, Addex will regain rights to intellectual property and know-how and can pursue the program independently.

Addex Pharmaceuticals (www.addexpharma.com) discovers and develops an emerging class of small molecule drugs, called allosteric modulators, which have the potential to be more specific and confer significant therapeutic advantages over conventional "orthosteric" small molecule or biological drugs. The company uses its proprietary discovery platform to address receptors and other proteins that are recognized as attractive targets for modulation of important diseases with unmet medical needs. The Company's two lead products are being investigated in Phase IIa clinical testing: dipraglurant (ADX48621, an mGluR5 negative allosteric modulator or NAM) is being developed by Addex to treat Parkinson's disease levodopa-induced dyskinesia (PD-LID); and, ADX71149 (mGluR2 positive allosteric modulator or PAM) is being developed by our partner Janssen Pharmaceuticals, Inc., to treat schizophrenia. Addex also is advancing several preclinical programs including: mGluR2 NAM for treating Alzheimer's disease and depression; mGluR4 PAM for Parkinson's and other diseases; GLP1R PAM for type 2 diabetes; FSHR NAM for endometriosis and benign prostate hyperplasia; and GABABR PAM for chronic pain, urinary incontinence and other disorders. In addition, Addex has discovery programs to identify allosteric modulators of: receptor tyrosine kinase (RTK) superfamily, including TrkB PAM for treating neurodegenerative diseases (e.g. Alzheimer's, Parkinson's and Huntington's diseases); TNF receptor superfamily, including TNFR1 NAM for inflammation (e.g. rheumatoid arthritis); and, interleukin receptor family, such as IL1R1 NAM for gout and type II diabetes.
Addex and Merck & Co. Collaborate to Develop Drugs for Parkinson's Disease

Collaboration Targets a Non-Dopaminergic Approach to Treating Parkinson's Disease

Geneva, Switzerland - Allosteric modulation company Addex Pharmaceuticals (SWX:ADXN) announced today that it has entered an exclusive collaboration and license agreement with Merck & Co., Inc. (through its affiliate Merck Sharp & Dohme Research Ltd) with the goal of developing a new class of orally available drugs, initially as candidates for the treatment of Parkinson's disease and potentially other undisclosed indications. The partners will discover and develop positive allosteric modulators (PAMs) targeting the metabotropic glutamate receptor 4 (mGluR4). The deal includes lead mGluR4 PAMs discovered by Addex.

“We are proud to have established this collaboration with Merck because their researchers have helped to define the therapeutic potential of targeting mGluR4 to treat Parkinson's disease,” Vincent Mutel, CEO of Addex, said. “This is another important validation of our leadership in allosteric modulation.”

“Addex has made exceptional progress in the area of mGlu receptor allosteric modulation,” said Darryle D. Schoepp, Ph.D., senior vice president and franchise head, Neuroscience, at Merck Research Laboratories. “This partnership is key to us jointly establishing a leadership position in the promising area of mGluR4 receptor modulation for Parkinson's disease. Merck scientists are excited to work with Addex to extrapolate the full value of this novel mechanism for a range of neuroscience disorders.”

Parkinson's disease is a debilitating movement disorder. Current treatments focus on dopamine-replacement strategies, however most patients reach a stage where these treatments are no longer effective. There can also be debilitating side effects with current treatments and many patients limit doses so their symptoms are less cumbersome. The recent success of surgical approaches suggests that bypassing the dopamine system may provide a more effective treatment strategy. It is believed that selective activation of mGluR4 is one way to do this and could correct the circuitry that modulates motor excitability. This has the potential to provide significant palliative benefit in Parkinson's disease.

Under the terms of the agreement, Addex will receive $3 million upfront and is eligible for up to $106.5 million in research, development and regulatory milestones for the first product developed for multiple indications. Additional milestones of up to $61 million would be payable if a second and third product is developed. Addex is eligible to receive undisclosed royalties on sales of any products resulting from this collaboration.

Addex and Merck will collaborate on preclinical development. Merck will be responsible for clinical development. Addex has an option to co-promote in certain European Union countries and will participate in the joint oversight committee for clinical development. Addex will host a webcast & teleconference (see below).

Targeting glutamate receptors

Like dopamine and serotonin, glutamate is a key neurotransmitter in the human brain, an important signaling molecule involved in control of multiple brain functions ranging from motor control to mood. Although marketed drugs modulate specific receptors involved in both the dopaminergic and serotonergic systems, it has been difficult to develop drugs that target specific G protein coupled receptors in the glutamatergic system.

Merck has been a pioneer in research on mGlu receptors and the metabotropic glutamatergic system for multiple indications. For example, research by Merck scientists provided the first evidence that mGluR4 activation has potential for treatment of Parkinson's disease. However, a remaining challenge has been to make drug-like molecules that activate mGluR4 in a specific fashion. Addex is a pioneer in developing truly selective small molecule drug candidates targeting glutamate receptors and has previously disclosed programs targeting mGluR5 and mGluR2.

mGluR4 in Parkinson's disease

Published research* shows that mGluR4 activators, like those in development at Addex, could work via two distinct mechanisms to alleviate symptoms of Parkinson's disease and, potentially, even slow the progression of the disease: 1) mGluR4 activation triggers a compensatory mechanism that may spare or potentiate the use of dopamine receptor activators; 2) mGluR4 activation may have a neuroprotective effect that helps to preserve the brain’s dopaminergic neurons.


About Parkinson's disease

Parkinson's disease is a brain disorder. It occurs when certain nerve cells (neurons) in a part of the brain called the substantia nigra die or become impaired. Normally, these cells produce a signaling molecule (neurotransmitter) known as dopamine. Among other things, dopamine allows smooth, coordinated function of the body's muscles and movement. When approximately 80 percent of the dopamine-producing cells are damaged, the symptoms of Parkinson's disease appear.

Parkinson's disease affects both men and women in almost equal numbers. It shows no social, ethnic, economic or geographic boundaries. In the United States, it is estimated that 60,000 new cases are diagnosed each year, joining the 1.5 million Americans who currently have Parkinson's disease. While the condition usually develops after the age of 65, 15 percent of those diagnosed are under 50.
Most symptoms associated with Parkinson’s disease, like tremor, rigidity and slowness, are caused by a lack of dopamine. Marketed medicines help to ease the symptoms of Parkinson’s disease by either replacing or mimicking dopamine. Currently, no marketed products slow the disease progression. No marketed products work via non-dopaminergic mechanisms.

About Addex

Addex Pharmaceuticals discovers and develops allosteric modulators, an emerging class of small molecule therapeutic agents. Allosteric modulation may offer more sophisticated ways to normalize biological signaling compared to classical orthosteric agonist or antagonist drugs. Allosteric, literally translated from its Greek roots, means: other site. Thus, allosteric modulators bind receptors at sites that are distinct from the binding sites of classical small molecule orthosteric agonist and antagonist drugs.

The most advanced drug candidate, ADX10059, a negative allosteric modulator (NAM) of metabotropic glutamate receptor 5 (mGluR5), recently demonstrated clinically and statistically significant efficacy in separate Phase IIa clinical trials in gastroesophageal reflux disease (GERD) patients and migraine headache patients. Data from another Phase IIa clinical trial of ADX10059 in acute anxiety are due around the end of 2007.

The Addex discovery capability has previously been validated through a collaboration with Ortho-McNeil, a Johnson & Johnson company. The deal is limited to discovery and development of allosteric modulators of metabotropic glutamate receptor 2 (mGluR2).

In May 2007, Addex completed an initial public offering on the SWX Swiss Exchange, raising CHF137 million ($111 million / €83 million). The IPO was the largest biotech IPO in Europe in three years.

Addex Achieves First Milestone in Parkinson’s Disease Collaboration with Merck & Co., Inc.

Collaboration Targets a Non-Dopaminergic Approach to Treating Parkinson’s Disease

25 February 2008

Geneva, Switzerland – Allosteric modulation company Addex Pharmaceuticals (SWX:ADXN) announced today that the first preclinical milestone has been achieved in a recently announced exclusive collaboration and license agreement with Merck & Co., Inc. (through its affiliate Merck Sharp & Dohme Research Ltd). The collaboration is focused on developing an emerging class of oral drugs, allosteric modulators, that target the metabotropic glutamate receptor 4 (mGluR4) for Parkinson’s disease and other undisclosed indications.

“The achievement of this first preclinical milestone provides additional validation for the strategy of activating mGluR4 to treat Parkinson’s disease” Vincent Mutel, CEO of Addex, said. “The speed with which the milestone was reached, within three months of signing the agreement, stems from our joint commitment to the project and the efforts of the excellent team involved in this collaboration.”

Addex will receive $250,000 for achieving the first preclinical milestone. Under the terms of the agreement, first announced in December 2007, Addex received $3 million upfront and is eligible for up to $106.5 million in research, development and regulatory milestones for the first product developed for multiple indications. Additional milestones of up to $61 million would be payable if a second and third product is developed. Addex is eligible to receive undisclosed royalties on sales of any products resulting from this collaboration. Merck is responsible for clinical development.

mGluR4 in Parkinson's disease

Parkinson’s disease is a debilitating movement disorder. Current treatments focus on dopamine-replacement strategies, however most patients reach a stage where these treatments are no longer effective. There can also be debilitating side effects with current treatments and many patients limit doses so their symptoms are less cumbersome. The recent success of surgical approaches suggests that bypassing the dopamine system may provide a more effective treatment strategy. It is believed that selective activation of mGluR4 is one way to do this and could correct the circuitry that modulates mot or excitability. This has the potential to provide significant palliative benefit in Parkinson’s disease.

Published research* shows that mGluR4 activators, like those in development at Addex, could work via two distinct mechanisms to alleviate symptoms of Parkinson’s disease and, potentially, even slow the progression of the disease: 1) mGluR4 activation triggers a compensatory mechanism that may spare or potentiate the use of dopamine receptor activators; 2) mGluR4 activation may have a neuroprotective effect that helps to preserve the brain’s dopaminergic neurons.


Targeting glutamate receptors

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Merck has been a pioneer in research on mGlu receptors and the metabotropic glutamatergic system for multiple indications. For example, research by Merck scientists provided the first evidence that mGluR4 activation has potential for treatment of Parkinson's disease. However, a remaining challenge has been to make drug-like molecules that activate mGluR4 in a specific fashion. Addex is a pioneer in developing truly selective small molecule drug candidates targeting glutamate receptors and has disclosed allosteric modulator programs targeting mGluR5 and mGluR2.

About Parkinson's disease

Parkinson's disease is a brain disorder characterized by movement disorders and other symptoms. It occurs when certain nerve cells (neurons) in a part of the brain called the substantia nigra die or become impaired. Normally, these cells produce a vital chemical known as dopamine. Dopamine allows smooth, coordinated function of the body's muscles and movement. When approximately 80% of the dopamine-producing cells are damaged, the symptoms of Parkinson's disease appear.

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The most advanced drug candidate, ADX10059, a negative allosteric modulator (NAM) of metabotropic glutamate receptor 5 (mGluR5), recently demonstrated clinically and statistically significant efficacy in separate Phase IIa clinical trials in gastroesophageal reflux disease (GERD) patients and migraine headache patients.

About Addex

Addex Pharmaceuticals announced today that the second preclinical milestone has been achieved in an exclusive collaboration and license agreement with Merck & Co., Inc. (through its affiliate Merck Sharp & Dohme Research Ltd). The collaboration is focused on developing an emerging class of drugs, called allosteric modulators, for treatment of Parkinson's disease and other undisclosed indications. Allosteric modulators have broad potential to address important therapeutic targets; this collaboration with Merck is focused on developing drugs that specifically activate the metabotropic glutamate receptor 4 (mGluR4). The preclinical study showed the desired non-dopaminergic activity profile after oral administration of mGluR4 positive allosteric modulator (PAM) in an animal model of Parkinson's disease.

"We are pleased that these preclinical data show such promise in the animal model used," said Emmanuel Le Poul, head of the CNS Business Unit at Addex. "This work is a further validation of the target and the strength of our collaboration, as both teams have contributed to this achievement."

"Innovative non-dopaminergic therapies represent a significant opportunity to address an important unmet medical need in Parkinson's disease patients," said Vincent Mutel, CEO of Addex. "We are proud that our allosteric modulation drug discovery and development platform has generated highly innovative products in Parkinson's disease in addition to other important indications with unmet medical need including: gastroesophageal reflux disease, migraine, schizophrenia and anxiety."

Addex will discuss the mGluR4 PAM collaboration and its clinical and preclinical stage allosteric modulator pipeline and discovery platform during its R&D Day on July 16, 2009. A webcast and recording of the Addex R&D Day will be made available at www.addexpharma.com.

Addex will receive $500,000 for achieving the second preclinical milestone. Addex received $250,000 after achieving the first preclinical milestone during the first quarter of 2008. Under the terms of the agreement, first announced in December 2007, Addex received $3 million upfront and is eligible for up to $106.5 million in research, development and regulatory milestones for the first product developed for multiple indications. Additional milestones of up to $61 million would be payable if a second and third product is developed. Addex is eligible to receive undisclosed royalties on sales of any products resulting from this collaboration. Merck is responsible for clinical development.
mGluR4 may play an important role in Parkinson's disease, which is a debilitating movement disorder. Current treatments focus on dopamine-replacement strategies, however most patients reach a stage where dopaminergic treatments are no longer effective. There can also be debilitating side effects with dopaminergic treatments and many patients limit doses so their side effects will be less cumbersome. The recent success of surgical approaches suggests that bypassing the dopamine system may provide a more effective treatment strategy. It is believed that selective activation of mGluR4 is one way to do this and could correct the circuitry that modulates motor excitability. This has the potential to provide significant benefit in Parkinson's disease.

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Glutamate, like dopamine and serotonin, is a key neurotransmitter in the human brain, an important signaling molecule involved in control of multiple brain functions ranging from motor control to mood. Although marketed drugs modulate specific receptors involved in both the dopaminergic and serotonergic systems, it has been difficult to develop drugs that can selectively target specific receptors of glutamate, which has many different receptors, some of which can cause serious side effects if improperly modulated.

Merck has been a pioneer in research on mGlu receptors and the metabotropic glutamategic system for multiple indications. For example, research by Merck scientists provided the first evidence that mGluR4 activation has potential for treatment of Parkinson's disease. However, a remaining challenge has been to make drug-like molecules that activate mGluR4 in a specific fashion. Addex is a pioneer in developing allosteric modulators, truly selective small molecule drug candidates, for human health.

Parkinson's disease is a brain disorder characterized by movement disorders and other symptoms. It occurs when certain nerve cells (neurons) in a part of the brain called the substantia nigra die or become impaired. Normally, these cells produce a vital chemical known as dopamine. Dopamine allows smooth, coordinated function of the body's muscles and movement. When approximately 80% of the dopamine-producing cells are damaged, the symptoms of Parkinson's disease appear.

About 1.5 million Americans currently have Parkinson's disease, and about 60,000 new cases are diagnosed each year. Parkinson's is one of the fastest growing diseases, driven by the ageing population. Parkinson's disease drugs had global sales of around $2.5 billion in 2005, which analysts believe could grow to $3.8 billion by 2010.

Although no marketed products slow the disease progression, there are a number of medicines that effectively ease the symptoms. The medicines most commonly prescribed attempt to either replace or mimic dopamine. They can improve the tremor, rigidity and slowness associated with Parkinson's disease but they also can cause side effects like dyskinesia (involuntary movements) and eventually stop working, as the dopaminergic neurons continue to die.

Addex Pharmaceuticals (www.addexpharma.com) discovers and develops allosteric modulators for human health. Allosteric modulators are a different kind of orally available small molecule therapeutic agent, which we believe will offer a competitive advantage over classical drugs. Our lead allosteric modulator product, ADX10059, has achieved clinical proof of concept and is in Phase Ib testing for the treatment of GERD and, separately, migraine headache. Both are important diseases for which existing products with limited efficacy have established multi-billion dollar markets despite sub-optimal efficacy. ADX10059 is a first-in-class mGluR5 inhibitor, a therapeutic strategy that also is being pursued in multiple indications by large pharma competitors.

Our products and technology already have proven their value through our partnerships with four of the top 10 pharmaceutical companies in the world. Specifically, two separate agreements with Merck & Co., Inc., are focused on developing allosteric modulators as drugs to treat Parkinson's disease and schizophrenia, respectively. A third agreement with Ortho-McNeil-Jansen Inc. is focused on development of allosteric modulators to treat anxiety and schizophrenia. In addition, GlaxoSmithKline and Roche have made equity investments in Addex.
Developing innovative non-dopaminergic drugs for Parkinson's disease is an increasingly important part of our work at Addex," said Vincent Mutel, CEO of Addex. "We are proud to be advancing mGluR4 PAMs with our collaborators at Merck."

Under the terms of the exclusive collaboration and license agreement, first announced in December 2007, Addex received $3 million upfront and has received two preclinical milestones of $250,000 and $500,000, to date. Addex is eligible to receive up to $106.5 million in research, development and regulatory milestones for the first product developed for multiple indications. Additional milestones of up to $61 million would be payable if a second and third product is developed. Addex is eligible to receive undisclosed royalties on sales of any products resulting from this collaboration. Merck is responsible for clinical development. Extension of the research collaboration allows Addex to recognize $1.8 million in research funding over 12 months beginning on December 1, 2009.

Glutamate, like dopamine and serotonin, is a key neurotransmitter in the human brain, an important signaling molecule involved in control of multiple brain functions ranging from motor control to mood. In Parkinson's disease, the death of dopamine producing neurons leads to excess glutamate signaling.

Parkinson's disease is a degenerative disease of the brain that often impairs motor skills, speech, and other functions. It is estimated that 60,000 new cases are diagnosed each year in the U.S., where more than 1.5 million people currently have PD. While the condition usually develops after the age of 65, 15% of those diagnosed are under 50. PD affects both men and women in almost equal numbers.

mGluR4 may play an important role in Parkinson's disease. Current treatments focus on dopamine-replacement strategies, however most patients reach a stage where dopaminergic treatments are no longer effective. There can also be debilitating side effects with dopaminergic treatments, especially levodopa induced dyskinesia, and many patients are encouraged to limit doses so their side effects will appear later and be less cumbersome. The recent success of surgical approaches suggests that bypassing the dopamine system may provide a more effective treatment strategy. It is believed that selective activation of mGluR4 is one way to do this and could correct the circuitry that modulates motor excitability via a non-dopaminergic mechanism.

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Filing Data

Not available.

Contract

Not available.