

BIOWORLD® TODAY

Ophthotech, Novartis in ex-U.S. pact worth up to \$1B, with \$200M up front

May 20, 2014

By Randy Osborne

Audience Reach: 3,110

Still signing up patients for its phase III trial with Fovista, the antiplatelet-derived growth factor agent that would be used with anti-VEGF therapy in wet age-related macular degeneration (AMD), Ophthotech Corp. pulled down a \$200 million up-front ex-U.S. deal with Novartis AG that could end up being worth \$1 billion.

The deal keeps Fovista "anti-VEGF" agnostic, so physicians have a choice of which therapy they might use with it, said David Guyer, CEO of New York-based Ophthotech, who spoke to *BioWorld Today* ahead of a conference call with investors on Monday.

"Part of choice also is that some physicians may want a co-formulation, and market conditions change over time, so we like the ability to have it both ways," said Guyer. Included in the agreement is the possibility of mixing Fovista with an anti-VEGF from Novartis, of Basel, Switzerland, which will also develop a Fovista pre-filled syringe.

"They certainly have great expertise with that technology," Guyer said. In March, Novartis disclosed that it had come up with one for the wet AMD anti-VEGF therapy Lucentis (ranibizumab, Roche AG).

Along with Lucentis, another compound for which Fovista was designed to add extra punch is Eylea (afibercept, Regeneron Pharmaceuticals Inc.). Used off-label for wet AMD is Avastin (bevacizumab, Roche AG). Anti-VEGFs keep abnormal blood vessels from growing behind the eye, which can cause eventual blindness, and Fovista is designed to make the same blood vessels shrink away.

Under terms of the deal, Ophthotech gets \$200 million up front, plus another \$130 million in enrollment-based milestone payments related to the phase III trial with Fovista, which Guyer described as "purely about recruitment." The study is "on target for top-line data in 2016. Since the endpoint for the trial is 12 months, you can subtract a year, and that's when recruitment is expected to be finished," he said, and the remaining milestone money would be paid.

Also included in the Novartis deal are contingent, ex-U.S. marketing approval-based milestone payments totaling as much as \$300 million, and sales milestones outside the U.S. that could add up to another \$400 million. Novartis would pay Ophthotech royalties, too.

Ophthotech said earlier this month that the phase III Fovista program had opened trial sites for the company's third experiment, testing the drug in combination with Avastin and Eylea. The work builds on the strength of a phase IIb trial that tested Fovista 0.3 mg in combination with Lucentis 0.5 mg, Fovista 1.5 mg with Lucentis 0.5 mg, or sham with Lucentis 0.5 mg. Patients in the 1.5 mg Fovista/0.5 mg Lucentis group gained a mean of 10.6 letters of vision on the ETDRS standardized chart after 24 weeks of treatment, compared to 6.5 letters for patients receiving Lucentis monotherapy, with no significant safety issues in either treatment group.

Wet AMD therapies sold for \$5 billion last year, despite a 60 percent penetrance by off-label Avastin, which means the market is much larger still, and destined to grow as the population ages, Guyer said. Ophthotech went public in September 2013 and more than doubled the hoped-for amount, selling 7.6 million shares at \$22 each to garner \$167 million.

Ophthotech's shares (NASDAQ:OPHT) were up 22 percent in after-hours trading, or \$7.15, selling for \$38.61.

Ophthotech, Novartis In Ex-U.S. Pact Worth Up To \$1B, With \$200M Up Front

May 19, 2014

By Randy Osborne

Audience Reach: 3,110

Still signing up patients for its phase III trial with Fovista, the antiplatelet-derived growth factor agent that would be used with anti-VEGF therapy in wet age-related macular degeneration (AMD), Ophthotech Corp. pulled down a \$200 million upfront ex-U.S. deal with Novartis AG that could end up being worth \$1 billion.

The deal keeps Fovista “anti-VEGF” agnostic, so physicians have a choice of which therapy they might use with it, said David Guyer, CEO of New York-based Ophthotech, who spoke to *BioWorld Today* ahead of a conference call with investors on Monday.

“Part of choice also is that some physicians may want a co-formulation, and market conditions change over time, so we like the ability to have it both ways,” said Guyer. Included in the agreement is the possibility of mixing Fovista with an anti-VEGF from Novartis, of Basel, Switzerland, which will also develop a Fovista pre-filled syringe. “They certainly have great expertise with that technology,” Guyer said. In March, Novartis disclosed that it had come up with one for the wet AMD anti-VEGF therapy Lucentis (ranibizumab, Roche AG).

Along with Lucentis, another compound for which Fovista was designed to add extra punch is Eylea (aflibercept, Regeneron Pharmaceuticals Inc.). Used off-label for wet AMD is Avastin (bevacizumab, Roche AG). Anti-VEGFs keep abnormal blood vessels from growing behind the eye, which can cause eventual blindness, and Fovista is designed to make the same blood vessels shrink away. (See *BioWorld Insight*, July 22, 2013.)

Under terms of the deal, Ophthotech gets \$200 million up front, plus another \$130 million in enrollment-based milestone payments related to the phase III trial with Fovista, which Guyer described as “purely about recruitment.” The study is “on target for top-line data in 2016. Since the endpoint for the trial is 12 months, you can subtract a year, and that’s when recruitment is expected to be finished,” he said, and the remaining milestone money would be paid.

Also included in the Novartis deal are contingent, ex-U.S. marketing approval-based milestone payments totaling as much as \$300 million, and sales milestones outside the U.S. that could add up to another \$400 million. Novartis would pay Ophthotech royalties, too.

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Ophthotech’s shares (NASDAQ:OPHT) were up 22 percent in after-hours trading, or \$7.15, selling for \$38.61.



Ophthotech jumps on Novartis deal

May 19, 2014

Audience Reach: 53,746

Ophthotech Corp. (NASDAQ:OPHT) jumped \$7.54 (24%) to \$39 in early after-hours trading after granting Novartis AG(NYSE:NVS; SIX:NOVN) exclusive, ex-U.S. rights to develop and commercialize Fovista, which is in Phase III testing to treat wet age-related macular degeneration (AMD). Ophthotech, which retains sole commercialization rights in the U.S., will receive \$200 million in cash up front. The company is also eligible for up to \$830 million in milestones, plus mid-30% royalties on Fovista sales. The milestones include \$130 million tied to enrollment of an ongoing Phase III trial of Fovista to treat wet AMD in combination with anti-VEGFs. Top-line data from the trial are expected in 2016. Fovista is a pegylated aptamer against platelet derived growth factor B (PDGFB; PDGF2).

Novartis is responsible for other clinical trials and costs for ex-U.S. approvals, including a development program in Asia. The pharma and Ophthotech also will develop a co-formulation of Fovista with a Novartis anti-VEGF drug in a pre-filled syringe. Ophthotech received options to acquire U.S. commercialization rights for the co-formulated product. Ophthotech will be eligible for royalties of "approximately equal value" to the Fovista royalties on sales of a co-formulated product.

The companies announced the deal after market close. Ophthotech was up \$0.38 to \$31.46 on Monday.

THE WALL STREET JOURNAL.

Ophthotech, Novartis in Fovista Drug Pact

May 19, 2014

By Maria Armental

Audience Reach: 7,955,125

Ophthotech to Get \$200 Million Upfront Payment With Potential for More Than \$1 Billion

Swiss drug maker Novartis AG said it has entered into an exclusive agreement with Ophthotech Corp. to commercialize the biopharmaceutical company's wet age-related macular degeneration treatment Fovista outside the U.S.

Shares of New York-based Ophthotech surged 24% to \$38.95 in recent after-hours trading, as the companies said Ophthotech would receive an upfront fee of \$200 million, with the potential to secure more than \$1 billion over the length of the agreement with milestone payments.

Ophthotech will retain the rights to commercialize the treatment in the U.S., and is also entitled to royalties from non-U.S. Fovista sales, the companies said.

Under the agreement, Novartis will commercialize Fovista as stand-alone treatment and as a co-formulation with a Novartis proprietary product, the Swiss drug maker said.

Fovista in combination with currently available treatments could further improve outcomes of patients suffering from avoidable vision loss, said David Epstein, division head of Novartis Pharmaceuticals.

"If approved, Fovista is expected to be the first to market in this class of therapies for wet AMD confirming our commitment and leadership in the ophthalmology space," he added.

Meanwhile, Ophthotech Chief Executive David Guyer described the pact as one of the largest ex-US partnering deals ever in the biotechnology industry, and noted the collaboration with Novartis "is potentially transformational for Ophthotech."

Ophthotech will continue to lead the global Fovista Phase 3 wet AMD pivotal clinical program, which is expected to have initial, top line data available in 2016, the company said.

Through Monday's close, shares of Ophthotech, which made its public trading debut in September, have slipped 2.8% since the start of the year.



Ophthotech Licenses Experimental Eye Drug To Novartis

May 19, 2014

By Vrinda Manocha and Sriraj Kalluvila

Audience Reach: 4,980,338

Ophthotech Corp said it could potentially receive over \$1 billion in payments as part of a licensing deal for its experimental eye drug with Novartis AG.

Ophthotech's shares rose as much as 29 percent in trading after the bell.

The company said on Monday that a unit of Novartis will market its lead experimental eye drug, Fovista, outside the United States.

Ophthotech said it could receive immediate and near-term milestone payments of up to \$330 million and is eligible to get ex-US marketing approval and sales milestone payments of up to \$700 million.

The payments do not include future royalties from sales of the drug outside the United States, the company said. "The deal validates Fovista, while importantly allowing the company to retain and fund the drug's development and US commercialization," J.P. Morgan analyst Geoff Meacham said in a note.

Ophthotech is testing Fovista in late-stage studies to treat wet age-related macular degeneration (AMD), in combination with standard treatments including Regeneron Pharmaceuticals Inc's Eylea and Roche Holding AG's Avastin and Lucentis.

Ophthotech said it expects initial data from Fovista's development program in 2016.

Wet AMD is caused by abnormal blood vessels leaking blood or fluid into the retina and is the more advanced form of AMD, the most common cause of blindness in the elderly.

Fovista is designed to strip cells that wrap around newly-formed blood vessels in the eye, allowing the standard treatments to inhibit the growth of new blood vessels.

Ophthotech said Novartis would develop and market the technology such as a pre-filled syringe to deliver the injectable eye drug.

The company also said Fovista could be used in a fixed combination with an experimental treatment of Novartis.

Ophthotech said it will file for approval of the drug in the United States, and will collaborate with Novartis to seek approval outside the country.

The company's shares, priced at \$22 in its IPO in September, closed at \$31.46 on the Nasdaq on Monday.

Novartis commits \$1bn for ex-US rights to Ophthotech AMD Drug

May 20, 2014

By Mandy Jackson

Audience Reach: 55,000

Ophthotech will almost double its cash balance with a \$200m upfront payment and \$130m in near-term milestone fees under a deal worth up to \$1.03bn plus royalties that gives Novartis ex-US rights to Fovista for wet age-related macular degeneration (AMD).

New York-based Ophthotech had \$290.8m in cash as of 31 March, which previously would have carried the company until 2016 when top-line results are expected from the ongoing Phase III program for Fovista, a platelet-derived growth factor (PDGF) inhibitor. The new money will enable planned expansion studies for the biologic, which is designed for co-administration with vascular endothelial growth factor (VEGF) inhibitors, and clinical trials for other assets.

Ophthotech chairman and CEO David Guyer told *Scrip* that Novartis was the best partner to oversee Fovista's development and launch outside of the US, because the Swiss pharma company is "a recognized international leader with unparalleled reach in eye disease."

Novartis sells the blockbuster Roche/ Genentech VEGF inhibitor Lucentis (ranibizumab) outside of North America, but the company has an undisclosed anti-VEGF therapy of its own that it may develop in a fixed-dose combination with Fovista.

Ophthotech closed up 1.2% at \$31.46 per share on 19 May, but jumped another 22.8% in after-hours trading to \$38.64 following the late-afternoon Novartis deal announcement.

Under the terms of the transaction, Ophthotech will receive \$200m up front plus up to \$130m in near-term clinical trial milestone fees, \$300m dependent on ex-US regulatory approvals, up to \$400m in ex-US sales milestone fees, and royalties in the mid-30% range on Fovista sales outside the US.

Dr Guyer said Ophthotech was able to negotiate favorable terms with Novartis based on the \$5bn-plus market size for AMD and the successful Phase IIb program for Fovista, which showed statistically significant and clinically meaningful results.

Ophthotech claims that the agreement is one of the largest ex-US biotechnology deals ever transacted. The arrangement also gives Novartis the right to develop a fixed-dose combination (FDC) of Fovista with a proprietary Novartis anti-VEGF therapy as well as a pre-filled syringe formulation of Fovista. Ophthotech has rights to opt in to US development of the FDC and pre-filled syringe products.

Ophthotech's executives are quick to point out, however, that the company's preferred delivery of Fovista and anti-VEGF therapies is as separate injections so that doctors can choose which of the VEGF inhibitors he or she wants to use.

"Our market data shows physicians want the choice," Dr Guyer said. "But there is potential for a single [fixed-dose] injection to provide additional flexibility for physicians."

The deal with Novartis does not impact Ophthotech's financial flexibility, which the company carefully engineered last year. Ophthotech raised \$50m in venture capital and got a commitment for up to \$125m in

royalty financing from Novo A/S in May. Then the company grossed \$167.2m with an initial public offering in September.

"We did the Novo financing almost in lieu of doing a partnering transaction so that a) we had financing success going into the IPO and b) we knew we had the strength to be selective choosing an ex-US partner," Ophthotech chief financial and business officer Bruce Peacock told *Scrip*.

Ophthotech's cash resources will take the company at least into 2016 when it will report the first top-line Phase III data for Fovista. Two Phase III clinical trials are under way for Fovista plus Lucentis, but a third Phase III trial will test the anti-PDGF therapy with physician's choice of Genentech's Avastin (bevacizumab) or the Sanofi and Regeneron Pharmaceuticals VEGF inhibitor Eylea (aflibercept).

Before 2016, Ophthotech may report data from some smaller, exploratory studies for Fovista and begin clinical trials for Zimura. The drug is a chemically synthesized aptamer that inhibits complement factor C5, which may be a central component of the complement cascade involved in development of AMD.

Novartis hands Ophthotech a \$1B deal for heavyweight wet AMD contender

May 19, 2014

By John Carroll

Audience Reach: 35,363

Novartis (\$NVS) has scooped up the ex-U.S. rights to Ophthotech's Fovista--its late-stage therapy for wet age-related macular degeneration (AMD) that hopes to one day rival heavyweight franchises controlled by Roche (\$RHHBY) and Regeneron (\$REGN)--in a package deal potentially worth more than \$1 billion. And Ophthotech (\$OPHT), which touted the deal as one of the biggest ever for ex-U.S. drug rights, gets \$330 million of that in a hefty upfront and near-term milestones for the Phase III work.

The biotech went public last year amid a wave of new offerings, gathering \$165 million--which ranks in the top 10 biotech IPOs of the year--as investors bought into the blockbuster potential of Fovista. CEO Dr. David Guyer and President Dr. Samir Patel had developed the drug at Eyetech, then plucked the asset out for a spinoff after selling the company.

The treatment is an aptamer that's designed to inhibit platelet-derived growth factor subunit B, which regulates the cells found on the walls of blood vessels. In a Phase IIb study that was completed in the fall of 2012, investigators say that the drug used in combination with Lucentis, one of the dominant VEGF drugs on the market, significantly improved visual acuity when compared to a patient group which was treated only with Lucentis. And it helped that the company has been hanging on to the worldwide rights up to now. Ophthotech currently has a market cap of \$1 billion, making it one of the biggest benefactors of the IPO boom.

In the deal Novartis is paying \$200 million upfront, \$130 million for Phase III milestones, up to \$300 million for ex-U.S. marketing approvals and \$400 million for meeting certain sales goals. That \$330 million in upfront and near-term payments also marks one of the biggest licensing pacts of the last decade, signaling once again that Big Pharma is ready and willing to pay the big bucks when they see the right opportunities come along.

Ophthotech's shares soared 24% on the news Monday evening.

Wet AMD is unfortunately a blockbuster market and getting bigger. The disease afflicts a growing number of the elderly, and Novartis is angling to grab a share of it for themselves. In addition to partnering on a drug that can be used in combination with any anti-VEGF therapy, Novartis is also planning to study a combination of Fovista with a proprietary anti-VEGF drug of its own.

"As one of the largest ex-US partnering deals ever in the biotechnology industry, this collaboration with Novartis is potentially transformational for Ophthotech," said Guyer. "This agreement represents an important achievement for the company as we continue to execute on a strategy to deliver science-driven retinal products and offer physicians multiple treatment options to improve patient outcome. The collaboration also supports our previously stated plan to partner Fovista outside the United States while we retain sole commercialization rights to Fovista in the United States. The collaboration not only provides a substantial strategic and financial benefit to Ophthotech, it also begins to put in place essential elements designed to expand the reach of Fovista outside the United States, following potential regulatory approvals."

Novartis in up to \$1 billion deal to acquire ex-US rights to Fovista

May 20, 2014

Audience Reach: 8,070

Swiss pharma major Novartis (NOVN: VX) has signed a licensing and commercialization agreement with US biotech firm Ophthotech for the exclusive rights to market Fovista (anti-PDGF aptamer) outside the USA. News of the deal saw Ophthotech's shares rocket 24% to \$38.95 in after-hours trading last night.

Under the financial terms of the deal, Ophthotech could potentially receive over \$1 billion in upfront and milestone payments during the course of the collaboration, not including future royalties.

Ophthotech could receive immediate payment and near-term milestones totaling up to \$330 million, including an upfront fee of \$200 million and Fovista Phase III enrollment-based milestones of up to \$130 million;

Ophthotech is eligible to receive contingent future ex-US marketing approval milestones totaling up to \$300 million and ex-US sales milestones up to \$400 million; and

Ophthotech is entitled to receive royalties on ex-US Fovista sales.

Fovista under investigation of wet AMD

Fovista is being studied in combination with anti-VEGF agents for patients suffering from wet age-related macular degeneration (wet AMD). Novartis will also develop a co-formulation of Fovista with a Novartis proprietary anti-VEGF treatment. Ophthotech will hold the marketing rights to Fovista in the USA.

Fovista is the most advanced anti-PDGF agent in development for the treatment of wet AMD and, if approved, is expected to be first to market in this class of therapies for wet AMD, noted Ophthotech.

"Novartis is committed to addressing key unmet needs in medical retina. Fovista in combination with currently available anti-VEGF treatments could further improve outcomes of patients suffering from avoidable vision loss," said David Epstein, division head, Novartis Pharmaceuticals, adding: "If approved, Fovista is expected to be the first to market in this class of therapies for wet AMD confirming our commitment and leadership in the ophthalmology space."

Transformational deal drug Ophthotech

"As one of the largest ex-US partnering deals ever in the biotechnology industry, this collaboration with Novartis is potentially transformational for Ophthotech. The collaboration not only provides a substantial strategic and financial benefit to Ophthotech, it also begins to put in place essential elements designed to expand the reach of Fovista outside the United States, following potential regulatory approvals," said Ophthotech chief executive David Guyer.

Fovista offers a new mechanism of action to address unmet need to further improve visual acuity and potentially slow disease progression. In Phase II clinical studies, combination therapy of Fovista and Lucentis (ranibizumab) significantly improved baseline visual acuity in wet AMD patients. No new safety signals were observed with Fovista/Lucentis adjunctive therapy as compared to Lucentis monotherapy. Lucentis is marketed by Novartis and rival Swiss drug major Roche. Novartis expects to develop Fovista and the co-formulation in its proprietary, innovative pre-filled syringe as part of this agreement.



Novartis Buys Ex-U.S. Rights to Ophthotech's Fovista for Up to \$1B

May 20, 2014

Audience Reach: 304,159

Novartis has acquired from Ophthotech exclusive rights to market the eye drug candidate Fovista® outside the U.S., while retaining U.S. marketing rights, under a licensing and commercialization agreement that could net Ophthotech more than \$1 billion.

Novartis agreed to pay Ophthotech \$200 million upfront, and \$130 million in payments tied to Phase III patient enrollment milestones. In addition, Ophthotech is eligible to receive up to \$300 million contingent on winning future marketing approval milestones outside the U.S., and up to \$400 million tied to sales milestones outside the U.S. million. Additionally, Ophthotech is entitled to royalties on ex-US sales of Fovista.

"As one of the largest ex-US partnering deals ever in the biotechnology industry, this collaboration with Novartis is potentially transformational for Ophthotech," David R. Guyer, M.D., Ophthotech's CEO and chairman, said in a statement. "This agreement represents an important achievement for the Company as we continue to execute on a strategy to deliver science-driven retinal products and offer physicians multiple treatment options to improve patient outcome.

Fovista is an anti-PDGF aptamer now under study in combination with anti-VEGF agents for patients suffering from wet age-related macular degeneration (wet **AMD**). Fovista offers a new mechanism of action designed to further improve visual acuity and potentially slow disease progression.

"Fovista in combination with currently available anti-VEGF treatments could further improve outcomes of patients suffering from avoidable vision loss," added David Epstein, division head, Novartis Pharmaceuticals. Ophthotech said it will continue to lead the global Fovista Phase III wet AMD pivotal clinical program, which is expected to enroll up to 1,866 patients in three trials in more than 225 centers worldwide, and release initial, topline data in 2016. Ophthotech will continue to lead the effort to win U.S. registration of Fovista, while joining with Novartis on pursuing regulatory approvals outside the U.S.

Novartis hopes to commercialize Fovista both as a standalone drug and with an undisclosed anti-VEGF treatment, in hopes of staking a claim in the increasingly lucrative wet AMD market. For example, Eylea® (aflibercept) last year generated \$1.409 billion in U.S. sales for Regeneron and a combined \$472 million outside the U.S. for Regeneron and co-marketing partner Bayer HealthCare.

As part of the agreement, Novartis will seek to develop and commercialize alternative delivery technologies for Fovista, such as a prefilled syringe, and will also develop a co-formulation of Fovista with one of its undisclosed anti-VEGF compounds.

The agreement comes more than a year after Ophthotech reported promising Phase II results showing that the combination therapy of Fovista and Lucentis® (ranibizumab) met the primary endpoint of mean vision gain in wet AMD patients, who saw a mean 10.6 letters on the ETDRS standardized chart after 24 weeks of treatment, vs. 6.5 letters for patients taking Lucentis alone. No new safety signals were observed with Fovista / Lucentis adjunctive therapy as compared to Lucentis monotherapy.

Novartis announces exclusive agreement to extend leadership in ophthalmology, leveraging novel anti-PGDF therapy Fovista®

May 20, 2014

Audience Reach: 11,999

Novartis announced today the signing of a licensing and commercialization agreement with Ophthotech Corporation (Ophthotech) for the exclusive rights to market Fovista® (anti-PDGF aptamer) outside the United States. Under the financial terms of the agreement, Ophthotech will receive an immediate payment of an upfront fee of USD 200 million plus potential future recruitment and other milestone payments. In addition, Ophthotech is eligible to receive royalties on ex-US Fovista® sales. Fovista is being studied in combination with anti-VEGF agents for patients suffering from wet age-related macular degeneration (wet AMD). Novartis will also develop a co-formulation of Fovista with a Novartis proprietary anti-VEGF treatment. Ophthotech will hold the marketing rights to Fovista in the United States.

“Novartis is committed to addressing key unmet needs in medical retina. Fovista in combination with currently available anti-VEGF treatments could further improve outcomes of patients suffering from avoidable vision loss,” said David Epstein, Division Head, Novartis Pharmaceuticals. “If approved, Fovista is expected to be the first to market in this class of therapies for wet AMD confirming our commitment and leadership in the ophthalmology space.”

Fovista offers a new mechanism of action to address unmet need to further improve visual acuity and potentially slow disease progression. In Phase II clinical studies, combination therapy of Fovista and Lucentis® (ranibizumab) significantly improved baseline visual acuity in wet AMD patients. No new safety signals were observed with Fovista / Lucentis adjunctive therapy as compared to Lucentis monotherapy.

Novartis expects to develop Fovista and the co-formulation in its proprietary, innovative pre-filled syringe as part of this agreement.



Novartis acquires non-US rights to Ophthotech's experimental wet AMD drug Fovista

May 19, 2014

By Joe Barber

Audience Reach: 190,000

Novartis and Ophthotech announced Monday an agreement giving the former exclusive rights to commercialise the experimental wet age-related macular degeneration (AMD) therapy Fovista (anti-PDGF aptamer) outside the US for \$200 million up front and other milestone payments. Ophthotech, which estimated that the agreement could be potentially worth more than \$1 billion, will retain US rights to the drug. David Epstein, head of pharmaceuticals at Novartis, said "if approved, Fovista is expected to be the first to market in this class of therapies for wet AMD confirming our commitment and leadership in the ophthalmology space."

Under the terms of the agreement, Novartis said it will pay Ophthotech up to \$130 million in milestones related to enrolment in an ongoing Phase III programme for Fovista, which is expected to have interim, topline data available in 2016.

Ophthotech is also eligible to receive non-US approval milestones of as much as \$300 million and sales milestones outside the US of up to \$400 million. In addition, as part of the collaboration, the companies will develop a co-formulation of Fovista with a Novartis proprietary anti-VEGF treatment.

"The collaboration not only provides a substantial strategic and financial benefit to Ophthotech, it also begins to put in place essential elements designed to expand the reach of Fovista outside the United States, following potential regulatory approvals," remarked Ophthotech CEO David R. Guyer. Shares in the company rose nearly 24 percent on the news.

Ophthotech, Novartis enter into ex-US licensing and commercialization agreement

May 20, 2014

By David Mullen

Audience Reach: 200,016

Ophthotech Corporation has entered into an ex-U.S. licensing and commercialization agreement with Novartis Pharmaceuticals for Fovista, an anti-PDGF in development for the treatment of wet age-related macular degeneration, according to a press release.

This agreement entitles Novartis to commercialize Fovista in markets outside of the United States. Ophthotech will continue to commercialize Fovista in the United States and lead the Fovista phase 3 wet AMD clinical program.

“This agreement represents an important achievement for the company as we continue to execute on a strategy to deliver science-driven retinal products and offer physicians multiple treatment options to improve patient outcome,” **David R. Guyer, MD**, Ophthotech chief executive officer and chairman of the board, said in the release.

Under this agreement, Ophthotech could receive more than \$1 billion in upfront and milestone payments, excluding future royalties. The company could also potentially receive up to \$330 million in immediate payment, upfront fee and near-term milestones, as well as \$300 million in contingent future ex-U.S. marketing approval milestones, \$400 million in ex-U.S. sales milestones, and royalties on ex-U.S. sales, the release said.



Novartis announces licensing deal with US firm

May 20, 2014

Audience Reach: 32,653

Novartis has entered into a licensing agreement with American pharmaceutical company Ophthotech, for the non-US commercial rights to its wet age-related macular degeneration (AMD) treatment Fovista.

Potential payments to Ophthotech under the agreement could total over \$1bn (USD), not including future royalties. The company also retains sole rights to market Fovista in the US. The announcement, which was made on May 19, saw Ophthotech's shares rise by 29%.

Wet AMD is caused by abnormal blood vessels leaking blood or fluid into the retina and is the more advanced form of AMD, the most common cause of blindness in the elderly.

Fovista is designed to facilitate the action of existing wet AMD treatments by stripping the cells that wrap around abnormal blood vessels that are characteristic of the condition. Ophthotech, is currently testing Fovista in late-stage studies and expects initial data from the development programme in 2016.

The two companies will collaborate on acquiring approval for the drug from both US and international authorities. Ophthotech has also stated that Novartis will develop alternative delivery technologies for Fovista, such as a pre-filled syringe.

David Epstein, division head of Novartis, said: "If approved, Fovista is expected to be the first to market in this class of therapies for wet AMD, confirming our commitment and leadership in the ophthalmology space."

Ophthotech Soars On \$1 Billion Novartis Partnership

May 20, 2014

By Amy Reeves

Audience Reach: 737,731

Shares of small biotech **Ophthotech** (OPHT) surged 21% in morning trading on the stock market today, after the firm announced a big-pharma partnership for its eye-drug candidate late Monday.

Ophthotech inked a deal worth as much as \$1 billion with **Novartis** (NVS) to commercialize Fovista, a treatment for wet age-related macular degeneration (AMD) now in phase-three testing. Novartis will pay \$200 million upfront followed by a series of milestone payments related to the drug's clinical development. If it passes through the trials, Novartis will market Fovista outside the U.S. and pay a royalty to Ophthotech, which will sell it in the U.S.

Leerink analyst Joseph Schwartz wrote in a note late Monday that Ophthotech has been saying since its IPO in September that it would seek a big-pharma partner for this purpose, but the terms were more favorable than Schwartz expected.

"In the agreement, OPHT stands to earn (more than) \$1 billion in milestones and royalties in the mid-30% range on ex-US Fovista sales, which are above our base case assumption in which we model a royalty rate of 25% and do not credit OPHT with any milestones," he wrote.

He also noted that Novartis has experience marketing wet AMD drugs, since it currently markets **Roche** (RHHBY) unit Genentech's blockbuster Lucentis abroad.

The two companies also agreed to develop a co-formulation of Fovista with a Novartis anti-VEGF product, which is the same class of product as Lucentis and **Regeneron's** (REGN) Eylea. In a research note Tuesday, RBC Capital Markets analyst Adnan Butt pointed out that Regeneron is also developing a co-formulation of Eylea with an anti-PDGFR (the same class as Fovista) in collaboration with **Bayer** (BAYRY).

"Other companies have previously announced their attempts at developing a dual combination into a single injection," he wrote. "However, no one has presented data so far and REGN appears to be in the lead."

Regeneron stock was down 1.7% in morning trading Tuesday.



Ophthotech, Novartis Team up on \$1B Deal for Eye Drug

May 19, 2014

Ben Fidler

Audience Reach: 65,717

Ophthotech has said for some time that it's been looking for a partner to help with international sales of Fovista, its experimental drug for age-related macular degeneration in clinical trials. Today the location New York-based company is announcing that it has found such a partner in Novartis, and has cut a deal with Swiss pharma giant that could be worth over \$1 billion when all is said and done.

Under the deal, Novartis is getting international rights to Ophthotech's Fovista, which is designed to treat the "wet" form of AMD, in which abnormal blood vessels grow and leak fluid in the retina, causing distorted vision and potentially blindness. In return, the Swiss pharma giant is giving Ophthotech a \$200 million up front, and potentially another \$130 million when it finishes enrolling patients in the Phase 3 studies for Fovista. Ophthotech also stands to receive another \$700 million in regulatory and sales milestones, and a royalty stream on the drug's international sales through the deal. Ophthotech still owns the drug's U.S. rights.

"The collaboration not only provides a substantial strategic and financial benefit to Ophthotech, it also begins to put in place essential elements designed to expand the reach of Fovista outside the United States, following potential regulatory approvals," said Ophthotech CEO and chairman David Guyer, in a statement.

Shares of Ophthotech skyrocketed close to 24 percent in after-hours trading on Monday.

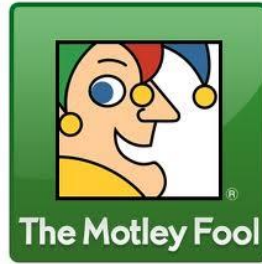
Wet AMD used to be treated with laser surgeries, but now patients typically get one of a group of drugs injected into the eye that block the a molecule called vascular endothelial growth factor (VEGF) that researchers believe causes the condition to worsen. Roche/Genentech's cancer drug bevacizumab (Avastin) works this way, and is commonly prescribed for the condition off-label. Ranibizumab (Lucentis)—sold in the U.S. by Genentech, and internationally by Novartis—and Regeneron's (NASDAQ: REGN) aflibercept (Eylea) have similarly become big successes as well.

Wet AMD has become the focal point of a huge amount of R&D spending, and dealmaking, in pharma and biotech. Regeneron, for instance, has risen to prominence through aflibercept, and just cut a \$640+ million deal with Avalanche Biotechnologies, a startup out of California, to develop a gene therapy for the disorder. Several companies like Kala Pharmaceuticals, Ohr Pharmaceutical (NASDAQ: OHRP), and PanOptica, are trying to develop eye drops for it.

Ophthotech is trying to be the first to market with a drug that targets platelet-derived growth factor (PDGF) instead of VEGF. The idea is rather than just stopping abnormal blood vessels from continuing to grow, an anti-PDGF agent, when combined with an anti-VEGF drug, would cause those blood vessels to recede.

Ophthotech is running three Phase 3 studies to prove that the approach works, and just went public last year to help finance the effort. It's testing Fovista in combination with ranibizumab in two of those studies, and with either aflibercept or bevacizumab in the other one.

Ophthotech is enrolling almost 1,900 patients and has said it expects to produce top-line data in 2016. As part of today's deal, Novartis and Ophthotech plan to work on a co-formulation of Fovista and a proprietary Novartis anti-VEGF product, so patients could be treated with one combined injection, instead of separate injections of Fovista and an anti-VEGF agent.



Tuesday's Top Health Care Stories: Ophthotech, Dendreon, Edwards Lifesciences, and Medtronic

May 20, 2014

By Leo Sun

Audience: 9,122,881

Let's take a look at four stocks -- **Ophthotech** (NASDAQ: OPHT) , **Dendreon** (NASDAQ:DNDN) , **Edwards Lifesciences** (NYSE: EW) , and **Medtronic** (NYSE: MDT) -- which could all make waves in the health care sector this Tuesday morning.

Ophthotech surges after signing a deal with Novartis

Shares of Ophthotech are up almost 20% this morning in pre-market trading, after signing an agreement with **Novartis** (NYSE: NVS) to commercialize its wet AMD (age-related macular degeneration) treatment Fovista outside the U.S. Ophthotech will retain the rights to commercialize Fovista in the U.S.

Ophthotech will receive an upfront payment of \$200 million, and be entitled to over \$1 billion in potential milestones, as well as additional royalty payments. Fovista is currently in three late-stage trials in the U.S.

Analysts believe that Fovista could generate peak sales as high as \$3.5 billion if approved. Two other prominent treatments in Wet AMD -- Novartis and Roche's Lucentis and **Regeneron** and **Bayer's** Eylea -- are both proven blockbusters. Lucentis and Eylea respectively generated over \$4 billion and \$1.9 billion in global sales in 2013.

Ophthotech has no marketed products. Fovista is its most advanced product, followed by Zimura, another Wet AMD treatment currently in phase 2 trials.

The Street



Why Ophthotech (OPHT) Stock Is Surging Today

May 20, 2014

By Andrew Meola

Audience Reach: 4,992,981

NEW YORK (TheStreet) -- **Ophthotech** (OPHT) surged Tuesday after the company announced it granted the rights to market its experimental eye drug Fovista outside the U.S. to a **Novartis** unit.

Ophthotech announced it could earn immediate payments including upfront fees of \$200 million and milestone payments of \$130 million as part of the arrangement. The company also said it could get more than \$1 billion in upfront and milestone payments over the life of the deal, excluding royalties on potential Fovista sales.

J.P. Morgan increased its price target on Ophthotech to \$51 from \$40 and reiterated its "overweight" rating in the wake of the deal. **Stifel Nicolaus** also increased its price target to \$58 from \$55 and reiterated its "buy" rating, as the firm thinks the deal strategically positions Ophthotech's Fovista drug for longer-term commercial success.



Ophthotech Corp (OPHT), Novartis Enter ex-U.S. Licensing Agreement for Wet AMD Treatment

May 19, 2014

Audience: 100,860

Ophthotech Corporation (Nasdaq: OPHT) announced that the Company has entered into an ex-US licensing and commercialization agreement with Novartis Pharmaceuticals (NYSE: NVS) focused on the treatment of wet age-related macular degeneration (AMD). Under the agreement, Ophthotech grants Novartis exclusive rights to commercialize Ophthotech's lead product candidate, Fovista®, in markets outside the United States while Ophthotech retains sole rights to commercialize Fovista® in the United States. Potential payments to Ophthotech under the agreement could total over \$1 billion in upfront and milestone payments, not including future royalties. Fovista® is the most advanced anti-PDGF agent in development for the treatment of wet AMD and, if approved, is expected to be first to market in this class of therapies for wet AMD.

Ophthotech will continue to lead the global Fovista® Phase 3 wet AMD pivotal clinical program which is expected to have initial, topline data available in 2016. Ophthotech will continue its lead role in the potential registration of Fovista® in the United States, while Ophthotech and Novartis will collaborate to seek regulatory approvals outside the United States.

This collaboration continues the Fovista® development strategy to remain agnostic with respect to the choice of the anti-VEGF agent administered in combination with Fovista®. Separate injections of the anti-VEGF agent and Fovista® would allow physicians to choose their preferred anti-VEGF agent for the combination therapy. The collaboration also provides for the potential development of a fixed combination delivery of a co-formulation of Fovista® with a Novartis proprietary anti-VEGF product which would result in additional flexibility for physicians. Novartis will also seek to develop and commercialize alternative innovative delivery technologies such as a Fovista® pre-filled syringe as part of this collaboration.

"As one of the largest ex-US partnering deals ever in the biotechnology industry, this collaboration with Novartis is potentially transformational for Ophthotech," stated David R. Guyer, M.D., Chief Executive Officer and Chairman of the Board of Ophthotech. "This agreement represents an important achievement for the Company as we continue to execute on a strategy to deliver science-driven retinal products and offer physicians multiple treatment options to improve patient outcome. The collaboration also supports our previously stated plan to partner Fovista® outside the United States while we retain sole commercialization rights to Fovista® in the United States. The collaboration not only provides a substantial strategic and financial benefit to Ophthotech, it also begins to put in place essential elements designed to expand the reach of Fovista® outside the United States, following potential regulatory approvals."

Under the financial terms of the agreement:

Ophthotech to potentially receive over \$1 billion in upfront and milestone payments during the course of the collaboration, not including future royalties.

Ophthotech could receive immediate payment and near-term milestones totaling up to \$330 million, including an upfront fee of \$200 million and Fovista® Phase 3 enrollment-based milestones of up to \$130 million.

Ophthotech is eligible to receive contingent future ex-US marketing approval milestones totaling up to \$300 million and ex-US sales milestones up to \$400 million.

Ophthotech is entitled to receive royalties on ex-US Fovista® sales.

WilmerHale acted as legal counsel for Ophthotech in connection with the transaction. Ophthotech Corp (NASDAQ: OPHT)



Ophthotech, Novartis enter into ex-U.S. licensing, commercialization agreement

May 19, 2014

Audience Reach: 260,395

Ophthotech (OPHT) announced that the company has entered into an ex-US licensing and commercialization agreement with Novartis Pharmaceuticals (NVS) focused on the treatment of wet age-related macular degeneration, or AMD. Under the agreement, Ophthotech grants Novartis exclusive rights to commercialize Ophthotech's lead product candidate, Fovista, in markets outside the United States while Ophthotech retains sole rights to commercialize Fovista in the U.S. Potential payments to Ophthotech under the agreement could total over \$1B in upfront and milestone payments, not including future royalties. Ophthotech will continue to lead the global Fovista Phase 3 wet AMD pivotal clinical program which is expected to have initial, topline data available in 2016. Ophthotech will continue its lead role in the potential registration of Fovista in the U.S., while Ophthotech and Novartis will collaborate to seek regulatory approvals outside the U.S. This collaboration continues the Fovista development strategy to remain agnostic with respect to the choice of the anti-VEGF agent administered in combination with Fovista. Separate injections of the anti-VEGF agent and Fovista would allow physicians to choose their preferred anti-VEGF agent for the combination therapy. The collaboration also provides for the potential development of a fixed combination delivery of a co-formulation of Fovista with a Novartis proprietary anti-VEGF product which would result in additional flexibility for physicians. Novartis will also seek to develop and commercialize alternative innovative delivery technologies such as a Fovista pre-filled syringe as part of this collaboration.



Novartis licenses Ophthotech eye drug in \$1bn deal

May 20, 2014

Fovista is a potential first-in-class treatment for wet AMD

Novartis has fleshed out its portfolio of drugs for diseases of the eye by licensing Ophthotech's Fovista in a deal valued at around \$1bn.

The Swiss pharma giant has licensed rights to Fovista (anti-PDGF aptamer) outside the US in a deal that brings Ophthotech \$200m upfront, another \$130m in near-term milestones and \$700m-plus in potential regulatory and commercial payments.

Fovista is claimed to be the closest to market of all anti-PDGF (platelet derived growth factor) drugs in development and could be a first-in-class therapy for the wet form of age-related macular degeneration (AMD), a leading cause of acquired blindness.

Novartis already sells anti-VEGF (vascular endothelial growth factor) drug Lucentis (ranibizumab) for wet AMD - as well as other indications such as pathological myopia and macular oedema - and achieved sales of more than \$4bn with the brand in 2013, making it the 19th **biggest-selling drug on the market** according to the PMLiVE Top Pharma List.

Competition in the AMD sector is on the increase, however, with Lucentis jostling for market share with **Regeneron and Bayer's Eylea** (aflibercept) as well as off-label use of **Roche's Avastin (bevacizumab)**, so the Ophthotech deal gives Novartis an alternative therapeutic option as well as the possibility of developing a combination treatment.

Novartis and Ophthotech confirmed that Fovista would also be developed as a fixed-dose combination with "a Novartis proprietary anti-VEGF product" as well as new formulations of the drug such as a prefilled syringe version.

As a single agent for wet AMD Fovista is currently in three phase III trials involving more than 1,800 patients that are due to generate top-line data in 2016.

Ophthotech has retained rights to the drug in the US and will also earn royalties on overseas sales. The firm's chief executive David Guyer said the deal was the largest ex-US partnering deal ever in the biotechnology industry and "potentially transformational" for the company.



Here's Why Ophthotech's Shares Surged In Extended Trading

May 20, 2014

By Bill Ashton

Ophthotech announced yesterday that it has signed an exclusive agreement with Novartis in which the latter will be granted marketing rights for an experimental eye drug to all regions barring the US

Ophthotech Corporation (**OPHT**) saw its shares rise 22.8% after the closing bell yesterday, on news that the company has given the license to market its lead product candidate, Fovista, to one of Novartis AG's (**NVS**) arms. Under the agreements signed, **the Switzerland-based drug giant** will now be exclusively responsible for commercializing Fovista, which is used to treat wet age-related macular degeneration (AMD), in all regions except for the US. Ophthotech will retain the rights to market the drug in the domestic market.

Market Size

AMD is a common eye condition and a leading cause of vision loss among people over fifty years of age. The disease is the third-most-common cause of blindness, after cataract and glaucoma. BBC News reported in March 2011 that the number of people with AMD could increase 25% by 2020, due to the shifts in the population demographic. Approximately one-fifth of all AMD cases reported are Wet AMD cases.

Wet AMD causes damage to the macula, which is a small spot near the central portion of the retina. The damage results in the formation of abnormal blood vessels. The disease, which can cause rapid and irreversible vision loss, affects an estimated 200,000 US-residents every year.

Treatment options aim to seal leaking blood vessels and preventing the damaged blood vessels from growing back. As of now, Regeneron Pharmaceuticals Inc.'s (**REGN**) drug Eylea and Roche Holding Ltd.'s (**RHHBY**) Lucentis are two of the most popular drugs used to treat the disease.

According to Ophthotech's S-1 filing, the two drugs generated revenues of \$4.8 billion from FY10-FY12. Of this, Lucentis held the lion's share; \$4 billion of the total revenues generated were attributable to the drug's sales in the US and the EU. In 2012, Eylea, which had launched only recently, brought in only \$0.8 billion in sales for Regeneron. Eylea's sales rose to \$1.41 billion in FY13 while Lucentis sales increased 3.6% on a YoY basis in FY13.

The two drugs' sales picked up because the occurrence of the disease is rising by double digits due to changes in the population demographic across the world.

In light of the market size and the frequency of the occurrence of the disease, Fovista has the potential to address a \$5 billion market. Moreover, Fovista is not a competing therapy that could be used for the treatment of Wet AMD. Instead, the drug is being tested as an add-on therapy to Lucentis and Eylea, which essentially means that Fovista holds the potential to tap into a wider market base than what Eylea and Lucentis currently do on their own.

Progress So Far

Fovista is currently in the late stages of its testing phase. The drug, which is expected to be used along with standard treatments that include Eylea and Lucent, will be the first drug in its class of therapies for the treatment of wet AMD.

Ophthotech has begun a Phase 3 clinical program to evaluate the safety and efficacy of its drug. Initial data from this program is expected to become available in 2016. If the results are statistically significant, the company will submit an application to gain rights to market the drug in the US and Europe before the end of 2016.

What's In It for Ophthotech?

Ophthotech is expected to receive an immediate payment of up to \$330 million as a result of the agreement. This amount includes an upfront fee of \$200 million, while the remaining \$130 million is for expenses pertaining to Fovista Phase3 enrollment-based milestones.

The company may also get about \$700 million to \$1 billion in upfront and milestone payments from the collaboration. Ophthotech is due to receive future royalties from the agreement in the future.

Share Price

Ophthotech went public in September last year. The company bagged \$165 million in its IPO, which was marked as one of the top ten **biotech IPOs** of the year. The successful IPO represented investors' faith in Fovista to become a blockbuster drug.

The company's shares were priced at \$22 when it began trading in September 2013, and since then they have been on the rise. The stock closed at \$31.75 yesterday, up 1.22%. The shares then rallied 22.8% in after-hours trading.

On the other hand, Novartis's stock slipped 0.4% to close at \$89.52 on Monday. Novartis's share price has remained relatively stable on news of the licensing agreement with Ophthotech.

Sell Side Estimates

Ophthotech is well financed, as evident from the fact that the company took on no debt in FY13, and in between FY11-FY12, only issued \$11 million as short-term debt.

All of the four analysts covering the company have a Buy rating on the stock, with the target price coming out to be \$60.67 per share, at a premium of 92% to the company's share price at the end of yesterday's trading session.



Ophthotech Signs Marketing Deal For Eye Drug With Novartis; Shares Surge

May 19, 2014

Audience Reach: 54,000

Shares of Ophthotech Corp. (OPHT: Quote) surged 23 percent after the bio-pharmaceutical company said it has granted Novartis AG (NVS: Quote) the license to market its macular degeneration drug Fovista outside the US.

Ophthotech has granted Novartis exclusive rights to commercialize its lead product candidate, Fovista, in markets outside the US, while Ophthotech retains the US marketing rights.

Ophthotech said it could receive immediate payments of up to \$330 million, including an upfront fee of \$200 million and Fovista Phase 3 enrollment-based milestones of up to \$130 million. Ophthotech said it could potentially get over \$1 billion in upfront and milestone payments during the course of the collaboration, not including future royalties.

Fovista, a developmental stage drug, is being developed for the treatment of wet age-related macular degeneration. If approved, Fovista is expected to be first to market in this class of therapies for wet AMD.

Age-related macular degeneration is a disease characterized by progressive degenerative abnormalities in the macula of the eye, a small area in the central portion of the retina.

"As one of the largest ex-US partnering deals ever in the biotechnology industry, this collaboration with Novartis is potentially transformational for Ophthotech," stated David Guyer, CEO of Ophthotech.

OPHT closed Monday's trading at \$31.46, up \$0.38 or 1.22%, on the Nasdaq. The stock surged \$7.54 or 23.97% in after-hours trade.

NVS closed Monday's trading at \$89.52, down \$0.36 or 0.40%, on the NYSE. The stock further slipped \$0.01 or 0.01% in after-hours trade.

Ophthotech (OPHT) Mega Million Deal With Novartis (NVS), Oncolytics Biotech (ONCY) Brain Cancer Trial Positive Data, Tarena International (TEDU) Solid Results

May 20, 2014

By Mike Zaman InstaBlog

Audience Reach: 2,708,842

Ophthotech Corporation (OPHT)

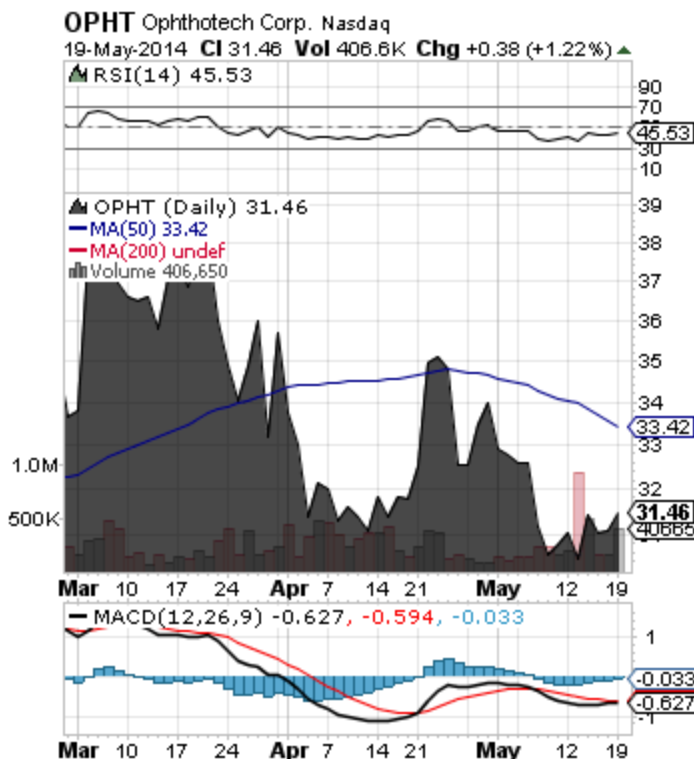
OPHT said that it has entered into an ex-US licensing and commercialization agreement with Novartis Pharmaceuticals (NVS) focused on the treatment of wet age-related macular degeneration (AMD).

Under the agreement, the company grants Novartis exclusive rights to commercialize **OPHT's** Fovista®, in markets outside the United States while **OPHT** retains sole rights to commercialize Fovista® in the U.S.

Potential payments to OPHT under the agreement could total over \$1 billion in upfront and milestone payments, not including future royalties. **OPHT** could receive immediate payment and near-term milestones totaling up to \$330 million, including an upfront fee of \$200 million and Fovista® Phase 3 enrollment-based milestones of up to \$130 million. **OPHT** is entitled to receive royalties on ex-US Fovista® sales.

OPHT's Fovista® is the most advanced anti-PDGF agent in development for the treatment of wet AMD and, if approved, is expected to be first to market in this class of therapies for wet AMD.

Brokerage firm JPMorgan has raised its price target for **OPHT** from \$40.00 to \$51.00 per share



OPHT is a biopharmaceutical company specializing in the development of novel therapeutics to treat diseases of the eye, with a focus on developing innovative therapies for age-related macular degeneration (AMD).

Round Ups

Bloomberg

**Bloomberg
Businessweek**

U.S. Stock-Index Futures Little Changed Before Earnings

May 20, 2014

By Namitha Jagadeesh

Audience: 6,975,021

Share Offering

Ophthotech Corp. jumped 23 percent to \$38.64 in late New York trading. The drug developer granted Novartis AG the exclusive rights to commercialize its Fovista treatment in markets outside the U.S. Ophthotech said potential royalty revenue from the deal could exceed \$1 billion, including \$200 million upfront and further payments if it reaches some targets.



Stocks to Watch: Staples, TJX, Urban Outfitters

May 20, 2014

By Maria Armental and Tess Tynes

Audience Reach: 7,955,125

Swiss drug maker **Novartis** AG NOVN.VX -0.38% reached an exclusive agreement with **Ophthotech** Corp. OPHT +24.53% to commercialize wet age-related macular degeneration treatment Fovista outside the U.S. Ophthotech shares rose 18% to \$37.19 premarket.



Unusual 11 Mid-Day Movers 05/20: (NEWL) (ARX) (OPHT) Higher; (DKS) (WHX) (SPLS) Lower

May 19, 2014

Audience: 100,860

Ophthotech Corporation (Nasdaq: OPHT) 21.9% HIGHER; announced that the Company has entered into an ex-US licensing and commercialization agreement with Novartis Pharmaceuticals focused on the treatment of wet age-related macular degeneration (AMD). Under the agreement, Ophthotech grants Novartis exclusive rights to commercialize Ophthotech's lead product candidate, Fovista®, in markets outside the United States while Ophthotech retains sole rights to commercialize Fovista® in the United States. Potential payments to Ophthotech under the agreement could total over \$1 billion in upfront and milestone payments, not including future royalties. Fovista® is the most advanced anti-PDGF agent in development for the treatment of wet AMD and, if approved, is expected to be first to market in this class of therapies for wet AMD.

Ophthotech Raises \$175M for Solo Run in Phase III

Cover Story

May 29, 2013

By Catherine Shaffer

At a time when a majority of biotech companies are partnering up with big pharma for Phase III trials, Ophthotech Corp., of Princeton, N.J., is building a war chest to go it alone.

The company raised \$175 million to support a global Phase III program for Fovista, an antiplatelet-derived growth factor (anti-PDGF) agent, in combination with anti-VEGF therapy for age-related macular degeneration (AMD).

The \$175 million breaks down into \$125 million from Novo A/S, in exchange for royalties on Fovista sales, and \$50 million in Series C preferred stock financing from Novo A/S and other venture investors. The financing overall will be structured in three equal tranches.

"We retain all worldwide rights for this asset," Ophthotech CEO David Guyer told BioWorld Today. Because Fovista showed "outstanding" results in Phase IIb, and because Ophthotech estimated that it has "huge market potential," the company decided to break with tradition and do a solo Phase III program, rather than the well-trodden path of seeking a partner after a successful Phase IIb proof-of-concept trial.

That randomized, controlled Phase IIb study assessed efficacy and safety of Fovista 0.3 mg in combination with Lucentis (ranibizumab, Roche AG) 0.5 mg, Fovista 1.5 mg with Lucentis 0.5 mg, or sham with Lucentis 0.5 mg. Patients in the 1.5 mg Fovista/0.5 mg Lucentis group gained a mean of 10.6 letters of vision on the ETDRS standardized chart after 24 weeks of treatment, compared to 6.5 letters for patients receiving Lucentis monotherapy.

There were no significant safety issues in either treatment group.

"With this funding, Ophthotech is well positioned to bring this drug Fovista rapidly to market. We're very grateful to our investors for their profound confidence," Guyer said, adding that Fovista is a "potential game-changing therapy to improve outcomes for people with wet AMD."

The financing is expected to cover a "substantial portion of the costs" of the Phase III program for Fovista.

The Phase III trial will be designed based on the successful Phase IIb trial. Beginning in the third quarter, it will enroll about 1,900 patients across 200 clinical centers worldwide. Ophthotech plans to release additional details of the study design at a later date.

Guyer said Ophthotech looked at many different financing strategies before settling on the current format. "The investors in the syndicate are kind of bullish," Guyer said. "We believe that taking this asset to the next inflection point would provide the best value for the shareholders."

In terms of competition, there are no other companies at the Phase III stage with an anti-PDGF therapy in combination with an anti-VEGF agent, according to Ophthotech.

The company does not share market projections for Fovista, but Guyer pointed out that sales of anti-VEGF products are approaching the \$5 billion level.

Eylea (aflibercept, Regeneron Pharmaceuticals Inc.) and Lucentis are the major anti-VEGF players in the AMD market, with off-label competition from Avastin (bevacizumab, Roche).

Either product could be an attractive pairing for combination therapy. Ophthotech used Lucentis in its Phase IIb trial design, leaving Eylea somewhat out in the cold. Regeneron's stock (NASDAQ:REGN) took a temporary hit in June 2012, falling 12.5 percent when Fovista's trial results were released. The stock has since more than doubled, closing at \$251.45 Tuesday.

At the time, there was speculation over which product Ophthotech would choose for the Phase III pairing. Steve Yoo, an analyst with Leerink Swann, noted that "both Roche and Regeneron have vested interest in keeping Fovista as a standalone therapy off the market. If Fovista is priced so that it could be used in conjunction with Avastin, it could seriously degrade the market share of both Eylea and Lucentis."

One potential solution would be for Ophthotech to carry out its Phase III trial using both Eylea and Lucentis, to increase competitive bidding pressure between the two companies.

"We are finalizing the clinical trial protocol and will disclose it at a later date. We certainly have the flexibility to use all anti-VEGF therapies primarily used in the wet AMD marketplace today," Guyer said.

In conjunction with the financing, Ophthotech has expanded its management team. Guyer, the company's chairman, has moved into the position of CEO. Co-founder and President Samir Patel was appointed vice chairman. The new arrangement will allow Guyer to direct the company's corporate and financial strategy, while Patel focuses on clinical development.

Although Ophthotech is going it alone for Phase III for the time being, Guyer said the company has not ruled out partnering. "We would carefully consider any proposals. The board is also looking at various strategies."

Part-Way Financing

The Bernstein Report: Ebb & Flow Edition

Cover Story

June 3, 2013

Ophthotech Corp. did two deals last week that could bring in \$175 million, but the biotech expects it still will need additional capital to complete a Phase III trial of Fovista for wet age-related macular degeneration.

The company raised \$16.7 million in the first tranche of a \$50 million series C round from existing investors Novo A/S; SV Life Sciences; Clarus Ventures; and HBM Partners.

Ophthotech also received \$41.7 million in the first tranche of a \$125 million deal with Novo in exchange for future undisclosed royalties on Fovista sales. Ophthotech is eligible for two more equal tranches based on recruitment milestones in the Phase III trial, which is slated to begin in 3Q13.

Ophthotech CEO David Guyer said Novo suggested the royalty structure, which shareholders preferred because the majority of the financing is non-dilutive.

Novo's Thomas Dyrberg told BioCentury the deal is Novo's first investment tied to a royalty stream, but doesn't expect such deals to become a regular part of its investment strategy. Dyrberg sits on Ophthotech's board.

Guyer said Ophthotech has enough cash to cover a "substantial portion" of the Phase III trial, which is expected to enroll 1,900 patients.

The international study will evaluate Fovista, a pegylated aptamer against platelet derived growth factor B (PDGFB; PDGF2) in combination with an anti-VEGF therapy. Guyer would not disclose which combination would be used but said: "We certainly have flexibility to use all or any VEGF therapies that are in the marketplace today."

Guyer expects recruitment "will be very fast" given Fovista's positive Phase IIb data.

Last year, Ophthotech announced data from Phase IIb trial in 449 AMD patients showing that a once-monthly combination of Fovista and Lucentis ranibizumab from Roche (SIX:ROG; OTCQX:RHHBY) met the primary endpoint of improving mean visual acuity from baseline to week 24 vs. Lucentis alone (10.6 letters vs. 6.5 letters).

In 2007, Ophthotech licensed rights to Fovista (formerly E10030) from Eyetech Inc., then a unit of OSI Pharmaceuticals Inc.



Ophthotech Raises \$58.3 Million for AMD

May 29, 2013

Ophthalmic company Ophthotech Corp. (New York, N.Y.) raised \$58.3 million on Wednesday, including the first \$16.7 million tranche of a planned \$50 million series C round from existing investors Novo A/S; SV Life Sciences; Clarus Ventures; and HBM Partners. The funding also includes the first \$41.7 million tranche from a separate, planned \$125 million investment from Novo. In exchange for its separate investment, Novo is eligible for undisclosed royalties on sales of Ophthotech's Fovista, which is slated to start Phase III testing to treat age-related macular degeneration (AMD) next quarter. Additionally, the company said Chairman David Guyer was named CEO.

Last year, Ophthotech said once-monthly intravitreal Fovista plus Lucentis ranibizumab met the primary endpoint vs. Lucentis alone in a Phase IIb trial to treat AMD. Ophthotech has rights to the pegylated aptamer against platelet derived growth factor B (PDGFB; PDGF2) from OSI Pharmaceuticals Inc., now part of Astellas Pharma Inc. (Tokyo:4503), under a 2007 deal. The Genentech Inc. unit of Roche (SIX:ROG; OTCQX:RHHBY) markets Lucentis in the U.S., while Novartis AG (NYSE:NVS; SIX:NOVN) markets it elsewhere.

Ophthotech Raises \$175M, Plans Phase III Macular Degeneration Studies

May 29, 2013

By Brian Gormley

Ophthotech Corp., whose drug may help improve vision in patients with the vision-stealing disease macular degeneration, has raised \$175 million in royalty and equity financing as it prepares to test this product in Phase III clinical trials.

In October, Ophthotech said its drug, Fovista, when used with the Genentech drug Lucentis, improved vision compared to Lucentis alone in a Phase IIb study of 449 patients with the wet form of age-related macular degeneration. AMD is a leading cause of vision loss in older adults, according to the National Eye Institute. The wet form of the disease can cause rapid vision loss.

The market for wet AMD drugs has become more competitive in recent years with the introduction of Lucentis, approved in 2006, and the 2011 approval of Eylea, a drug from Regeneron Pharmaceuticals Inc. Ophthotech is one of several venture-backed companies developing treatments for the wet or dry forms of AMD. Others targeting the wet form include Kala Pharmaceuticals Inc. and Promedior Inc.

In Ophthotech's Phase IIb clinical trial, patients receiving its drug, Fovista, and Lucentis gained a mean of 10.6 letters on a standardized chart, compared to 6.5 letters for those who received only Lucentis. In the third quarter Ophthotech plans to launch multinational Phase III studies of 1,900 macular degeneration patients at more than 200 centers.

The \$175 million, to be distributed in three equal tranches, will fund a substantial portion of that study, said David Guyer, who is joining Ophthotech as its chief executive. Samir Patel, co-founder and president, is taking on the additional role of vice chairman. Dr. Guyer will direct Ophthotech's corporate and financial strategy, and Dr. Patel will focus on clinical development.

Dr. Guyer, who had been a partner with Ophthotech backer SV Life Sciences, has also been chairman of Ophthotech since its inception in 2007. In addition to being CEO he'll also be a venture partner with SV Life Sciences, he said. Before joining the firm Dr. Guyer was CEO of Eyetech Pharmaceuticals Inc., which developed the macular degeneration drug Macugen.

The financing consists of \$125 million from Novo A/S in exchange for royalties on Fovista sales. The remaining \$50 million is a Series C financing from Novo and Ophthotech's existing backers, which, in addition to SV, include Clarus Ventures, HBM Healthcare Investments and Novo Ventures.

Dr. Guyer declined to discuss further specifics about the royalties or the total amount of venture capital Ophthotech has raised. This financing helps protect existing investors and employees, and leaves Ophthotech free to make other deals, Dr. Guyer said.

Ophthotech's Fovista is an aptamer directed against platelet-derived growth factor subunit B, which regulates neovascular pericytes, or cells associated with the walls of newly formed small blood vessels. Growth of these new blood vessels is a hallmark of the wet form of age-related macular degeneration. Lucentis is an antibody directed against vascular endothelial growth factor. Both drugs are administered through intravitreal injection.



Ophthotech Nabs \$175M To Fund Late-Stage Trial For Eye Drug

May 29, 2013

By Ben Fidler

Ophthotech was founded by former Eyetech Pharmaceuticals executives to change the standard of care for the “wet” form of age-related macular degeneration: the leading cause of blindness among adults in the western world.

With a new \$175 million round of financing the New York company will get its shot to prove its new drug candidate works in a large-scale clinical trial.

New York-based Ophthotech announced today that it has raised the new round of cash from Novo A/S and its current investors, which include SV Life Sciences, Novo Ventures (the VC arm of Novo Nordisk), HBM Healthcare Investments, and Clarus Ventures.

The financing comes in a couple parts. One is a \$50 million Series C round of preferred equity financing, which is being supplied by both Novo, and Ophthotech’s other investors. The remaining \$125 million is being committed by Novo Nordisk as part of a product royalty sale agreement. Essentially, Ophthotech is providing Novo with an undisclosed percentage royalty on future sales of its drug candidate E10030 (which it hopes to market under the name Fostiva). In return, Novo has agreed to pay \$125 million in three equal installments. The first part of the Series C and the royalty financing deal has already closed, which means that Ophthotech should have about \$58.3 million of new cash for its coffers today, and that it stands to collect roughly another \$116.7 million from Novo and its other investors if its drug can hit all of its milestones.

Ophthotech will use the cash to bankroll a large late-stage study of E10030, a treatment for the wet form of AMD, a condition in which blood vessels leak behind the eye, leading to distorted vision and potentially blindness. Ophthotech hasn’t revealed the design of the study yet, but it will include 1,900 patients across 200 testing sites, and begin before the end of September.

The market for age-related macular degeneration has exploded over the past several years, as the standard of care has changed from laser therapies that didn’t actually improve patients’ vision—rather, it stopped their vision from getting worse while destroying the very retinal tissue clinicians were trying to save—to injectable pharmaceuticals that do. Roche/Genentech’s ranibizumab (Lucentis) and bevacizumab (Avastin), and Regeneron Pharmaceuticals’ aflibercept (Eylea) have all become hit drugs for treating the disease. All of them, however, fight AMD by inhibiting the vascular endothelial growth factor (VEGF) that researchers say causes the condition to worsen. Ophthotech’s E10030, instead, blocks platelet-derived growth factor (PDGF), a different protein that has also been implicated in the wet form of AMD.

This is important because the essential problem in the wet form of AMD is abnormal blood vessel growth in the macula, a part of the retina. While blocking VEGF on its own only stops those abnormal blood vessels from continuing to grow, scientists believe adding PDGF to the equation may cause them to recede. Ophthotech’s plan is to combine the two treatments into one regimen, giving patients one injection of an anti-VEGF such as ranibizumab, and another of E10030. While the idea of getting two injections in the eye in one sitting certainly isn’t a fun idea for potential patients, Ophthotech’s selling point is that combining the two simply works better than solely using any anti-VEGF on its own.

“Giving combination therapy via two injections does not increase the treatment burden for the patient or physician,” says Ophthotech CEO David Guyer. “The patient visits are unchanged.”

Ophthotech isn't the only company to target PDGF—a startup in Waltham, MA called Kala Pharmaceuticals is developing a drug, for example, that blocks both VEGF and PDGF—but Ophthotech is the farthest along in development. The company in 2012 completed a mid-stage study of 449 patients over 24 weeks. In the study, patients randomly received either injections of 0.3 mg of E10030 and 0.5 mg of ranibizumab; 1.5 mg of E10030 and 0.5 mg of ranibizumab; or 0.5 mg of ranibizumab and a placebo injection. Ophthotech reported in October that the group taking the largest dose of E10030 with Roche's drug had better results than those taking ranibizumab alone: in the former group, patients read an average of 10.6 letters on a standardized visual acuity chart more than they had at the beginning of the study. By comparison, patients taking ranibizumab alone could read an average of 6.5 more letters than they could before—a 62 percent benefit. Ophthotech reported that it was a statistically significant improvement, meaning it was highly unlikely that the results were due to chance, and that the drug was well tolerated by patients.

Guyer says that the next study will test patients who haven't yet been treated for wet AMD, meaning the company hopes to establish the combination regimen with any anti-VEGF as a first-line therapy for the disorder.

“We are anti-VEGF agnostic,” Guyer says. “We believe that our drug will be shown to work with any of the anti-VEGF's.”

He added that the primary goal for the study—which is also the standard FDA regulatory endpoint for approval of such drugs—will be the same. The only difference will be that the late-stage trial will test patients over the course of a full year instead of 24 weeks.

Guyer is the co-founder and former CEO of Eyetech Pharmaceuticals, which crafted the first VEGF blocker, pegaptanib (Macugen), to be approved by the FDA for wet AMD. Eyetech had already developed what is now known as E10030 when it was acquired by OSI Pharmaceuticals for \$935 million in 2005—the year before ranibizumab was approved by the FDA and stole that drug's thunder. Guyer, who subsequently left the company to work as a partner at SV Life Sciences, licensed the newer drug from OSI in 2007 and formed Ophthotech around it with Eyetech's other co-founder, Samir Patel (Patel is now Ophthotech's president).

“It's a drug we've known for a very long time and we're fortunate enough to do the development on,” he says.

Guyer wouldn't reveal how much money Ophthotech has raised to date, though he did say that Novo Ventures has been a part of the investment group since the company's inception. Guyer added that though he believes a small company like Ophthotech can successfully sell E10030 in the U.S., the company would likely look to find a partner to help sell the drug internationally.

Novo Spearheads \$175M Financing To Back Ophthotech's Phase III AMD Study

May 29, 2013

By John Carroll

New York-based Ophthotech has rounded up a whopping \$175 million in financing to cover a pivotal late-stage study of its lead drug for wet age-related macular degeneration (AMD). The biotech signed a deal to share its royalties on Fovista--earlier dubbed E10030--with Novo A/S in exchange for \$125 million. And Novo stepped up to lead a \$50 million Series C round for the company.

Ophthotech, which was set up by Eyetech veterans, is taking the big step into Phase III after reporting positive results from a Phase IIb study of Fovista last summer. Investigators reported data on the 449 patients recruited for the study, who were split between one arm that received a combination of Fovista and Lucentis and another group that received only Lucentis. The primary endpoint was vision acuity.

The patients receiving a combination of Fovista (1.5 mg) and Lucentis gained a mean average of 10.6 letters of vision on a standardized chart test after 24 weeks of therapy, compared to 6.5 letters for patients receiving Lucentis monotherapy, a 62% added vision benefit. Now the company wants to see if it can safely replicate those results in Phase III.

The company was built on the notion that their aptamer would bind to platelet-derived growth factor subunit B and inhibit the growth of blood vessels needed for the development of wet AMD. Combined with an anti-VEGF drug, they reckoned, this new treatment could provide a one-two punch against wet AMD that could go on to become a new standard of care. Clarus Ventures led the \$30 million B round in 2009, joined by SV Life Sciences, Novo A/S and HBM BioVentures.

Along with the financing the biotech announced a reshuffling on the management side of the business. Eyetech founder and Ophthotech Chairman David R. Guyer stepped into the CEO role to handle the money end of the business while company co-founder Samir Patel will focus entirely on the clinical development program.

"We are grateful to our investors for their profound confidence in Ophthotech and Fovista as a potential game-changing therapy that we hope will improve outcomes for millions of people with wet AMD," Guyer said in a statement.

“The Pink Sheet”

Royalty Rights to AMD Drug Spur \$175 Million Capital Raise For Ophthotech

May 30, 2013

By Joe Haas

Money will finance 1,900-patient, 200-site Phase III trial for wet AMD drug Fovista, expected to work in concert with anti-VEGF therapies such as Lucentis to restore eye function. The transaction is just the latest ophthalmology financing involving Novo AS, SV Life Sciences and executives once with Eyetech.

The legacy of Eyetech Inc. continues, as its successor, Ophthotech Corp., has raised \$175 million to fund a huge Phase III trial for its wet age-related macular degeneration (AMD) candidate, *Fovista*. The transaction announced May 29 comprises a \$50 million Series C round for the privately held biotech, plus \$125 million from long-time investor Novo AS in exchange for undisclosed royalty rights to Fovista.

The financing is just the latest in a web of transactions involving the now-defunct Eyetech, Novo AS, the corporate venture arm of Novo Nordisk AS, and other players in the ophthalmology space, including VC firm SV Life Sciences. New York-based Ophthotech was created and is led by the co-founders of Eyetech, Chairman and CEO David Guyer and President Samir Patel. Following the sale of Eyetech to OSI Pharmaceuticals Ltd., Guyer was a principal at SV Life Sciences, which focuses much of its investment on eye care companies.

The financing includes the sale of \$50 million in Series C preferred stock to Novo AS and the biotech's other prior investors: SV, Clarus Ventures and HBM BioVentures. Those four participated in Ophthotech's \$30 million Series B round in 2009, while Novo, SV and HBM were the investors in the biotech's \$36 million Series A in 2007.

But Novo AS also is ponying up \$125 million against future royalties on the sale of Fovista, an anti-platelet-derived growth factor (PDGF) drug slated to enter Phase III during the third quarter of this year. In an interview, Guyer declined to provide specifics on the royalty agreement, such as percentage of sales or whether the royalties would be capped by dollar amount or a certain date.

As an affiliate of diabetes-focused Novo Nordisk, Novo AS (through VC outfit Novo Ventures) has made numerous investments in ophthalmology start-ups, including a \$40 million Series A in October 2011 for dry AMD-focused Imagen Biotech Inc.. SV also participated in that round, along with Fidelity Biosciences. Earlier in 2011, Novo and SV provided \$13.2 million in Series A funding to KalVista Pharmaceuticals Ltd., a spinout from Vantia Therapeutics Ltd. focused on developing small-molecule kallikrein inhibitors for diabetic macular edema.

Combination Therapy With Lucentis

Ophthotech intends to launch a 1,900-patient Phase III trial of Fovista at more than 200 sites internationally during the third quarter. Guyer would not speculate on when the trial might read out data. The company will attempt to build upon the success of a Phase IIb trial in which Fovista, an injectable dosed monthly with Genentech Inc.'s anti-VEGF therapy Lucentis (ranibizumab), demonstrated efficacy superior to solo therapy with Lucentis. Patients dosed with the combo gained a mean 10.6 letters of vision

on a standard visual acuity chart compared with 6.5 letters for the control group, an additional benefit of 62%, the company said.

Guyer would not specify whether the Phase III trial also would test Fovista with an anti-VEGF drug against anti-VEGF solo therapy. However, upon its founding in 2007, Ophthotech's focus was on coming up with a second drug that could augment the benefit of anti-VEGF drugs (such as Lucentis or Regeneron Pharmaceuticals Inc.'s Eylea (aflibercept)) ("Ophthotech Corp." —START-UP, July 2009).

"We are finalizing our Phase III trial protocol and will disclose it at a later date, but we certainly have the flexibility to use all or any anti-VEGF therapies that are primarily used in the wet AMD marketplace today in our trial," Guyer said.

Previous research by Ophthotech demonstrated that PDGF inhibition appears to destabilize the formation of unwanted blood vessels by blocking the recruitment and maturation of pericytes, specific cells that dot the forming vasculature and protect them by producing cell-survival signals even in the presence of VEGF inhibitors. In preclinical study, "extra blood vessels melted away," Ophthotech's Patel told *The Pink Sheet DAILY's* sister publication, Start-Up, in 2009.

In tandem with the financing, Ophthotech announced a management restructuring in which Guyer is moving into the CEO's office to direct corporate and financial strategy, while Patel will take the title of Vice Chairman of the Board and focus fully on clinical development of Fovista. Guyer noted that he and Patel have worked together for roughly 25 years, beginning in the academic setting and proceeding through the creation of Eyetech and the approval and launch of its anti-VEGF drug *Macugen* (pegaptinib sodium).

"We co-founded Ophthotech in 2007, so we've consistently worked together throughout," Guyer said.

"This is an extremely large trial [and] we're doing it ourselves, without a partner, so we felt it was very important to enhance management so that Patel could concentrate on all of these important clinical operations and strategies while we allowed the company to continue to grow in other ways. The clinical program is a 24/7 job in itself."

Taking On The U.S. Market Alone

At Eyetech, Guyer and team eventually brought in Pfizer Inc. as a development and commercialization partner, before selling the company to OSI. OSI later sold Macugen to Canadian specialty pharma Valeant Pharmaceuticals International Inc., which announced a major increase in its emphasis on eye care May 27 with the planned \$8.7 billion acquisition of Bausch & Lomb Inc. ("Eye On The Prize: For \$8.7 Billion, Valeant Will Acquire Bausch & Lomb" — "The Pink Sheet" DAILY, May 28, 2013).

Guyer said he thinks Ophthotech, where two-thirds of the personnel are former Eyetech employees, will be able to commercialize Fovista by itself in the U.S., by focusing primarily on approximately 2,000 retinal surgeons.

"At Eyetech, we had a sales force of 35 so we believe a small sales force in this indication of wet AMD can commercialize on its own," he said. "In our case, while we took the lead with the retinal specialists, Pfizer did back us up to general ophthalmologists. And we certainly can do the same."

"But ex-U.S., I think it's difficult for any small company to distribute and sell, so at the correct time we will look to do an ex-U.S. partnership," the executive added. "In addition, the board has and will continue to look at all potential financial and strategic options and see what brings the greatest value to the shareholders."

Guyer did not comment directly on the Valeant gambit for B&L or the possibility of continued consolidation in ophthalmology but he said the sector, after years of neglect from big pharma and investors alike, should only grow.

“When I started Eyetech, I had to convince the world that this is a multi-billion dollar opportunity,” he said.

“Today, we can see that at least for the anti-VEGF market sales will approach \$5 billion this year. So, I think we’ve seen validation of the commercial market in back-of-the-eye diseases.”

Going forward, the sector offers several multi-billion dollar therapeutic opportunities, Guyer asserted. Beyond AMD, these might include diabetic retinopathy, glaucoma and dry eye, he said.

Ophthotech Raises \$175M For Fovista Phase III In Wet AMD

May 30, 2013

By Mandy Jackson

Ophthotech raised \$175 million, mostly in the form of royalty financing from Novo A/S, to fund a 1,900-patient Phase III clinical trial for its anti-platelet-derived growth factor (anti-PDGF) aptamer Fovista in combination with an anti-VEGF therapy for the treatment of wet age-related macular degeneration (AMD).

Company

New York-based Ophthotech was founded in 2007 with a \$36 million Series A venture funding round, the acquisition of Fovista rights (formerly E10030) from OSI Pharmaceuticals and a license for Archemix's aptamers targeting factor C5 of the complement cascade.

But Ophthotech's connection to Fovista goes back long before the company's acquired the rights to the anti-PDGF aptamer from OSI.

Ophthotech chairman and newly-appointed CEO David Guyer was co-founder and CEO of Eyetech, and Ophthotech president and vice chairman Samir Patel was co-founder and chief medical officer at Eyetech when OSI bought the company, which developed Fovista and Macugen (pegaptanib sodium) – the first anti-VEGF drug ever approved by the US FDA.

The Archemix deal yielded Ophthotech's mid-stage AMD drug candidate ARC1905, which is a potent and selective inhibitor of C5. The company has not announced plans for the asset beyond its completed Phase I/II clinical trial.

Technology

PDGF regulates pericytes – one of two types of cells involved in the new blood vessel formation, or neovascularization, associated with AMD. By inhibiting PDGF, Fovista strips pericytes from neovascular tissue. Co-administration with an anti-VEGF therapy, which attacks vascular endothelial cells, stops blood vessel growth and may cause neovascular regression.

"It allows a more potent VEGF attack by removing these pericytes," Dr Guyer told *Scrip*.

Market opportunity

Anti-VEGF drugs, including Roche/ Genentech's Lucentis (ranibizumab) and Regeneron Pharmaceuticals' and Sanofi's Eylea (aflibercept), have become the standard of care for wet AMD. Worldwide anti-VEGF drug sales exceed \$4 billion, but Ophthotech says a significant unmet medical need remains, because most patients treated with anti-VEGF monotherapy do not significantly regain any visual acuity.

Data so far

Fovista administered in combination with Lucentis improved visual outcomes 62% more than Lucentis monotherapy in a 449-patient Phase IIb clinical trial. Patients with wet AMD treated with 1.5mg of Fovista plus Lucentis gained a mean of 10.6 letters on the standard ETDRS eye chart at 24 weeks compared with 6.5 letters for patients treated with Lucentis monotherapy (p=0.019).

Amount raised

Novo provided \$125 million in financing in exchange for a share of royalties from Fovista sales. Ophthotech also raised \$50 million in a Series C funding round with participation from Novo and the company's previous investors, which include SV Life Sciences, Novo Ventures, HBM Healthcare Investments and Clarus Ventures. The capital will be distributed in three tranches.

Key investor

Novo A/S is the private limited liability company owned by the Novo Nordisk Foundation. It also is the holding company in the Novo Group and is responsible for managing the foundation's \$30 billion-plus in assets, including pharmaceuticals in the Novo Nordisk and Novozymes portfolios. Novo A/S also provides seed funding and venture capital to development-stage life science companies, among other investments in the industry.

Use of funds

Ophthotech plans to initiate its 1,900-patient Phase III clinical trial in the treatment of wet AMD during the third quarter of 2013 in more than 200 clinics worldwide. The company will release more details on the trial design, including the anti-VEGF therapy that will be combined with Fovista for the study, at a later date. Dr Guyer noted that Fovista is "anti-VEGF agnostic," since it appears to work no matter which drug the anti-PDGF is combined with.

He declined to elaborate on the length of the Phase III study, including when final data will be available, but said: "We think that AMD trials recruit really well and with the exciting Phase II data the recruitment will be fast."

Impact

The funding will give Ophthotech the capacity to gather Phase III data for Fovista and add value to its anti-PDGF therapy prior to seeking an ex-US partner for the drug candidate.

"The [Ophthotech] board has and will continue to look at all financial and strategic partnership options. However, we believe a small company can develop, launch and commercialize in the US alone," Dr Guyer said.

Comment

Scrip contributor and Aetia Limited fund manager Andy Smith noted in a recent *Stockwatch* column that anti-VEGF and anti-PDGF therapies, which are injected into the eye monthly or bi-monthly, may soon face tough competition from radiation or laser therapies that are administered less frequently and at a lower cumulative cost.

But asked about the threat to anti-VEGF and anti-PDGF drugs, Dr Guyer dismissed the alternative treatments, saying: "We do not see them as major competitive threats. Laser is a destructive therapy and recent radiation trials have failed."



Venture Capital Deals

May 29, 2013

By Dan Primack

Ophthotech Corp., a Princeton, N.J.-based developer of therapies for wet and dry age-related macular degeneration, has raised \$175 million in new private financing. The first \$125 million comes from Novo AS, in exchange for royalties on the company's lead compound for wet AMD. The other \$50 million in a Series C round from Novo AS and existing backers like Clarus Ventures, HBM Partners and SV Life Sciences.



Ophthotech Raises \$175 Million To Fund Phase 3 Trial of Wet AMD Drug Candidate

May 29, 2013

With \$175 million in financing in place, Ophthotech plans to begin a global phase 3 trial of its lead anti-PDGF compound with anti-VEGF therapy for the treatment of wet age-related macular degeneration, according to a company news release.

The trial is slated to begin in the third quarter and will involve almost 1,900 subjects at more than 200 centers globally.

A randomized, controlled phase 2b trial of Fovista in combination with Lucentis (ranibizumab, Genentech) found superior efficacy when compared with ranibizumab monotherapy and no significant safety issues.

Ophthotech raised \$125 million from Novo A/S, which was granted royalties on Fovista sales. A Series C preferred stock offering involving Novo A/S and current venture investors raised \$50 million, the release said.

Ophthotech also announced that David R. Guyer, MD, chairman of the board, was named CEO, and Samir Patel, MD, Ophthotech co-founder and president, was appointed vice chairman of the board. Guyer will direct corporate and financial strategy, while Patel will focus on clinical development.

Novo AS Invests In Ophthotech Corporation

May 29, 2013

In an announcement made today, Ophthotech Corporation said it was able to raise US\$175 million in funding to finance the global Phase 3 clinical program of its lead medication Fovista. The medication is an anti-platelet growth factor that works in combination anti-VEGF therapy in the treatment of neovascular age determined macular degeneration.

The fund consists of an investment worth US\$125 million by Novo AS. The investment was done after the signing of a royalty agreement for the eventual revenues generated from Fovista. The US\$50 million is in the form of Series C preferred stock financing also from Novo AS. This financing is broken down into three equal tranches, where the first one was completed at the close of the funding round.

According to Henrik Gurtler CEO of Novo AS, "We are excited to lead this very large financing to drive Phase 3 development of Fovista. Ophthotech is well positioned to bring this important drug rapidly to market, based on the strength of Phase 2b results and the proven medical, regulatory and commercial capabilities of its management team."



HBM Healthcare Investments AG : Ophthotech Secures Financing Of USD 175 Million For Phase-III Clinical Trial Of FovistaTM

May 29, 2013

Ophthotech secures financing of USD 175 million for phase-III clinical trial of FovistaTM

Ophthotech Corporation, a privately held company in the portfolio of HBM Healthcare Investments, has concluded a USD 175 million financing deal. The funds will be used to conduct a pivotal phase-III clinical study of Ophthotech's lead compound FovistaTM. The study is expected to begin in the third quarter of 2013, and will encompass around 1,900 patients across over 200 centres world-wide.

The USD 175 million in financing consists of USD 125 million from the holding company Novo A/S, in exchange for royalties on future sales of FovistaTM, and a capital increase of USD 50 million, financed by both Novo A/S and existing Ophthotech shareholders. The overall financing package can be called up by Ophthotech in three equal tranches, the first of which has already been completed.

HBM Healthcare Investments has been invested in Ophthotech since 2007. When this financing round is completed, it will hold approximately 14% of the company. The terms of the financing raise the book value of the investment in Ophthotech to USD 42.1 million. This lifts the net asset value (NAV) per HBM share to CHF 78.23 as at 28 May 2013, which corresponds to an increase of 3.9% compared to the last published NAV as per mid May 2013 or 33% since the beginning of calendar year 2013.

FovistaTM is an anti-PDGF inhibitor which is being tested in combination with an anti-VEGF inhibitor for the treatment of age-related macular degeneration (wet AMD). In June 2012, data from the phase 2b trial in 449 patients showed that those patients who received FovistaTM in combination with the existing drug Lucentis[®] experienced a 62% greater improvement in visual acuity than patients treated with Lucentis[®] alone.

Wet AMD is the major cause of age-related blindness. The global market for drugs to treat this condition is currently worth over USD 5 billion and is expanding strongly. The current market is essentially shared by the two anti-VEGF therapies Lucentis[®] (distributed by Roche and Novartis) and Eylea[®] (distributed by Regeneron Pharmaceuticals and Bayer).

HBM Healthcare Investments Ltd

"The Pink Sheet"
DAILY

Shire Collaboration Brings Validation to ArmaGen's Drug-Delivery Technology

By Joseph Haas

July 23, 2014

Audience Reach: 45,000

Shire PLC has signed on as the first collaboration with the privately held ArmaGen Technologies Inc., and the work on the specialty pharma's Hunter syndrome drug Elaprase (idursulfase) could be a valuable validation of ArmaGen's experimental blood-brain barrier drug-delivery technology.

Based on the research of University of California, Los Angeles professor William Pardridge, ArmaGen obtained \$17 million in Series A funding in November 2012, with Shire joining the venture arms of Boehringer Ingelheim GMBH, Takeda Pharmaceutical Co. Ltd. and Mitsui & Co. Ltd. in the round [See Deal]. It was clear early on, ArmaGen CEO James Callaway said in an interview, that Shire wanted in on the ground floor of a technology that could enable its Hunter syndrome therapy to address central nervous system symptoms as well as the systemic manifestations it already helped with.

"From my interactions with them, Shire clearly wanted a front-row seat to evaluate the technology to deliver Elaprase across the blood-brain barrier," the executive noted. "From that privileged position, for which they paid equity dollars, they got an opportunity to see the compelling data we've been generating prior to the Series A and since, and became motivated to invest more deeply in ArmaGen."

Under the transaction announced July 23, Shire obtains a worldwide license to AGT-182, a late preclinical-stage asset that will fuse the iduronate-2-sulfatase enzyme – which Elaprase replenishes in Hunter syndrome sufferers – with an antibody attracted to the blood-brain barrier's insulin receptor. AGT-182 is slated to go into Phase I/II proof-of-concept study later this year. ArmaGen will conduct that trial, with research funding from Shire, which then will take over the program at Phase III.

ArmaGen gets \$15 million upfront split between cash and an equity investment. The biotech can earn another \$210 million under the deal, including the research funding, development and commercial milestones and royalties that could reach double digits, Callaway said. ArmaGen has not yet filed an IND, but he said discussions with FDA so far suggest the trial will enroll about 24 patients and produce final data in 2016.

"Our technology enables Elaprase not only to be delivered systemically, as it currently is, but to cross the blood-brain barrier and then treat the manifestations of the disease within the central nervous system, which include reduction in cognitive development, mental retardation and are a contributor to premature death," Callaway explained.

Elaprase is a weekly intravenous infusion product approved by FDA in 2006 and in Europe in 2007 ("Shire's Elaprase Approved For Hunter Syndrome" — "The Pink Sheet" DAILY, Jul. 24, 2006). The indication per FDA-approved labeling states that the drug "has been shown to improve walking capacity in patients five years and older," but that "in patients 16 months to five years of age, no data are available to demonstrate improvement in disease-related symptoms or long term clinical outcome; however, treatment with Elaprase has reduced spleen volume similarly to that of adults and children five years of age and older." Shire is conducting a 15-year

long-term outcomes study for the product, which could refine the labeling claims ("Shire's Elaprase For Hunter Syndrome To Undergo Long-Term Outcomes Study" — "The Pink Sheet," Jul. 31, 2006).

Broad Implications For Large Molecules

The implications of producing delivery technology to transfer large-molecule therapies across the blood-brain barrier are significant, because only about 2% of small-molecule drugs and no large molecules currently can enter the brain via the bloodstream ("In ArmaGen, Investors Seek A Brain-Penetrating Breakthrough" — START-UP, June 2013).

While the partnership with Shire around Elaprase is ArmaGen's first, Callaway noted that the company also is working on AGT-181, a nearly clinic-ready combination of its technology with Sanofi/Genzyme Corp.'s Hurler syndrome drug Aldurazyme (laronidase). In addition, it is conducting preclinical programs to apply the technology in other lysosomal storage disorders, such as metachromatic leukodystrophy and Sanfillippo A syndrome.

"[AGT-182] is the first of many opportunities that ArmaGen has to make second-generation products in the case of some of these lysosomal storage disease enzymes as well as to transform the treatment of neurological diseases more broadly," Callaway explained. "We've reached out and fused Enbrel (etanercept) to this antibody and shown that we can retain full biological activity and demonstrate impact in animal models, including Parkinson's disease models."

It also is working on using the technology with erythropoietin, he said. "That's the real thrust of ArmaGen, to take complex biologics and get them across the blood-brain barrier with this antibody fusion that binds to the insulin receptor and triggers what's called receptor-mediated transcytosis," he added. "We can infuse virtually anything – whether it be protein peptides, nucleic acid – and deliver it across the blood-brain barrier, and have reduced it to practice in over a dozen different molecules."

The Shire/ArmaGen collaboration arrives shortly on the heels of AbbVie Inc.'s July 18 announcement of an agreement in principle to acquire and merge with Shire for nearly \$54 billion ("AbbVie/Shire Merger To Create Rare Disease Business Unit Headed By Ornskov" — "The Pink Sheet" DAILY, Jul. 18, 2014). While motivated mainly by a plan to re-domicile AbbVie in the U.K., which would confer significant tax benefits, the pharma made clear that it also wanted to diversify with Shire's rare disease portfolio, which also includes enzyme replacement therapies for Fabry and Gaucher disease.

No Shire executive was available to comment for this story, but a spokesperson told "The Pink Sheet" DAILY that Shire remains an independent company and therefore did not need AbbVie's prior approval to complete the deal with ArmaGen. Callaway implied that ArmaGen's negotiations with Shire around AGT-182 pre-dated the start of merger talks with AbbVie, saying the deal took more than a quarter but less than half a year to finalize.

Shire continues its own development program to create an intrathecally delivered formulation of Elaprase, which in theory also could enable the drug to address CNS symptoms.

While Callaway would not divulge the amount of Shire's increased investment in ArmaGen, he said the deal makes the specialty firm one of its lead investors. It currently is determining whether to seek a Series B funding round to provide additional capitalization.

"We are debating that topic currently versus other opportunities to sell assets, but it's an expensive business," Callaway said. "This deal is a nice start on top of a Series A, but money has to come from somewhere, so it's either going to be a Series B mezzanine or another asset sale, either an individual product or a collection of products."

'In Transition' Shire Strikes Deal for Follow-on Hunter Syndrome Product

By Lucie Ellis

July 23, 2014

Audience Reach: 55,000

Shire is teaming up with biotechnology firm ArmaGen Technologies in order to develop an investigational enzyme replacement therapy (ERT) for the treatment of Hunter syndrome.

Under the agreement, Shire will hold worldwide commercialization rights to ArmaGen's compound AGT-182. In return the Calabasas, California-based biotech will receive payments up to approximately \$225m, including an initial upfront payment of \$15m in cash and equity, an additional equity investment, R&D funding, development and sales milestones, as well as future royalties up to double digits.

ArmaGen CEO James Callaway told Scrip that Shire, which holds a seat on the privately held biotech's board, has had its eye on the ArmaGen Hunter syndrome candidate for some time. Shire had "always been paying attention to our technology in general but of course specifically this asset because it is in exactly the same population as one of its lead products, Elaprase (idursulfase)," Dr Callaway said. It was this specific interest that spurred Shire to "jump into a negotiation", he said. Elaprase was approved in the US in 2006 for Hunter syndrome a rare, life-threatening genetic condition that results from the absence or insufficient levels of the lysosomal enzyme iduronate-2-sulfatase.

AGT-182– which has been granted orphan drug status from both the US FDA and the European Medicines Agency – uses the body's natural system for transporting products across the blood-brain barrier (BBB) by binding to the same receptor that delivers insulin to the brain. ArmaGen plans to begin a Phase I/II study of AGT182 in Hunter syndrome (also known as mucopolysaccharidosis type II, or MPS II) before the end of 2014 in collaboration with Shire.

"Shire will participate in development of AGT-183 as a member of the steering committee but ArmaGen will have operational responsibility for the development of the product," Mr Callaway told Scrip. "We have agreed development and clinical plans and ArmaGen is responsible for executing these. Shire will provide a level of stewardship as this is an area they know very well and also they will provide full financial support through this proof-of-concept study," he said.

A Shire/AbbVie Deal?

Dr Callaway also said it was a relief to be able to close this collaborative deal with Shire during a time where its prospective partner is undergoing takeover discussions with US pharma AbbVie (scripintelligence.com, 18 July 2014). "There were points of discussion that were difficult and we had what looked to be very different views of what each company needed out of the deal, so it was a challenging and fragile process at many stages," Dr Callaway said. "We're glad the deal has been done especially considering the timing."

As for the future of its arrangement with Shire, Dr Callaway wasn't overly concerned: "Uncertainty is certainly the code word for the day when you're talking of mergers and acquisitions," he said. "I think Shire has a business to run right now and until further notice it needs to execute plans. This is an important program for them as a second generation of one of

their lead assets and we're going to operate in that spirit until we're told otherwise. But I think it's a logical deal for the company whether it's Shire or AbbVie," he said.

Dr Philip J Vickers, global head of research and development at Shire said in a statement about the deal that: "AGT-182 has the potential to be an important new therapy to our existing portfolio of Hunter syndrome programs.

"Our agreement with ArmaGen strengthens our long-standing commitment to the Hunter syndrome community to bring forward novel therapies that have the potential to dramatically redefine the treatment paradigm and address the most critical unmet needs," he said.

Who Is ArmaGen?

The arrangement with Shire marks the first deal for ArmaGen for the development of its products but the company was founded back in 2004 by University of California, Los Angeles (UCLA) professor Dr William Partridge with cash from the NIH. ArmaGen survived until December 2012 when it secured Series A financing from a group of pharma investors: Boehringer Ingelheim Venture Fund, Takeda Pharmaceutical, Shire, and Japanese firm Mitsui Pharmaceuticals. The company now has secure financing for several years, Dr Callaway told Scrip.

ArmaGen's pipeline includes three other early stage programs: AGT-181 in development for the treatment of Hurler syndrome; AGT-183 being studied in metachromatic leukodystrophy; and AGT-184 for the treatment of Sanfilippo A syndrome.

The firm said it planned to pursue other collaborative deals for its products "particularly partners that are attempting to get complex biologics across the BBB." ArmaGen is aiming to get its three programs in to clinical studies and consummate the proof-of-concept of the two leads (AGT-181 and AGT-182) by the end of 2016.

BioWorld TODAY

Across Barrier Carrier? ArmaGen, Shire Team in Hunter Transcytosis

By Randy Osborne

July 24, 2014

Audience Reach: 53,700

\$15M NOW; \$225M POTENTIAL

Angling to strengthen its position in Hunter syndrome by way of a method past the blood-brain barrier, Shire plc – already an investor in Armagen Technologies Inc. – paid \$15 million up front and added an equity investment, sweetening the deal to develop the enzyme replacement therapy AGT-182 for somatic as well as central nervous system (CNS) effects of Hunter syndrome.

"They will become one of our lead investors," said Armagen CEO James Callaway. The pact could be worth as much as \$225 million for Calabasas, Calif.-based Armagen, counting R&D funding from Shire, of Dublin, plus payment for the achievement of development and sales milestones. Armagen is eligible for royalties up to the double digits, too.

"We've been very quiet" since the company was formed about a decade ago, Callaway said. "This is the first deal we've done, and there hasn't been a reason to make noise."

Hunter syndrome is caused by a malfunction or deficiency in the iduronate-2-sulfatase (IDS) enzyme. AGT-182 fuses a replacement version to an antibody that is attracted to the insulin receptor on the blood-brain barrier and thus can travel through it by way of receptor-mediated transcytosis.

The platform, which has generated other candidates and could yield "almost an endless supply of deal-making," also exploits the transferrin receptor (responsible for transporting iron in and out of the brain), Callaway said.

Shire already markets Elaprase (idursulfase) for Hunter syndrome, which "does a nice job of treating the systemic manifestations of the disease, including pulmonary obstruction and limited joint mobility," Callaway told BioWorld Today. "Sadly, to a large extent, [Elaprase] does not extend the life, because the CNS effects progress unabated." Mucopolysaccharides build up, causing mental and physical retardation. "The majority of these children don't make it past the second decade of life," he said.

Under the terms of the deal, a joint steering committee of people from both companies will oversee progress, with Armagen conducting a phase I/II study that will start before the end of this year, and Shire taking AGT-182 the rest of the way, through commercialization worldwide. "I wouldn't call [AGT-182] early stage, especially in orphan drugs where the pipeline can accelerate very quickly."

Armagen has research in the works to transport Enbrel (etanercept, Amgen Inc.) across the blood-brain barrier, as well as erythropoietin and glial cell-derived neurotrophic factor. "We've published data on all of these, but the lysosomal storage diseases are particularly attractive," since replacing an enzyme is relatively straightforward and gets the job done, Callaway said.

Farther back in the pipeline are prospects for Hurler syndrome, metachromatic leukodystrophy and Sanfilippo A syndrome. Armagen has eight other constructs "that are characterized, biologically active and contain either enzymes or proteins and cytokines," Callaway said, noting that the company also has an antibody against beta-amyloid.

In Hunter syndrome, Green Cross Corp., of Seoul, South Korea, has the biosimilar Hunterase available in some parts of the world, but "there isn't a lot of competition when you get to patient numbers this small," Callaway said.

Others have done research with transcytosis, including South San Francisco-based Genentech Inc. (now part of Roche AG) and Montreal-based Angiochem Inc., though Armagen is "the leader in that field," Callaway said. "We have the largest intellectual property, and we've been involved since the late 1970s" with research that originated in the University of California at Los Angeles, from which the company spun out in 2004, he added. (See BioWorld Today, June 27, 2011.)

Taking its name from the notion of "an arm that binds to a receptor and drags with it the enzyme or protein of interest," Armagen "survived from 2004 to 2012 on SBIR grants," Callaway said.

In November 2012, the firm secured \$17 million in series A cash, all from pharma venture funds that included those from Boehringer Ingelheim GmbH, of Ingelheim, Germany, and Osaka, Japan-based Takeda Pharmaceutical Co. Ltd. Also in the mix: Shire, placing itself "front and center" with Armagen, and "obviously in a good position to negotiate terms and generate this deal," Callaway said.

Shire To Spend About \$225M on Drug Collaboration

July 23, 2014

Audience Reach: 35 million

The drugmaker Shire plans to spend about \$225 million in a joint effort with a privately held, U.S. firm to develop a potential treatment for the rare and life-threatening genetic disorder Hunter syndrome.

The British company said Wednesday it will pay \$15 million upfront and then make additional payments to the firm, ArmaGen, to cover sales and development milestones and help fund research.

ArmaGen will be responsible for conducting early- and mid-stage research, expected to start before the end of this year, on its potential treatment. Shire then will take over further clinical testing, including late-stage studies, which are the final and most expensive trials a drug passes through before the pharmaceutical company submits it to regulators for approval.

The potential treatment, labeled AGT-182, has received an orphan drug designation from both U.S. and European regulators. That status can lead to some added marketing exclusivity if the drug is approved and a faster review by regulators.

Shire PLC also is in talks with U.S. drugmaker AbbVie over a roughly \$55 billion combination that would create a new company incorporated in the United Kingdom but controlled by shareholders of North Chicago, Illinois-based AbbVie Inc.

U.S.-traded shares of Shire climbed \$1.24 to \$255.20 in premarket trading Wednesday.



Shire Signs Licensing, Collaboration Agreement with Armagen

July 23, 2014

Audience Reach: 22 million

Shire Enters Strategic Licensing And Collaboration Agreement With Armagen

* Under terms of agreement, shire will obtain worldwide commercialization rights for agt-182 in exchange for payments of approximately \$225 million to ArmaGen

* Armagen will be responsible for conducting and completing phase i/ii study which it expects to initiate before end of 2014,

* Deal requires an initial upfront payment of \$15 million in cash and equity Source text for Eikon:
Further company coverage:

ArmaGen Licenses AGT-182 to Shire

July 23, 2014

Audience Reach: 53,746

ArmaGen Technologies Inc. (Calabasas, Calif.) granted Shire plc (LSE:SHP; NASDAQ:SHPG) exclusive, worldwide rights to develop and commercialize AGT-182, which is in development to treat mucopolysaccharidosis type II (MPS-II, Hunter's syndrome). ArmaGen will receive \$15 million up front in cash and equity. The company is also eligible for up to \$210 million in an additional equity investment, R&D funding and milestones, plus up to double-digit royalties. ArmaGen will conduct a Phase I/II trial of AGT-182, after which Shire will be responsible for further development and commercialization. ArmaGen expects to start the Phase I/II trial by year end.

AGT-182 is in development for both CNS and somatic manifestations of Hunter's syndrome, a rare lysosomal storage disorder caused by inadequate activity of the enzyme iduronate-2-sulfatase (IDS). AGT-182 is an enzyme replacement therapy comprised of IDS formulated with ArmaGen's Trojan horse technology. The technology creates a fusion protein of a therapeutic compound and a molecule that targets surface receptors on endothelial cells to facilitate transport across the blood-brain barrier.

AbbVie Inc. (NYSE:ABBV) is acquiring Shire for about £31.4 billion (\$53.8 billion) in a cash and stock deal slated to close next quarter (see BioCentury Extra, July 18).

With Acquisition Looming, Shire Still Making Deals

By John George

July 23, 2014

Audience Reach: 209,626

Shire isn't sitting idly by while its proposed \$ 54.8 billion sale to AbbVie goes through the regulatory approval process.

On Wednesday, Shire (NASDAQ: SHPG) entered into a worldwide licensing and collaboration agreement with ArmaGen, a privately held biotechnology company based in Calabasas, Calif.

Under the terms of the agreement, Shire will pay ArmaGen about \$225 million for commercialization rights to AGT-182, an experimental enzyme replacement therapy for patients with Hunter Syndrome. Shire is based in Dublin, Ireland, and has its U.S. headquarters in Wayne, Pa.

The deal calls for Shire to make an upfront payment of \$15 million in cash and equity and provide ArmaGen with an additional equity investment, research-and-development funding, development and sales milestones and royalty payments should the new drug candidate receive regulatory approval.

Shire, which specializes in therapies for rare diseases, developed the first approved treatment for Hunter Syndrome. That drug, Elaprase, received Food and Drug Administration approval in 2006. Hunter Syndrome, which afflicts about 1,800 people worldwide, is a life-threatening genetic disorder that results from the absence or insufficient levels of an enzyme known as iduronate-2-sulfatase. Without this enzyme, cellular waste products accumulate in a person's tissues and organs, causing them to malfunction.

Calabasas Biotech Signs License Agreement

By Joel Russell

July 23, 2014

Audience Reach: 40,000

ArmaGen, a private biotech firm, has signed a licensing agreement to fund development of AGT-182, an investigational enzyme to treat degenerative nerve disorder Hunter syndrome.

Under the agreement, Calabasas-based ArmaGen will receive payments up to \$225 million, including an initial upfront payment of \$15 million in cash and equity, from Shire plc, an Irish pharmaceutical company. In exchange, Shire will receive worldwide commercialization rights for AGT-182. The collaboration will be managed by a joint steering committee with representatives from both companies.

AGT-182 is ArmaGen's main investigational drug, and the company plans to start clinical trials before the end of the year.

"Shire is the ideal partner for AGT-182, based on the company's international reach and expertise in serving patients with Hunter syndrome," James Callaway, chief executive of ArmaGen, said in a statement.

Hunter syndrome is a rare, progressive and severe disorder in which the body can't break down complex sugars. The buildup of these chemicals interferes with the functioning of certain organs, leading to serious complications including developmental delays and mental impairment.

ArmaGen Licenses AGT-182 Rights To Shire For Up To \$225M

July 23, 2014

Audience Reach: 304,159

ArmaGen said today it licensed to Shire the worldwide commercialization rights to its investigational Hunter syndrome drug AGT-182, one of its two lead programs. The deal could net ArmaGen up to about \$225 million.

AGT-182 is an enzyme replacement therapy (ERT) designed to treat both the central nervous system (CNS) and somatic manifestations of Hunter syndrome by binding to the same receptor that delivers insulin to the brain. The ERT has received orphan drug designation from both the FDA and the European Medicines Agency (EMA).

AGT-182 is engineered by fusing a replacement for the enzyme iduronate-2-sulfatase (IDS), which helps break down complex sugars produced by the body, to an antibody that is attracted to the same receptor that delivers insulin to the brain. That enables the engineered enzyme to travel through the blood-brain barrier, attached to that antibody. Last month, ArmaGen said the U.S. Patent and Trademark Office issued a notice of allowance for a patent claiming the composition of AGT-182—a patent that, once issued, will be in force until at least 2030.

ArmaGen said it will be responsible for conducting a Phase I/II study of AGT-182, a trial it expects to initiate before the end of this year. Shire will oversee further clinical development, including Phase III trials, registration and commercialization of AGT-182 worldwide.

In return, Shire agreed to pay ArmaGen up to about \$225 million. That includes \$15 million in upfront cash and equity, as well as an additional equity investment, R&D funding, development and sales milestones, in addition to future royalties up to double digits.

“The agreement with Shire validates the clinical potential of ArmaGen’s lead therapy and its ability to cross the blood-brain barrier to treat the progressive and devastating neurological complications of Hunter syndrome,” ArmaGen CEO James Callaway, Ph.D., said in a statement. “Shire is the ideal partner for AGT-182, based on the company’s international reach and expertise in serving patients with Hunter syndrome.”

Shire’s global reach will broaden further if the company is acquired by AbbVie for roughly £32 billion (approximately \$55 billion), as announced by both companies last week. The combined company would be domiciled in the U.K., in the largest and latest tax-slicing “inversion” deal within biopharma.

Added Philip J. Vickers, Ph.D., Shire’s global head of research and development: “AGT-182 has the potential to be an important new therapy to our existing portfolio of Hunter syndrome programs. We plan to apply our proven ability to develop therapies for rare genetic diseases to progress AGT-182 as a potential treatment that offers hope to patients with Hunter syndrome and their families.”

Shire's Elaprase® (idursulfase), indicated for Hunter syndrome, was the company's second best-selling medicine last year, with \$546 million in sales. Shire pipeline includes a Phase II Hunter compound, SHP609, for CNS disorders associated with the syndrome.

AGT-182 is one of ArmaGen's two lead programs; the other is AGT-181, an ERT that is indicated for Hurler's syndrome. ArmaGen plans to launch a Phase I/II study of AGT-181 later this year in patients with the lysosomal storage disorder.

ArmaGen said a joint steering committee with representatives from both companies will oversee the ArmaGen-Shire collaboration.

Shire Inks a \$225M Rare Disease Deal on the Eve of Life with AbbVie

By Damian Garde

July 23, 2014

Audience Reach: 41,579

Shire (\$SHPG) has signed a \$225 million agreement to brighten its future in rare diseases, bolstering a major selling point for AbbVie (\$ABBV) as the two prepare for a \$54.7 billion merger.

Under the deal with Calabasas, CA's ArmaGen, Shire will hand over \$15 million up front and up to \$210 million more in equity investment and milestone payments to get its hands on a treatment for the rare Hunter syndrome. ArmaGen's candidate, AGT-182, is an orphan treatment designed to replace the missing enzyme at the root of the disease, in which buildups of cellular waste accumulate in tissues and organs, leading to serious complications and afflicting about one in 162,000 people, according to Shire.

Per the agreement, ArmaGen is solely responsible for a Phase I/II, which it expects to start before year's end. After that, Shire will step in and take full control of late-stage development and commercialization, the company said.

For Shire, the move dovetails with both its broad base of work in rare diseases and its efforts in Hunter's. The company's Elaprase, FDA approved in 2006, was the first marketed treatment for the disorder, and Shire is in the midst of Phase II with SHP-609, a treatment for the central nervous system manifestations of the disease that affect roughly two-thirds of Hunter's patients.

"Our agreement with ArmaGen marks our continued promise to the Hunter syndrome community to bring novel therapies that have the potential to dramatically redefine the treatment paradigm and address the most critical unmet needs," Shire R&D boss Philip Vickers said in a statement. "AGT-182 has the potential to be an important new therapy to our portfolio of programs for the treatment of both the CNS and somatic manifestations of Hunter syndrome."

Meanwhile, Shire expects to pull in \$3 billion in revenue from its rare disease business by 2020, and AbbVie, on the line to acquire the Irish company for \$54.7 billion in cash and stock, is similarly bullish about its future. The two expect to complete their union in the fourth quarter, talking up a combined company that will command a market cap of about \$137 billion, employing more than 30,000 people at 9 R&D centers and 14 manufacturing operations around the world.

Shire Plc (SHPG) Enters Licensing Agreement for AGT-182

July 23, 2014

Audience Reach: 148,891

Shire plc (Nasdaq: SHPG) announced a worldwide licensing and collaboration agreement for AGT-182, an investigational enzyme replacement therapy (ERT) for the potential treatment of both the central nervous system (CNS) and somatic manifestations in patients with Hunter syndrome (MPS II). This collaboration strengthens Shire's rare disease pipeline of innovative therapies where there is high unmet need, and underscores the company's long standing commitment to the Hunter syndrome community.

Under the terms of the agreement, Shire will obtain worldwide commercialization rights for AGT-182 in exchange for payments of approximately \$225 million to ArmaGen, including an initial upfront payment of \$15 million in cash and equity, an additional equity investment, R&D funding, development milestones and sales milestones, in addition to royalty payments. As part of the agreement, ArmaGen will be responsible for conducting and completing the Phase I/II study which it expects to initiate before the end of 2014, after which point Shire will be responsible for further clinical development, including Phase III trials, and commercialization.

Dr. Philip J. Vickers, Global Head of Research and Development at Shire, said, "Our agreement with ArmaGen marks our continued promise to the Hunter syndrome community to bring novel therapies that have the potential to dramatically redefine the treatment paradigm and address the most critical unmet needs. AGT-182 has the potential to be an important new therapy to our portfolio of programs for the treatment of both the CNS and somatic manifestations of Hunter syndrome. We look forward to collaborating with ArmaGen and leveraging our ability to successfully develop medicines to treat this rare, life-threatening disease."

Shire researched, developed and commercialized the first treatment approved for Hunter syndrome. This agreement with ArmaGen expands Shire's commitment to finding treatments for Hunter syndrome, which also includes SHP-609, Shire's product currently being investigated to treat the CNS manifestations associated with Hunter syndrome.

James Callaway, Ph.D., Chief Executive Officer of ArmaGen said, "Shire is the ideal partner for AGT-182, based on the company's international reach and expertise in serving patients with Hunter syndrome. We look forward to beginning the Phase I/II clinical trial of AGT-182 in collaboration with Shire and leveraging their expertise with these patients."

Shire in Strategic Licensing and Collaboration Agreement with ArmaGen

**By Sam Unsted
July 23, 2014**

Shire PLC Wednesday said it has entered a worldwide licensing and collaboration agreement with US biotechnology firm ArmaGen for AGT-182, an investigational enzyme replacement therapy, strengthening the FTSE 250-listed company's rare disease pipeline.

AGT-182 has been developed as a potential treatment for the central nervous system and somatic manifestations in patients with Hunter Syndrome.

Under the terms of the deal, Shire will pay approximately USD225 million for the worldwide commercialisation rights to AGT-182 to ArmaGen, including an initial upfront payment of USD15 million in cash and equity, an additional equity investment, research and development funding, development and sales milestones and royalty payments.

ArmaGen will be responsible for the Phase I/II study, expected to be initiated before the end of 2014, after which Shire will take responsibility for further clinical development, including Phase III trials, along with commercialisation.

Shire shares were trading 0.4% higher to 4,977 pence on Wednesday.



Shire, ArmaGen Partner To Develop AGT-182 Drug for Treatment of Hunter Syndrome

July 23, 2014

Audience Reach: 377,372

Shire plc (LSE: SHP, NASDAQ: SHPG), the global specialty biopharmaceutical company, and ArmaGen, a US privately held biotechnology company, today announced a worldwide licensing and collaboration agreement for AGT-182, an investigational enzyme replacement therapy (ERT) for the potential treatment of both the central nervous system (CNS) and somatic manifestations in patients with Hunter syndrome (MPS II). This collaboration strengthens Shire's rare disease pipeline of innovative therapies where there is high unmet need, and underscores the company's long standing commitment to the Hunter syndrome community.

Under the terms of the agreement, Shire will obtain worldwide commercialization rights for AGT-182 in exchange for payments of approximately \$225 million to ArmaGen, including an initial upfront payment of \$15 million in cash and equity, an additional equity investment, R&D funding, development milestones and sales milestones, in addition to royalty payments. As part of the agreement, ArmaGen will be responsible for conducting and completing the Phase I/II study which it expects to initiate before the end of 2014, after which point Shire will be responsible for further clinical development, including Phase III trials, and commercialization.

Dr. Philip J. Vickers, Global Head of Research and Development at Shire, said, "Our agreement with ArmaGen marks our continued promise to the Hunter syndrome community to bring novel therapies that have the potential to dramatically redefine the treatment paradigm and address the most critical unmet needs. AGT-182 has the potential to be an important new therapy to our portfolio of programs for the treatment of both the CNS and somatic manifestations of Hunter syndrome. We look forward to collaborating with ArmaGen and leveraging our ability to successfully develop medicines to treat this rare, life-threatening disease."

Shire researched, developed and commercialized the first treatment approved for Hunter syndrome. This agreement with ArmaGen expands Shire's commitment to finding treatments for Hunter syndrome, which also includes SHP-609, Shire's product currently being investigated to treat the CNS manifestations associated with Hunter syndrome.

James Callaway, Ph.D., Chief Executive Officer of ArmaGen said, "Shire is the ideal partner for AGT-182, based on the company's international reach and expertise in serving patients with Hunter syndrome. We look forward to beginning the Phase I/II clinical trial of AGT-182 in collaboration with Shire and leveraging their expertise with these patients."

Shire Gains Rights to ArmaGen's Experimental Hunter Syndrome Drug AGT-182

By Joe Barber

July 23, 2014

Audience Reach: 190,000

Shire entered a global licensing and collaboration agreement with ArmaGen for the latter's experimental Hunter syndrome drug AGT-182, the companies announced Wednesday. Philip Vickers, global head of R&D at Shire, said the enzyme replacement therapy "has the potential to be an important new therapy to our portfolio of programmes for the treatment of both the central nervous system (CNS) and somatic manifestations of Hunter syndrome."

Under the deal, Shire will obtain worldwide commercialisation rights for AGT-182 in exchange for payments of approximately \$225 million to ArmaGen, including an upfront payment of \$15 million, milestones tied to the achievement of certain development and sales goals, and up to double-digit future royalties. Meanwhile, ArmaGen agreed to conduct early- to mid-stage research on the drug, expected to begin later this year, with Shire holding responsibility for further clinical development, including late-stage trials.

Shire, which last week agreed to be acquired by AbbVie, said the partnership with ArmaGen strengthens its rare-disease pipeline. AGT-182, which is engineered via the fusion of the replacement IDS enzyme with an antibody that binds to a receptor on the blood-brain barrier, has received orphan drug status from both the FDA and European Medicines Agency. Shire noted that it is also investigating SHP-609 as a potential treatment for the CNS manifestations associated with Hunter syndrome.

Shire in Strategic Collaboration with ArmaGen for Hunter Syndrome

July 23, 2014

Audience Reach: 8,070

Ireland-headquartered drugmaker Shire (LSE: SHP) has entered into an agreement with US privately held biotech company ArmaGen for the worldwide licensing and collaboration of AGT-182, an investigational enzyme replacement therapy. This would potentially be used to treat the central nervous system and somatic manifestations in patients with Hunter syndrome (MPS II).

Shire will obtain worldwide commercialization rights for AGT-182 in exchange for payments of approximately \$225 million to ArmaGen, including an initial upfront of \$15 million in cash and equity, an additional equity investment, research and development funding, development milestones and sales milestones, in addition to royalties.

Shire responsible for further development

ArmaGen's role will be to conduct and complete a Phase I/II study which it expects to start before the end of the year. Shire will then be responsible for further clinical development, including Phase III trials, and commercialization.

Shire researched, developed and commercialized the first treatment to be approved for Hunter syndrome. Its product SHP-609 is currently being investigated to treat CNS manifestations associated with Hunter syndrome.

Philip Vickers, global head of R&D at Shire, said: "Our agreement with ArmaGen marks our continued promise to the Hunter syndrome community to bring novel therapies that have the potential to dramatically redefine the treatment paradigm and address the most critical unmet needs. AGT-182 has the potential to be an important new therapy to our portfolio of programs for the treatment of both the CNS and somatic manifestations of Hunter syndrome."

James Callaway, chief executive of ArmaGen, added: "Shire is the ideal partner for AGT-182, based on the company's international reach and expertise in serving patients with Hunter syndrome. We look forward to beginning the Phase I/II clinical trial of AGT-182 in collaboration with Shire and leveraging their expertise with these patients."

Shire Expands Rare Disease Reach

July 23, 2014

Audience Reach: 23,000

Shire, which is soon to be AbbVie, has finalized a deal with US biotech ArmaGen. The \$225-million deal gives Shire worldwide commercialization rights to the experimental enzyme replacement therapy AGT-182, which could be used to treat what the firms describe in a statement as “the central nervous system (CNS) and somatic manifestations in patients with Hunter syndrome.”

Hunter syndrome is a rare disease in which the body can't get rid of cellular waste. Around 1,200 patients have been diagnosed with the genetic disorder.

Shire Licenses ArmaGen ERT Candidate

July 23, 2014

Audience Reach: 18,295

Shire plc and ArmaGen have entered a worldwide licensing and collaboration agreement for AGT-182, an investigational enzyme replacement therapy (ERT) for the potential treatment of the central nervous system (CNS) and somatic manifestations in Hunter syndrome (MPS II).

Shire will obtain worldwide commercialization rights for AGT-182 for approximately \$225 million, including an initial upfront payment of \$15 million in cash and equity, an additional equity investment, R&D funding, development and sales milestones, as well as royalty payments. ArmaGen will be responsible for conducting the Phase I/II study, expected to begin this year, after which Shire will be responsible for further clinical development and commercialization.

Dr. Philip J. Vickers, global head of R&D at Shire, said, "Our agreement with ArmaGen marks our continued promise to the Hunter syndrome community to bring novel therapies that have the potential to dramatically redefine the treatment paradigm and address the most critical unmet needs. AGT-182 has the potential to be an important new therapy to our portfolio of programs for the treatment of both the CNS and somatic manifestations of Hunter syndrome. We look forward to collaborating with ArmaGen and leveraging our ability to successfully develop medicines to treat this rare, life-threatening disease."

James Callaway, Ph.D., chief executive officer of ArmaGen said, "Shire is the ideal partner for AGT-182, based on the company's international reach and expertise in serving patients with Hunter syndrome. We look forward to beginning the Phase I/II clinical trial of AGT-182 in collaboration with Shire and leveraging their expertise with these patients."

Shire Backs Hunter Syndrome Drug Development

July 23, 2014

Audience Reach: 2,708,842

Shire plc (SHPG +0.6%) commits up to \$225M to a joint development effort for a potential treatment for the life-threatening genetic disorder Hunter syndrome. It will pay privately-held California-based partner ArmaGen \$15M upfront followed by sales- and development-related milestone payments and funds for research.

ArmaGen will be responsible for early- and mid-stage development while Shire will manage the late-stage work.

The product candidate, AGT-182, has been designated an Orphan Drug by the FDA and EMA.



Shire Enters Licensing And Collaboration Agreement With ArmaGen

July 23, 2014

Audience Reach: 315,036

Shire and ArmaGen, a US privately held biotechnology company, announced a worldwide licensing and collaboration agreement for AGT-182, an investigational enzyme replacement therapy for the potential treatment of both the central nervous system and somatic manifestations in patients with Hunter syndrome. Shire will obtain worldwide commercialization rights for AGT-182 in exchange for payments of approximately \$225M to ArmaGen, including an initial upfront payment of \$15M in cash and equity, an additional equity investment, R&D funding, development milestones and sales milestones, in addition to royalty payments. ArmaGen will be responsible for conducting and completing the Phase I/II study which it expects to initiate before the end of 2014, after which point Shire will be responsible for further clinical development, including Phase III trials, and commercialization.



Shire in \$225 Million Licensing, Collaboration Deal with ArmaGen for AGT-182

July 23, 2014

Audience Reach: 54,800

Shire plc (SHP.L,SHPG: Quote) and ArmaGen, a US privately held biotechnology company, Wednesday announced a worldwide licensing and collaboration agreement for AGT-182, an investigational enzyme replacement therapy for the potential treatment of both the central nervous system and somatic manifestations in patients with Hunter syndrome.

As per the terms, Shire will obtain worldwide commercialization rights for AGT-182 in exchange for payments of about \$225 million to ArmaGen, including an initial upfront payment of \$15 million in cash and equity, an additional equity investment, R&D funding, development milestones and sales milestones, in addition to royalty payments.

Shire said the deal strengthens its rare disease pipeline of innovative therapies where there is high unmet need, and underscores the company's long standing commitment to the Hunter syndrome community.

As part of the agreement, ArmaGen will be responsible for conducting and completing the Phase I/II study which it expects to initiate before the end of 2014, after which point Shire will be responsible for further clinical development, including Phase III trials, and commercialization.

Shire researched, developed and commercialized the first treatment approved for Hunter syndrome.

AGT-182, which has received orphan drug designation from both the U.S. Food and Drug Administration and the European Medicines Agency, is designed to take advantage of the body's natural system for transporting products across the blood brain barrier by using the same receptor that delivers insulin to the brain.

Hunter syndrome or Mucopolysaccharidosis II is a rare, life-threatening genetic disorder that results from the absence or insufficient levels of the lysosomal enzyme iduronate-2-sulfatase. Without this enzyme, cellular waste products called mucopolysaccharides, also known as glycosaminoglycans accumulate in tissues and organs, which then begin to malfunction.

Shire, ArmaGen Ink Licensing Agreement for AGT-182

July 24, 2014

Audience Reach: 665,780

Shire (SHPG - Analyst Report) recently entered into a worldwide licensing and collaboration agreement with privately-held U.S.-based biotechnology company, ArmaGen.

The agreement is related to commercialization rights for pipeline candidate AGT-182, an experimental enzyme replacement therapy (ERT) which is being developed for the treatment of both the central nervous system (CNS) and somatic manifestations in patients with Hunter syndrome (MPS II).

As per the terms of the agreement, Shire will obtain worldwide commercialization rights for AGT-182 from ArmaGen. We note that the candidate enjoys orphan drug status both in the U.S. and EU.

In exchange, Shire will make payments of approximately \$225 million to ArmaGen. This includes an initial upfront payment of \$15 million in cash and equity, an additional equity investment, research and development funding, milestones payments along with royalty payments.

Meanwhile, ArmaGen will be responsible for conducting and completing the phase I/II study which is expected to start before 2014 end. Thereafter, Shire will be responsible for further clinical development, including phase III trials, and commercialization upon development.

The collaboration with ArmaGen is expected to strengthen Shire's rare disease pipeline. We note that Shire already has a drug, Elaprase, which is approved for treating Hunter Syndrome. Shire also has one candidate in its pipeline, SHP-609, which is being developed for the treatment of CNS manifestations associated with Hunter syndrome.

Last week, Shire announced that it has finally agreed to AbbVie's (ABBV - Analyst Report) acquisition proposal. Under the terms of the offer, shareholders of Shire will receive £53.19 for each Shire share (£24.44 in cash and 0.8960 ordinary shares of the merged company for each Shire share held).

Shire currently carries a Zacks Rank #3 (Hold). Investors looking for better-ranked stocks may consider companies like Allergan (AGN - Analyst Report) and Pfizer, Inc. (PFE - Analyst Report). While Allergan carries a Zacks Rank #1 (Strong Buy), Pfizer is a Zacks Rank #2 stock (Buy).

Shire Forms License Agreement with ArmaGen for Rare Disease Drug Candidate

Pharma News
July 24, 2014

In a move to strengthen its rare-disease drug pipeline, the specialty pharmaceutical company Shire plc has formed a worldwide licensing and collaboration agreement with ArmaGen, a US privately held biotechnology company, for AGT-182, an investigational enzyme replacement therapy for the potential treatment of both the central nervous system (CNS) and somatic manifestations in patients with Hunter syndrome.

Under the terms of the agreement, Shire will obtain worldwide commercialization rights for AGT-182 in exchange for payments of approximately \$225 million to ArmaGen, including an initial upfront payment of \$15 million in cash and equity, an additional equity investment, R&D funding, development milestones, sales milestones, and royalty payments. As part of the agreement, ArmaGen will be responsible for conducting and completing the Phase I/II study which it expects to initiate before the end of 2014, after which point Shire will be responsible for further clinical development, including Phase III trials, and commercialization.

Shire researched, developed and commercialized the first treatment approved for Hunter syndrome, according to the company. This agreement with ArmaGen expands Shire's commitment to finding treatments for Hunter syndrome, which also includes SHP-609, Shire's product currently being investigated to treat the CNS manifestations associated with Hunter syndrome.

AGT-182, which has received orphan drug designation from both the US Food and Drug Administration and the European Medicines Agency, is designed to take advantage of the body's natural system for transporting products across the blood brain barrier (BBB) by using the same receptor that delivers insulin to the brain. AGT-182 is engineered by the fusion of the replacement IDS enzyme to an antibody that binds to a receptor on the BBB. The IDS enzyme is designed to cross the BBB attached to that antibody.

Shire has made the deal following the announced acquisition by AbbVie of Shire for \$55 billion. Pending shareholder approval and customary closing and regulatory approvals, that deal is expected to close in the fourth quarter of 2014.

"The Pink Sheet" **DAILY**

More Than Window Dressing: Ornskov Seen as Key Asset in AbbVie's Buyout of Shire

By Joseph Haas

July 28, 2014

Audience Reach: 45,000

Executive Summary

The Shire CEO will oversee integration of his company into AbbVie and head a focused rare-disease unit in the new company, but longer-term might be in position to succeed AbbVie CEO Gonzalez. AbbVie may look to Sanofi's acquisition of Genzyme for a template on how to merge a rare diseases specialty play into big pharma.

It's not how biopharmaceutical mergers usually go, with the chief executive of the acquired company staying on as part of the new entity and reporting to the acquiring firm's CEO. But AbbVie Inc. has made clear that Shire PLC's CEO, rising industry star Flemming Ornskov, will be staying on to direct the integration process and head up a dedicated rare disease unit within the "New AbbVie."

Ornskov has been lauded widely for his smart stewardship at the helm of Shire, despite being in the job only 14 months – and it being his first shot at being a CEO. While AbbVie Chairman and CEO Rick Gonzalez, in response to the very first analyst question during a July 18 call announcing the merger, made clear that Ornskov had agreed to stay on and report to him, it's worth noting that Ornskov has not spoken publicly since the announcement nor made any clear commitment to stay on past the deal closing, expected during the fourth quarter.

It is unlikely legislation to prevent tax-inversion plays will pass before the deal closes, or that any such law will be retroactive.

Rare diseases, which makes up a significant portion of Shire's portfolio, "is an area that we are very, very excited about," Gonzalez said. "We believe it is a very high-touch kind of business, so we want to set it up in an individual business unit to make sure that we can maintain that patient focus that Shire has," he said ("AbbVie/Shire Merger To Create Rare Disease Business Unit Headed By Ornskov" — "The Pink Sheet" DAILY, Jul. 18, 2014).

Gonzalez also noted that two Shire board members – Chair Susan Kilsby and Dominic Blakemore – would be transferring over to AbbVie's board. Ornskov is being paid roughly \$9.9 million to stay on, about 150% of his current compensation, and about 30 of Shire's top-ranking executives also have signed deals that include significant retention bonuses if they stick around more than a year.

All of this gives the appearance that AbbVie, seen as motivated primarily by tax-inversion benefits that would accrue from being able to re-domicile in the U.K., is also deeply committed to the business diversification that Shire can offer. AbbVie apparently believes that it needs the Shire team to keep that business – built around enzyme-replacement therapies such as Replagal (agalsidase alfa) for Fabry disease, Vpriv (velaglucerase) for Gaucher disease, Elaprase (idursulfase) for Hunter syndrome and a pair of hereditary angioedema therapies,

Cinryze and Firazyr – on its current trajectory ("Shire, AbbVie Lay Out Competing Visions Ahead Of Expected New Offer" — "The Pink Sheet," Jun. 30, 2014).

Morningstar analyst Damien Conover, whose firm took something of an outlier view by asserting in a July 18 note that AbbVie may have paid too much for Shire, likened Ornskø to a premier free agent in professional sports. Still, Conover said it is difficult to assess whether Ornskø will be groomed for the top spot at AbbVie.

"Sometimes you can read the tea leaves pretty easily, but on this one I don't have any great insight," he said in an interview. "Gonzalez has been around for a while and he probably is looking for some sort of succession plan. ... That being said, I think people generally view the Shire management as pretty solid, so I think it might be Ornskø's decision. If he stays on, it might be a good signal that he is positioned pretty well."

Bernstein Research analyst Ronny Gal said he thought it was unlikely that someone with Ornskø's resume would stick around unless he had some assurances of a bright future at AbbVie.

"I think that what he has done since his first days at Shire is put forward a vision of making the company a roll-up play off the orphan diseases business," Gal said in an interview. "I believe the reason why Ornskø is staying with AbbVie is specifically to continue this roll-up. He's not a researcher, he's the guy who does the business strategy."

Sanofi/Genzyme As Template?

Before the AbbVie merger agreement, the company Shire often drew comparisons to was Genzyme Corp., the Cambridge, Mass.-based big biotech also focused on rare diseases and ERT drugs, including some of the same patient populations Shire serves, such as Fabry disease and Gaucher disease. French pharma Sanofi bought out Genzyme for \$19.4 billion in 2011, but has maintained the Genzyme legacy as a stand-alone rare disease-focused unit [See Deal].

Wall Street analysts think it's likely that AbbVie will use Sanofi's integration of Genzyme as a template for its absorption of Shire.

"I think [the rare disease-focused] half of Shire will probably stay as a stand-alone entity," Gal said. "That's pretty much the only way to run it, because of the deep science, the close relationships between researchers and doctors and patients, the very holistic experience needed to participate in that market. I think the rest of Shire will get absorbed into larger AbbVie."

Morningstar analyst Stefan Quenneville said AbbVie would need to tap Shire's expertise in rare disorders to get into the appropriate mindset for succeeding in that type of business.

"Pharma looks for large, broad markets, and rare diseases is more about transformational therapies that have a dramatic impact on a very small number of patients," he said in an interview. "It's a very different process from a clinical perspective and a regulatory perspective. In some ways, it takes a different mindset, so it makes sense to have a specific group of people within the organization focus on those things."

Quenneville's colleague Conover added that AbbVie will need to take that approach because there is almost no therapeutic overlap between the two companies. Rare diseases therefore will need to be an autonomous unit, he explained, albeit one that then can be primed for even greater success thanks to AbbVie's R&D, regulatory and commercial infrastructure.

The merger agreement, agreed to by both companies' boards, but still requiring approval by shareholder majorities, ends a saga begun in early May, when AbbVie made its first unsolicited bid to buy Shire ("Shire Rejects AbbVie Offer – But With Other Suitors Circling, Bidding War Is Likely" — "The Pink Sheet" DAILY, Jun. 20, 2014). Shire rejected four successive buyout offers from AbbVie, with each company presenting its strategic outlook to advisors and issuing dueling public statements as AbbVie called for non-confrontational negotiation and Shire contended its suitor's bids were too low.

An increased offer by AbbVie on July 8, however, brought about a change in tone, with Shire saying the £46.26-per-share bid came closer to one that the company could recommend to its board. A subsequent £53.20-per-share bid on July 14 led to negotiations that resulted in the July 18 merger announcement ("Shire Set To Recommend New AbbVie Offer After Latest Talks" — "The Pink Sheet" DAILY, Jul. 14, 2014).

Under the agreed-upon terms, AbbVie will pay £32 billion (nearly \$54 billion) for the acquisition, with Shire shareholders receiving £24.44 in cash and 0.8960 new AbbVie shares for each full share in Shire. Shire shareholders will own around 25% of the combined new company, with AbbVie shareholders getting a 75% stake.

Much discussion of the merger focused on the transaction's potential tax benefits – by domiciling in the U.K., AbbVie expects to reduce its corporate tax rate from 22% to 13% in 2016, while avoiding repatriation taxes on revenues accrued outside the U.S. – but AbbVie continued to assert that it was not motivated primarily by an accounting rationale, but also by an opportunity to diversify into rare diseases.

"The new company will be a larger, more diversified company with significant financial capacity for future strategic investment," Gonzalez said on the July 18 call. "I have been impressed by the strategic alignment between our two companies, which certainly reinforces my view that AbbVie and Shire represent a strong and compelling fit. We have a number of complementary strengths, which we will leverage to create an enhanced, strongly capitalized platform across research and development, manufacturing, and sales and marketing."

The new company will enjoy leadership positions in therapeutic sectors such as immunology, rare diseases, neuroscience, metabolic disease, hepatitis C, oncology and ophthalmology, he said. It also diversifies a company that has been over-reliant on immunology blockbuster Humira (adalimumab), which accounts for roughly 60% of AbbVie net sales.

Overcoming Declining Sales Of Humira

While AbbVie management has not given much outlook on potential synergies resulting from the deal, UBS Investment Research analyst Marc Goodman projected in a July 18 note that the pharma could realize savings of \$400 million by 2016.

Meanwhile, adding Shire's portfolio and pipeline to its own can drive AbbVie from being an \$18.8 billion net-sales earner in 2013 to \$27.1 billion in 2020, he estimated. Current Shire drugs and pipeline candidates would contribute nearly \$7.7 billion to that total in 2020 under the UBS modeling.

New revenue sources will be crucial because unlike some its big pharma brethren that already have gone through the worst of their patent cliffs, much of AbbVie's is yet to come, as Humira goes off patent in 2016. Goodman expects that the antibody product's sales erosion will be slow at first, but that revenue will slip from a peak of \$14.4 billion in net sales in 2016 to \$6.7 billion in 2020.

Nothing in the current AbbVie portfolio will make up for that loss, and with other patent expiries, Goodman projects that while the portfolio will yield sales of \$18.5 billion this year, those drugs

alone will garner just \$10.8 billion in 2020. Fortunately, AbbVie's three-drug hepatitis C regimen, now under FDA review, is expected to be a big seller ("Eye-Opening Phase III Data For AbbVie's HCV Combo Suggest A Tightened Race" — "The Pink Sheet" DAILY, Jan. 31, 2014). Goodman projects the HCV combo will earn just-below peak sales of \$2.5 billion in 2020, while other Phase III pipeline assets, including the GnRH antagonist elagolix, will bring home about \$1 billion combined that year.

But Shire's five-drug rare diseases portfolio will continue incremental sales increases between 2014 and 2020, he estimates, yielding just over \$3 billion combined in 2020. A drug-delivery partnership Shire signed with ArmaGen Technologies Inc. on July 23 may enable the Hunter syndrome drug to cross the blood-brain barrier, improving its efficacy ("Shire Collaboration Brings Validation To ArmaGen's Drug-Delivery Technology" — "The Pink Sheet" DAILY, Jul. 23, 2014). ADHD stalwart Vyvanse (lisdexamfetamine) will remain legacy-Shire's top seller, reaching \$2.6 billion in 2020, he added, with current Shire pipeline assets producing another \$1.3 billion in sales. Principal among those pipeline candidates is the dry-eye candidate lifitegrast ("Shire Course Corrects Lifitegrast And Eyes Ophthalmology Prospects" — "The Pink Sheet" DAILY, May 20, 2014).

Although the merger is yet to close, none of the analysts interviewed by "The Pink Sheet" see any significant obstacles standing in the transaction's way. Both groups of shareholders should be pleased with the terms, no white knight is expected to materialize seeking Shire's hand and potential U.S. tax legislation changing the rules for tax-inversion deals is unlikely to be enacted in time to derail AbbVie's strategy, they said.

"We view the deal as a high probability," Quenneville said. "I think the major wildcard, and it's a low-probability event, is if there is a major change in the U.S. rules allowing companies to invert. Legislatively, it would have to move through very quickly before the deal closes, which I think is highly unlikely, given the current state of politics here. I think there's an even lower probability, if something gets done, of [the legislation] being retroactive."