Acorda Therapeutics has entered into an agreement to acquire privately-held biopharmaceutical company Civitas Therapeutics for $525 million in cash. Acorda will obtain worldwide rights to CVT-301, a Phase 3 treatment candidate for OFF episodes of Parkinson’s disease (PD). The acquisition also includes rights to Civitas’ proprietary ARCUS™ pulmonary delivery technology and manufacturing facility with commercial-scale capabilities based in Chelsea, MA.

“This acquisition marks a great day for Acorda and Civitas,” said Acorda’s President and CEO Ron Cohen, MD. “The acquisition adds an exciting product candidate to Acorda’s pipeline that addresses a significant unmet need in Parkinson’s disease. It also leverages Acorda’s existing development and commercial capabilities and creates an opportunity for us to develop a global presence. In addition, Civitas’ ARCUS technology adds a proprietary platform with the potential for future development opportunities.”

“CVT-301 is a potentially transformative therapy for people with Parkinson’s disease to rapidly and predictably treat OFF episodes,” Dr. Cohen added. “Strongly positive data from a recent Phase 2b trial, together with a clearly defined regulatory pathway and extensive IP protection, make this a compelling opportunity, with estimated U.S. sales expected to exceed $500 million.”

Of the total consideration, $35 million will be used to pay costs related to a Civitas change-in-control. Subject to customary closing conditions, the acquisition is expected to be completed in the fourth quarter of 2014.

Read about Acorda’s investigational remyelinating agent rHIgM22 in “In the Pipeline” on p. 46.

FDA APPROVES MOVANTIK FOR OPIOID-INDUCED CONSTIPATION

FDA approved Movantik (naloxegol, Astra-Zeneca), an oral treatment for opioid-induced constipation in adults with chronic non-cancer pain. Movantik is peripherally acting opioid receptor antagonist.

Movantik’s safety and effectiveness were established in two clinical trials of 1,352 participants who had taken opioids for at least four weeks for non-cancer related pain and had opioid-induced constipation. Participants were randomly assigned to receive 12.5mg or 25mg of Movantik or placebo once daily for 12 weeks. The trials were designed to measure the change in the number of bowel movements per week from the start of the study.

In the first trial 44 percent of participants receiving 25mg of Movantik and 41 percent of participants receiving 12.5mg of Movantik experienced an increase in bowel movements per week, compared to 29 percent of participants receiving placebo. The second trial showed similar results.

Common side effects of Movantik include abdominal pain, diarrhea, headache and the experience of excessive gas in the stomach or intestinal area (flatulence).

The Agency is requiring a post-marketing study to further evaluate the potential risk of cardiovascular adverse events in patients taking Movantik. In June, FDA held a public meeting to discuss what studies might be required to assess the cardiac safety of peripherally acting opioid receptor antagonists, including Movantik, intended to treat opioid-induced constipation.

FDA GREEN-LIGHTS WRIST DEVICE FOR ASSESSMENT OF PARKINSON’S SYMPTOMS

FDA has cleared the marketing of the Personal KinetiGraph (PKG, Global Kinetics Corporation) tech-
Migraine in Middle Age Linked to Increased Risk of PD, Movement Disorders Later

People who experience migraine in middle age may be more likely to develop Parkinson’s disease, or other movement disorders later in life, a new study suggests. Those who have migraine with aura may be at double the risk of developing Parkinson’s, according to the study published online in Neurology (September 2014).

The study followed 5,620 people between the ages of 33 and 65 for 25 years. At the beginning of the study, a total of 3,924 of the participants had no headaches, 1,028 had headaches with no migraine symptoms, 238 had migraine with no aura and 430 had migraine with aura. Later, the investigators assessed whether the participants had any symptoms of Parkinson’s or had been diagnosed with Parkinson’s or had symptoms of restless legs syndrome (RLS)(also known as Willis-Ekbom disease).

The study found that people with migraine with aura were more than twice as likely to be diagnosed with Parkinson’s than people with no headaches. A total of 2.4 percent of those with migraine with aura had the disease, compared to 1.1 percent of those with no headaches. People with migraine with aura had 3.6 the odds of reporting at least four of six parkinsonian symptoms, while those with migraine with no aura had 2.3 times the odds of these symptoms. Overall, 19.7 percent of those with migraine with aura had symptoms, compared to 12.6 percent of those with migraine with no aura and 7.5 percent of those with no headaches. Women with migraine with aura were also more likely to have a family history of Parkinson’s disease compared to those with no headaches.

Plegridy Two-Year Data Confirm Maintenance of Efficacy and Safety

Biogen presented new data from the second year of its Phase III ADVANCE clinical trial that show the positive treatment effects of Plegidy (peginterferon beta-1a) were maintained in people with relapsing forms of multiple sclerosis (RMS) beyond the first year of the study. Results were presented at the sixth Triennial Joint Meeting of the Americas Committee for Treatment and Research in Multiple Sclerosis and the European Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS-ECTRIMS).

Post-hoc analyses from the two-year, Phase III ADVANCE clinical trial confirm that Plegidy’s positive effects on reducing disease activity and disability progression were maintained in year two of the study. A significantly higher proportion of patients taking Plegidy during both years of the study experienced no evidence of disease activity (NEDA)—defined as the absence of clinical and MRI disease activity over two years of treatment—compared to those who switched to Plegidy from placebo. Also, those treated with Plegidy for both years of the study had significant reductions in the risk of 24-week confirmed disability progression compared to patients treated with placebo during the first year.

In addition, new data from the second year of ADVANCE show that patients who took Plegidy throughout the study experienced statistically significant improvements in clinical and MRI outcomes—including annualized relapse rate (ARR), risk of relapse, risk of 24-week confirmed disability progression, and number of brain lesions—when compared to those who switched to Plegidy after taking placebo for the first year. This new data also showed that the safety profile of Plegidy was consistent between years one and two of the study.

Lemtrada (Alemtuzumab) Shows Positive Interim Results

Genzyme presented positive interim results from the second year of the extension study of Lemtrada (alemtuzumab) for multiple sclerosis at ACTRIMS-ECTRIMS.

THERAPEUTIC UPDATE

Technology designed to improve the assessment and monitoring of symptoms of Parkinson’s disease and other neurological disorders that affect movement.

The Personal KinetiGraph is a wrist-worn device that automatically records motion data over a period of up to ten days. The physician then receives detailed information about the patient’s mobility within minutes, identifying changes and trends that can be important considerations in the diagnosis and treatment of Parkinson’s disease. The device can also alert patients when it is time to take medication as prescribed and track when medication is taken to help improve treatment compliance.
In this analysis, relapse rates and sustained accumulation of disability remained low among patients who had previously received Lemtrada in either of the Phase III CARE-MS I and CARE-MS II studies. In these studies, Lemtrada was given as two annual courses, at the start of the study and 12 months later. Approximately 70% of patients who received Lemtrada in the studies did not receive further treatment with Lemtrada through the second year of the extension study. No new safety signals were identified.

The Phase III trials of Lemtrada were randomized, two-year pivotal studies comparing treatment with Lemtrada to high-dose subcutaneous interferon beta-1a (Rebif) in patients with relapsing-remitting multiple sclerosis who had active disease and were either new to treatment (CARE-MS I) or who had relapsed while on prior therapy (CARE-MS II).

More than 90% of the patients who were treated with Lemtrada in the Phase III trials enrolled in the extension study. These patients were eligible to receive additional treatment with Lemtrada in the extension study if they experienced at least one relapse or at least two new or enlarging brain or spinal cord lesions.

Pre-Injury Migraines Have No Effect In Post-Concussion Athletes

Preinjury migraine headaches do not appear to contribute to greater neurocognitive declines following a concussion, new findings show. A study in Athletic Training & Sports Health Care (September 16) compared outcomes between athletes with and without a history of preinjury migraine headaches. The study sought to examine the effect of preinjury migraine on neurocognitive performance and concussion symptomatology in athletes with concussion.

“I was somewhat surprising that there were no cognitive declines following a concussion in the pre-injury migraine group,” said lead study author Tracey Covassin PhD, and associate professor at Michigan State University in an interview with Practical Neurology™. “However, the study needs to be replicated with a larger sample size and more detail on migraines need to be obtained before really any conclusions can be drawn from one study.”

A total of 154 concussed athletes with (n=77) and without (n=77) a self-reported history of preinjury migraine headaches completed a neurocognitive test at baseline and at 3 and 9 days post-concussion. No differences were noted for interaction between time and preinjury migraine groups on verbal memory (P=.12), visual memory (P=.53), motor processing speed (P=.38), or reaction time (P=.97). A significant interaction was noted between time and the preinjury migraine group for the migraine-cognitive-fatigue (P=.029) and somatic symptom (P=.006) clusters.

“The latest concussion position statement suggests that migraines are considered a ‘modifier’ in the assessment and treatment of sport-related concussion,” Dr. Covassin said. “However, there is no direct research on sport-related concussed athletes to relate the current study to in regards to pre-injury migraines.”

Fishy Proposition For Seizure Treatment

A new study by researchers at the UCLA School of Medicine suggests that for epilepsy patients, improvement might come in the form of a few capsules of fish oil. The small randomized controlled study, published in September in the Journal of Neurology Neurosurgery & Psychiatry, shows that low doses of omega-3 fatty acids may help decrease the frequency of epileptic seizures when drug treatment no longer works.

In the study, around 1080mg of omega-3 fatty acids were found to significantly reduce the incidence of seizures in patients with so-called drug-resistant epilepsy.

The finding comes in contrast to previous studies using high doses of omega-3s that showed no clear beneficial effects. Those earlier, negative results were somewhat surprising because omega-3 fatty acids have been shown to cross into the central nervous system and to block calcium and sodium channels in nerve cells, thus preventing the repetitive firing of the cells that characterizes seizure.

“The blockade of these channels—especially sodium channels—is the basis for many antiepileptic drugs, like lamotrigine, lacosamide, and carbamazepine,” said Christopher DeGiorgio, a professor of neurology and the principal investigator of the new study.

The trial included 24 patients with epilepsy that could not be controlled by drug treatment. During the course of the study, each patient received three 10-week treatments, spaced 6 weeks apart: a low-dose fish oil regimen that consisted of three capsules of fish oil per day (equivalent to 1080mg of fish oil) plus three capsules of a corn oil placebo; a high-dose fish oil regimen of six capsules (2160 mg) per day; and a placebo regimen, consisting of six capsules of corn oil per day.

In patients taking low-dose fish oil, the average number of seizures decreased by 33.6 percent compared to the placebo.
group, from an average of just over 18 seizures per month to around 12 per month. Two patients on low-dose fish oil were completely seizure-free during the 10-week treatments. The high dose of fish oil, however, produced no significant decrease in seizure frequency. In addition, no patients taking the high dose—or the placebo—were seizure free.

**Potassium-Rich Foods Cut Stroke, Death Risks Among Older Women**

Postmenopausal women who eat foods higher in potassium are less likely to have strokes and die than women who eat less potassium-rich foods, suggests new research in the journal *Stroke*.

Researchers studied 90,137 postmenopausal women, ages 50 to 79, for an average 11 years. Women in the study were stroke-free at the start and their average dietary potassium intake was 2,611 mg/day. Results of this study are based on potassium from food, not supplements.

The researchers found:

- Women who ate the most potassium were 12 percent less likely to suffer stroke in general and 16 percent less likely to suffer an ischemic stroke than women who ate the least.
- Women who ate the most potassium were 10 percent less likely to die than those who ate the least.
- Among women who did not have hypertension (whose blood pressure was normal and they were not on any medications for high blood pressure), those who ate the most potassium had a 27 percent lower ischemic stroke risk and 21 percent reduced risk for all stroke types, compared to women who ate the least potassium in their daily diets.
- Among women with hypertension, those who ate the most potassium had a lower risk of death, but potassium intake did not lower their stroke risk.
- Researchers suggested that higher dietary potassium intake may be more beneficial before high blood pressure develops. They also said there was no evidence of any association between potassium intake and hemorrhagic stroke, which could be related to the low number of hemorrhagic strokes in the study.

**New Alzheimer’s Treatment Begins Testing**

A non-invasive, neuromodulatory approach to fighting Alzheimer’s is being tested in aged primates after its safety was proven in earlier results in mice.

Transcranial Electromagnetic Treatment (TEMT) is under development by NeuroEM Therapeutics, Inc., and according to Gary Arendash, President and CEO of the company, the primates make good test subjects due to their similarity to humans in brain structure and function.

“Aged primates (Rhesus monkeys) develop the same abnormal amyloid deposits in their brains as Alzheimer’s patients and they also become cognitively impaired during aging,” Dr. Arendash said. He and his colleagues had previously found that their TEMT technology reverses both Alzheimer’s brain pathology and severe memory impairment in aged Alzheimer’s mice. These mice had been genetically modified to produce human amyloid deposits.

For the study, researchers are administering TEMT to aged primates over several months while monitoring cognitive performance and brain function. TEMT has two ways it attacks the Alzheimer’s disease process. First, it disaggregates amyloid plaques both inside and outside of brain cells. Secondly, it increases brain metabolism by enhancing mitochondrial function.

“If our collaborative primate study is successful, clinical trials with TEMT administration to Alzheimer’s patients could begin by next summer,” indicated Dr. Arendash. “NeuroEM Therapeutics has a projected time line to commercialize its medical device of under 5 years, which is much faster than for an Alzheimer’s drug,” said Dr. Arendash.

**Thrombectomy Device OK’d in Asia**

Codman Neuro, part of DePuy Synthes Companies of Johnson & Johnson, received regulatory approval from the China Food and Drug Administration (CFDA), South Korea’s Ministry of Food and Drug Safety (MFDS), and the Taiwan Food and Drug Administration (TFDA) for the company’s REVIVE™ SE Thrombectomy Device, a next-generation self-expanding clot removal device intended to restore blood flow in patients with acute ischemic stroke secondary to intracranial occlusive vessel disease.

The REVIVE SE Device is designed to ease navigation through small and tortuous blood vessels and arteries in the cerebral vasculature. The new device enables rapid restoration of blood flow to the brain during an acute ischemic stroke.