

## Revimmune: Delivering a Knockout Punch to Autoimmune Diseases

By: Douglas Kerr, MD, PhD, and Adam Kaplin, MD, PhD

### Introduction

Autoimmune diseases are the third most common category of disease in the United States after cancer and heart disease, affecting approximately 5% to 8% of the population or 14 to 22 million people.<sup>1</sup> There are 80 recognized autoimmune diseases, and nearly three-fourths of those affected are women. Among the most prevalent autoimmune diseases are lupus, type I diabetes, scleroderma, multiple sclerosis (MS), Crohn's disease, chronic active hepatitis, rheumatoid arthritis, Graves' disease, myasthenia gravis, myositis, antiphospholipid syndrome (APS), Sjogren's syndrome, uveitis, polymyositis, Raynaud's phenomenon, and demyelinating neuropathies.

Autoimmune diseases occur when the body's immune system no longer differentiates between "self" and "other," meaning the immune system cells begin

attacking various organs and tissues. In the case of type I diabetes, the target tissues are insulin-producing islet cells in the pancreas; in lupus, it is connective tissues and sometimes major organs.

### Conventional Treatment

In recent years, more than 30 neurologic diseases have been recognized either to be caused primarily by autoimmune mechanisms or to have important autoimmune components. Although many of these diseases can be treated clinically by currently available conventional immunosuppressive regimens, important problems remain. Some patients are refractory to standard immunotherapy, and others respond only partially. In nearly all cases,

immunotherapy must be continued indefinitely, maintaining an impaired immune system, and often resulting in cumulative adverse side effects. Despite this, the vast majority of patients on conventional immunomodulatory treatment for MS continue to accrue disability.

Depending on the disease, immunomodulating treatments for autoimmune disease fall far short of the goals of safe, long-term relief and acceptable quality of life for many patients. Therapies must be administered chronically, from several times a day to every few weeks, for life. Many of these treatments are quite expensive, in the range of \$30,000 per year.

### Potential Treatment

A potential treatment for autoimmune diseases is Revimmune™, which includes high-dose cyclophosphamide. Revimmune, a patent-pending pharmaceutical treatment in late-stage development for a variety of autoimmune diseases, is a potential treatment option for severe, refractory, immune-mediated illnesses, such as MS. Revimmune uses an ultra-high intensity, short-course of an intravenous

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formulation of cyclophosphamide to “reboot” a patient’s immune system, thereby eliminating the autoimmunity.

Revimmune temporarily eliminates peripheral immune cells, including the immune cells causing the autoimmunity, while selectively sparing the stem cells in the bone marrow, which are subsequently able to repopulate the body with a nascent immune system. By inducing immunoablation and subsequent immune reconstitution, Revimmune eliminates or reduces dependence on chronic immunosuppressive therapies, which are potentially more toxic, carcinogenic, inadequate, inconvenient, and very expensive, especially in the case of monoclonal antibodies. Revimmune’s use would also obviate the risk and expense of allogeneic (donor) stem cell transplantation to treat severe cases of autoimmune diseases.

Accentia Biopharmaceuticals, Inc. has acquired the exclusive worldwide rights for Revimmune. Based on long-term follow-up showing durable remissions, there is substantial evidence that Revimmune has the potential to cure cases of severe refractory autoimmune diseases, such as aplastic anemia and myasthenia gravis. To date, more than 175 patients, mostly those with severe refractory autoimmune diseases, have been treated with Revimmune. The company believes that Revimmune is a “platform” technology that can be used in any autoimmune disease.

Revimmune is administered as an in-patient or outpatient infusion for 4 hours per day for 4 consecutive days. Patients can recover at home while their

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immune system reconstitutes itself during a 2- to 3-week period.

Revimmune includes a risk management program to enhance patient safety by ensuring appropriate patient selection, supportive care, and tracking of outcomes data, which could be critical to reimbursement coverage and malpractice protection for healthcare providers.

Developed by Dr. Richard Jones, Dr. Robert Brodsky, and colleagues at the Johns Hopkins University School of Medicine, Revimmune works by temporarily eliminating peripheral immune cells responsible for autoimmunity, while selectively sparing the stem cells in the bone marrow.

Investigators at Hopkins discovered that stem cells possess high levels of a protective enzyme that makes them impervious to Revimmune. Over the course of 2 to 3 weeks after treatment, these stem cells produce a new, improved immune system. Newly reconstituted peripheral immune system cells lack the misdirected immunity to self-antigens, which is characteristic of autoimmune diseases.

The principal investigator for the ongoing Revimmune MS study at the

Johns Hopkins University School of Medicine is Douglas Kerr, MD, PhD. In a follow-up of up to 2 years, most patients have shown substantial improvement and many have a complete elimination of signs of the disease. The co-principal investigators on this study are Dr. Daniel Drachman and Dr. Robert Brodsky.

“Revimmune offers the hope of sustained remissions and cures for autoimmune diseases, says Frank E. O’Donnell, Jr., MD, Chairman and CEO of Accentia. “Moreover, it eliminates the dependence on chronic immunosuppressive therapies, which are toxic, carcinogenic, inconvenient, not very effective, and in the case of monoclonal antibodies, quite expensive.”

Accentia is preparing an IND application for Revimmune for severe refractory MS, and is proposing to enter a Phase III clinical trial to support licensure under the abbreviated 505(b)(2) regulatory pathway. According to the National Multiple Sclerosis Society ([www.nationalmssociety.org](http://www.nationalmssociety.org)), approximately 400,000 people in the US suffer from the disease, 85% of whom are classified within the “relapsing-remitting” category, meaning that

symptoms wax and wane over time, with the overall trend toward worsening symptoms.<sup>2</sup> Two published studies of Revimmune in 20 MS patients found a reduction or elimination of new and enhancing lesions in all patients.<sup>3,4</sup> Furthermore, no patient experienced a clinical exacerbation following treatment, and most showed reductions or stabilization of clinical markers for the disease. In clinical studies, the drug regimen improves function in most patients and stops progression in over 90% of cases refractory to standard therapies.

## The Company

Accentia Biopharmaceuticals specializes in development of late-stage under-utilized drug products, in particular, approved medicines in new formulations and/or for new, patentable indications. The company's lead respiratory product candidate, SinuNase™, is currently in clinical development for treating chronic sinusitis (rhinosinusitis). SinuNase, a novel application and formulation of a known anti-fungal compound licensed from the Mayo Foundation for Medical Education and Research, has been fast-tracked by the FDA and is now in Phase III clinical trials. Accentia's other lead product, BiovaxID™, a patient-specific anti-cancer vaccine for treating non-Hodgkin's lymphoma, has also received FDA fast-track status and is in Phase III testing. ■

## References

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Dr. Douglas Kerr earned his MD and PhD from Jefferson Medical College at Thomas Jefferson University in Philadelphia. He then completed an internship in Medicine at The Graduate Hospital, also in Philadelphia. He went on to complete his residency in Neurology at The Johns Hopkins Hospital in Baltimore. Now an Associate Professor of Neurology at Johns Hopkins, Dr. Kerr serves as the Director of the Transverse Myelitis Center, focusing on comprehensive evaluation of TM. His research strives to determine the causes of TM and develop new treatment options. Dr. Kerr further focuses on stem cells as a tool for functional recovery in patients with TM and motor neuron diseases.



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Dr. Adam Kaplin graduated Magna Cum Laude from Yale University before earning his MD and PhD from The Johns Hopkins School of Medicine, where he was a Medical Science Training Program awardee. He went on to complete an internship in Internal Medicine at Johns Hopkins Bayview Medical Center and a residency in Psychiatry at Johns Hopkins Hospital, where he served as the Chief Resident of Psychiatry. Now an Assistant Professor of Psychiatry at Johns Hopkins, Dr. Kaplin focuses on the psychiatric complications of neurological diseases. He researches the immune-mediated mechanisms of depression and cognitive impairment in transverse myelitis, multiple sclerosis, and related autoimmune neurologic disorders, and the role of cytokines in these processes.

Dr. Kaplin is on the Board of Medical Advisors to the Transverse Myelitis Association (TMA) and the Montel Williams MS Foundation.