



OPEXA THERAPEUTICS

## Opexa Therapeutics

NASDAQ: OPXA  
52 wk: \$0.50-1.83  
May 15: \$0.55  
Mkt Cap: \$12.7MM

Cash: \$4.7MM  
Debt: \$0 MM  
Shares Outstd: 23 MM

Founded: 2003  
Employees: 25



Neil K. Warma,  
President & CEO,  
Director

Jaye Thompson, Ph.D.  
Senior Vice President of  
Clinical Development and  
Regulatory Affairs

Donna R. Rill  
Senior Vice President of  
Operations & Quality Systems

Don Healey, Ph.D.  
Vice President of Scientific  
Development & Manufacturing

John Ginzler, VP Finance

For more information, see  
profile on [OMP global  
database](#).

[CEO interview](#)

*NOTE: This summary was produced by OneMedPlace (OMP). Research based on information provided by the company and other sources. The mission of OMP Research is to identify promising investment opportunities in healthcare and life sciences*

## Could It Be the First Immunotherapy for Multiple Sclerosis?

**Rationale to follow OPXA:** The OPXA story is a marriage of two well-established concepts in biology --(i) Dysregulated Myelin Proteins are key causative agents of multiple sclerosis (MS) and (ii) immunotherapy is a viable therapeutic option to target diseases that implicate a few select antigens/proteins. Scientists at OPXA hence hypothesize that an autologous immunotherapy that targets T-cells that destroy the myelin proteins in the brain could be a viable therapeutic modality for patients with MS.

The stock is cheap, as the company has used these past two years to restructure and optimize many of its processes, including the manufacturing of its T-cell therapy, and investors now await the initiation of the upcoming phase II proof of principle trial in secondary progressive MS. Yet, with a huge addressable market dominated by big pharma companies, it is safe to say that should the phase II be successful, OPXA would likely be acquired. Many pharma companies want to enter the immunotherapy space and OPXA offers a plug-and-play technology that is procedurally simpler than current immunotherapies in the market/in development.

**Market opportunity:** Secondary progressive multiple sclerosis, the most advanced form of MS, affects more than 1 million people worldwide. Of the 400,000 cases of MS diagnosed each year in the United States, approximately half meet the diagnosis criteria of secondary progressive. Current MS therapies generate almost \$9B sales annually, and the market is expected to reach \$15B by 2015. The only current FDA-approved treatment for secondary progressive MS carries a "black box warning".

**Background:** Opexa Therapeutics is a biopharmaceutical company that is based on a technology platform that was originally created by Baylor School of Medicine and then in-licensed by OPXA in 2001. Their lead candidate Tcelna™ (formerly Tovaxin), is a patient-derived, hence patient-specific "concentrated" preparation of activated but attenuated myelin reactive T cells (MRTCs). Each subcutaneous (SC) dose of Tcelna contains 30-45 million such cells. This high dose of MRTCs "fools" the human immune system to mount a powerful dominant negative "regulatory T-cell response" against all MRTCs in general in this MS patient.

MRTCs are an established culprit (causative agent) for MS--they can migrate past the blood brain barrier into the central nervous system (CNS), where they "erroneously" trigger a signaling cascade that results in the destruction of the myelin sheath that protects human nerves. Simply put, MS is a demyelination disease of the CNS where the absence of the myelin sheath (by MRTC attacks) leads to synaptic "short-circuits". By abrogating these MRTCs, Tcelna can potentially stop myelin destruction and decelerate the pace of MS progression.

### **KEYPOINTS:**

**Tcelna is specific for each patient's own MS profile:** Scientists at OPXA believe that Tcelna can become a first-line treatment for every patient with MS, irrespective of what other treatment he or she is currently on or has formerly received. To be treated with Tcelna a candidate will undergo an initial blood draw of 120 ml at their neurologist's office which will be used to perform "epitope mapping". This is a proprietary procedure conducted at Opexa that screens for 109 different peptides that comprise the 3 key myelin proteins; MRTCs in the given MS patient's blood will selectively migrate towards only a few of these 109 peptides. We extrapolate that these must be the same peptides a given patient's MRTCs must be attacking inside the body. Over 99% of MS causing MRTCs are known to target one or more of these 109 myelin proteins and by identifying each patient's own culprit, Tcelna is a specific agent for that patient.

Once the predominant MS peptides have been identified, the patient now has to go to their nearest American Red Cross or Blood Group Alliance center where he or she will "donate" up to 450ml of blood. This bag of blood is couriered overnight to Opexa (Texas) where the T-lymphocytes are isolated and then clonally expanded in the presence of the predominant (up to 6) myelin peptides identified by epitope mapping. This gives the "bad" MRTCs a survival advantage such that up to 6 different pure MRTC cell-lines can be prepared per patient. Unlike with other known immunotherapies, each patient's cell lines have to be cultured only once and cryo-preserved until use. Patients are treated with 5 bolus doses of Tcelna administered subcutaneously-once monthly for the first four doses and then a booster dose 2 months after the 4th injection. Prior to administration, Opexa scientists thaw out vial(s) of Tcelna, irradiate to inactivate the MRTCs and courier overnight to the neurologist for administration.

**Tcelna is selective for the *in-vivo* immune response it triggers:** Tcelna, Opexa's therapy, selectively targets only the pathogenic T-cells and does not impact the entire T-cell population like many other MS drugs. Therefore, side effects of Tcelna are minimal. Irradiation of the MRTC prior to injection renders them



unable to replicate and triggers their apoptosis. They do, however, remain present long enough to educate and prime the T regs and other immune cells enabling them to selectively identify and downregulate the pathogenic cells. Signaling cascades working thru the Foxp3+ and Tr1 regulatory cells quickly learn what the "bad players" look like and can now eliminate identical disease-causing MRTCs that are circulating in that patient's bloodstream. It is hypothesized that by reducing the MRTCs' load in the bloodstream, the destruction of myelin and the progression of MS can be slowed--and this effect can be measured in clinical trials using imaging endpoints like reduction in whole-brain atrophy and "outcomes" endpoints like reduction in the annual relapse rate (ARR) and disease progression.

**What clinical trials reveal to date:** Under its previous management team, Opexa has run five phase I or II clinical trials-where a total of 196 patients with MS have been treated. All the patients presented with either the entry stage- relapsing-remitting MS (RRMS) or a more advanced form called Secondary Progressive MS (SPMS). Across all five trials, Tcelna therapy has been safe and well-tolerated, with no deaths or serious adverse events on therapy. Mild to moderate, but self-resolving injection site reactions have been reported.

While the initial phase I studies established dose (30-45 million MRTCs/injection) and schedule (q30d x 4, then 1 booster dose at month 6), the phase II trials demonstrated emergent signs of efficacy. In a phase IIb placebo controlled study trial of 150 RRMS patients Tcelna treated patients demonstrated a 37% reduction in ARR versus placebo (*statistical significance not reached*). With a 2-year follow-up, 77% of Tcelna patients remained relapse free, which is a very positive observation.

In a smaller cohort of patients from this study (N=50) who represented with more advanced disease (baseline ARR > 1), Tcelna demonstrated a more pronounced benefit-including a 56% improvement in ARR, and a 88% improvement in whole - brain atrophy. Also, improvement in MS disability (measured using the EDSS scale) reached statistical significance ( $p=0.05$ ) which is a high-bar given only 50 patients in this cohort. These results, taken together with results from other SPMS patients in phase I and in Baylor-run studies, warrant an exploration of Tcelna in SPMS.

While on one hand, the Tcelna results in SPMS are derived from retrospective analyses performed in small numbers of patients (small cohorts usually inflate results), the magnitude of benefit and statistical significance is undeniable. Also, the fact that most RRMS patients will eventually progress to SPMS and the world-wide prevalence of SPMS is > 1MM patients with only one approved agent, Novantrone (versus 7-10 agents for RRMS), creates a primed but untapped marketplace.

**New Management, New Vision, New Clinical Trials:** Under the leadership of CEO Neil Warma, and due to the immense pharma "interest" they have received, OPXA has decided to move to SPMS and start a phase II clinical trial for this indication. Should this be successful, every pharma company that has a presence in the RRMS marketplace will want to acquire OPXA to expand their offering to SPMS when their patients progress.

Although it presents as a stock-upsetting change of plans in the near-term, this "indication-shift" seems to be a carefully thought out clinical and commercial decision by Neil Warma's management team.

Pending a near-term capital raise to fund clinical development, the upcoming phase II U.S. and Canadian study will randomize 180 SPMS patients to receive either Tcelna or placebo (1:1). The dose and schedule for Tcelna remain unchanged. The primary endpoint of this study will be whole- brain atrophy at 2-years. Since slow onset agents like immunotherapies cannot alter the cumulative brain atrophy (demyelination) from previous years, a 2-year endpoint ensures enough time for Tcelna to be activated and elicit downstream beneficial effect after 6-months of therapy start. This trial will be 80% powered to demonstrate a 37.5% relative improvement assuming annual atrophy rate of 0.5 in the control subjects. The 88% atrophy improvement in the previous phase II suggests that the current expectation is fair and achievable.

**Manufacturing & Patents:** At its most basic level, the OPXA manufacturing process involved cell culture labs, scientists and incubators to generate the MRTC cell lines. For the upcoming phase II trial the drug production process has been optimized substantially and has been modified to a functionally closed system. OPXA will be ready to roll out a fully closed, automated system to produce Tcelna for commercial purposes. At its optimal output, this automated process should be able to generate 80-85% gross margins at current MS drug price levels.

OPXA has received composition of matter and method of use patents for Tcelna that are valid thru 2027. However, OMP research feels that for immunotherapy agents- process patents (product-by-process patents) provide for the most robust picket fence for their technology. Such a patent should be sought in parallel with FDA approval, so that the production trade secrets for Tcelna are not in the public domain before the drug is in the market.

### **2012 Catalysts**

- Financing deal to fund phase II trial initiation 1H2012
- Start of phase II study in SPMS 3Q2012