

OPEXA THERAPEUTICS, INC.

FORM 8-K (Current report filing)

Filed 03/24/14 for the Period Ending 03/24/14

Address	2635 TECHNOLOGY FOREST BLVD. THE WOODLANDS, TX 77381
Telephone	(281) 272-9331
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SIC Code	2834 - Pharmaceutical Preparations
Industry	Biotechnology & Drugs
Sector	Healthcare
Fiscal Year	12/31

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

**Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934**

Date of Report (date of earliest event reported): March 24, 2014

OPEXA THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Texas
(State or other jurisdiction of
incorporation)

001-33004
(Commission File Number)

76-0333165
(IRS Employer Identification No.)

2635 Technology Forest Blvd., The Woodlands, Texas
(Address of principal executive offices)

77381
(Zip Code)

Registrant's telephone number, including area code: **(281) 272-9331**
N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 - ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 - ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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Item 7.01 Regulation FD Disclosure

A copy of an investor slide presentation given by members of management of Opexa Therapeutics, Inc. (the “**Company**”) at an investor presentation on March 24, 2014 is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated hereby by reference. The presentation includes an overview of the Company’s ongoing clinical development program for Tcelna®, the Company’s lead therapy, in subjects with secondary progressive multiple sclerosis. The attached presentation will be made available on the Investor Relations page of the Company’s website at www.opexatherapeutics.com. The Company does not undertake to update this presentation.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
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99.1	Opexa Therapeutics, Inc. investor slide presentation.
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The information in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1, shall not be deemed “filed” for the purposes of Section 18 of the Securities Exchange Act of 1934 or otherwise subject to the liabilities under that Section, nor be deemed to be incorporated by reference into the filings of the registrant under the Securities Act of 1933.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Dated: March 24, 2014

OPEXA THERAPEUTICS, INC.

By: /s/ Neil K. Warma

Neil K. Warma

President & Chief Executive Officer

<u>Exhibit No.</u>	<u>Description</u>	<u>Exhibit Index</u>
99.1	Opexa Therapeutics, Inc. investor slide presentation.	



OPEXA THERAPEUTICS



Opexa Therapeutics, Inc.

NASDAQ: OPXA

March 2014
The Woodlands, TX

Forward-Looking Statements

- This investor presentation contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Statements contained in this presentation, other than statements of historical fact, constitute “forward-looking statements.” The words “expects,” “believes,” “anticipates,” “estimates,” “may,” “could,” “intends,” and similar expressions are intended to identify forward-looking statements. Forward-looking statements do not constitute guarantees of future performance. Investors are cautioned that statements which are not strictly historical statements, including, without limitation, statements regarding the development of our product candidate, Tcelna (imilecleucel-T), constitute forward-looking statements.
- Such forward-looking statements are subject to a number of risks and uncertainties that could cause actual results to differ materially from those anticipated. These risks and uncertainties include, but are not limited to, risks associated with: market conditions; our capital position; our ability to compete with larger, better financed pharmaceutical and biotechnology companies; new approaches to the treatment of our targeted diseases; our expectation of incurring continued losses; our uncertainty of developing a marketable product; our ability to raise additional capital to continue our development programs (including to undertake and complete any ongoing or further clinical studies for Tcelna); our ability to satisfy various conditions required to access the financing potentially available under the purchase agreements with Lincoln Park Capital Fund, LLC (“Lincoln Park”) or sell shares of our common stock to Lincoln Park or under our at-the-market (ATM) facility; our ability to maintain compliance with NASDAQ listing standards; the success of our clinical trials (including the Phase IIb trial for Tcelna in Secondary Progressive Multiple Sclerosis which, depending upon results, may determine whether Ares Trading SA (“Merck”) elects to exercise its option for an exclusive license to Tcelna for the treatment of multiple sclerosis (the “Option”)); whether Merck exercises the Option and, if so, whether we receive any development or commercialization milestone payments or royalties from Merck pursuant to the Option; our dependence (if Merck exercises the Option) on the resources and abilities of Merck for the further development of Tcelna; the efficacy of Tcelna for any particular indication; our ability to develop and commercialize products; our ability to obtain required regulatory approvals; our compliance with all FDA regulations; our ability to obtain, maintain and protect intellectual property rights; the risk of litigation regarding our intellectual property rights or the rights of third parties; the success of third party development and commercialization efforts with respect to products covered by intellectual property rights that we may license or transfer; our limited manufacturing capabilities; our dependence on third-party manufacturers; our ability to hire and retain skilled personnel; our volatile stock price; and other risks detailed in our filings with the SEC.
- These forward-looking statements speak only as of the date made. We assume no obligation or undertaking to update any forward-looking statements to reflect any changes in expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based. You should, however, review additional disclosures we make in our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K filed with the SEC.

Introduction to Opexa

- **Antigen specific T-cell immunotherapy platform**
 - Potential to address multiple therapeutic areas
 - Lower capital intensity by leveraging existing GMP manufacturing
 - Strong Patent Estate: 50 patents issued on T-cell platform (domestic and international)
- **Lead Program: Tcelna[®], in development for Multiple Sclerosis**
 - Phase IIb clinical trial in Secondary Progressive MS (SPMS)
 - Limited treatment options currently available for SPMS
 - Potential SPMS market in North America alone could exceed \$7 Billion
 - Fast Track designation from the U. S. Food and Drug Administration (FDA) for the treatment of SPMS
 - Option Agreement with Merck Serono, a strong potential commercial partner

Progress Update

- **Clinical**

- As of February 27, 2014, Opexa has randomized over 80% of the expected total number of patients in the Abili-T study in SPMS
- Expect completion of enrollment in Q2 2014
- Top line data expected in Mid 2016

- **Financial**

- As of December 31, 2013, Opexa had \$23.6 million in cash and cash equivalents
- Projected liquidity into Q4 2015, based on current operations and clinical activities

- **Management**

- Focused management team, recent addition of Tim Barabe and Dr. Hans-Peter Hartung to Opexa's Board of Directors, leading Scientific Advisory Board

Tcelna in Secondary Progressive MS

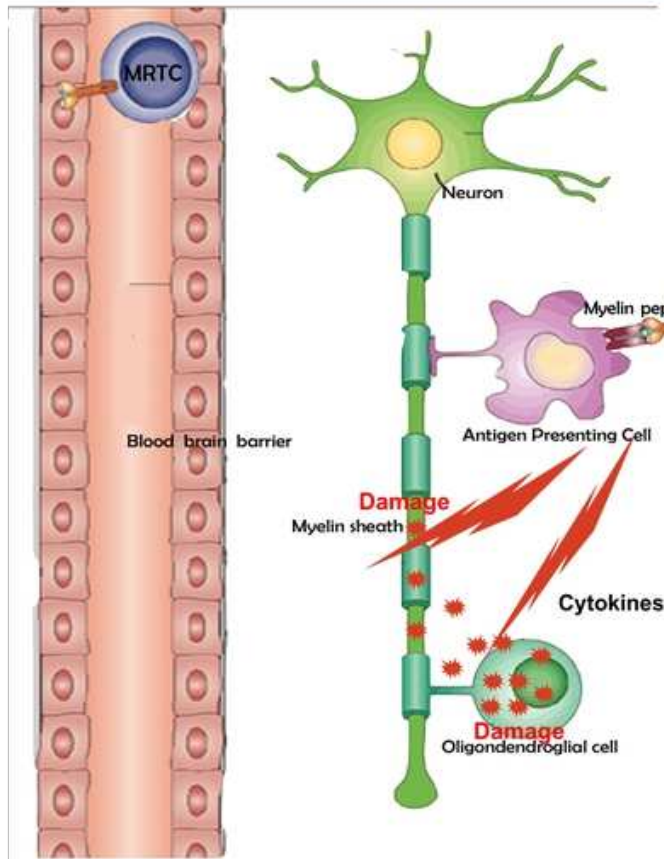
**450,000 Individuals in North America diagnosed with MS;
30-45 % potentially have an SPMS diagnosis**



- Potential SPMS market in North America alone could exceed **\$7 billion**
- Roughly 150,000 SPMS patients in North America
- Only one drug approved for SPMS in U.S. (none in EU or Asia)
 - Drug not suitable for chronic use due to severe side effects

Tcelna being developed to be a potential therapy of choice in SPMS

The Root Cause of Multiple Sclerosis: Activated T- cells Degrade Myelin and Damage Myelin Producing Cells



- In MS patients, the faulty immune system is not able to prevent the attack of a small sub-population of myelin reactive T-cells (MRTC)
- Myelin Reactive T-cells (MRTC) cross the blood brain barrier, enter the brain, and bind to antigen presenting cells (APC), causing a release of pro-inflammatory cytokines which lead to a two pronged attack through:
 1. Destruction of myelin sheath, the protective coating of nerve fibers
 2. Destruction of oligodendroglial cells, which are responsible for producing myelin

Result → Destruction of the myelin sheath and myelin producing cells, thereby preventing remyelination

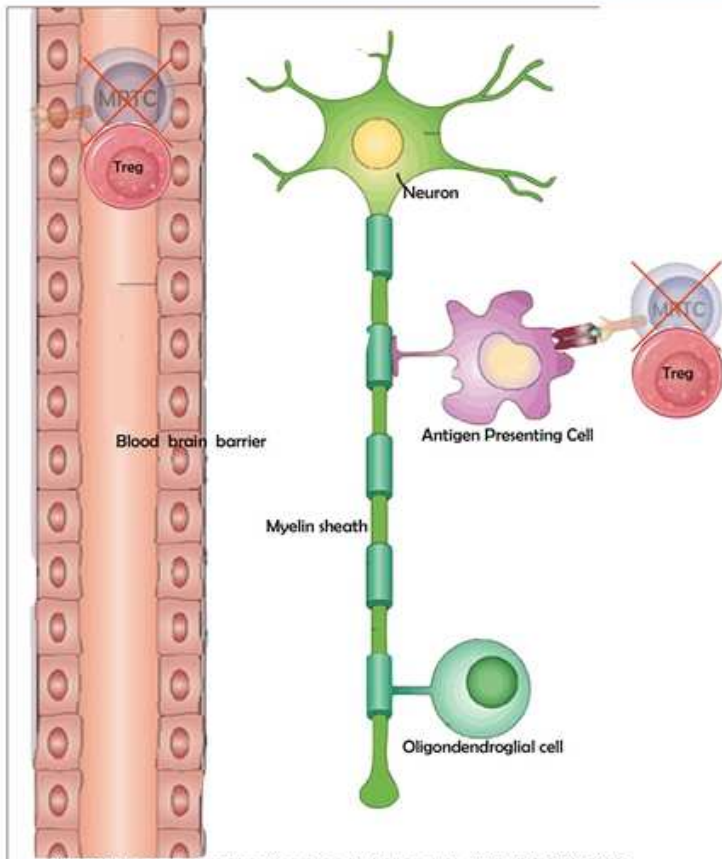
Tcelna[®] Consists of Attenuated Antigen Specific T-cell Clones



Tcelna: attenuated antigen specific T-cells

- Therapeutic dose of Tcelna (attenuated T-cell clones) is injected subcutaneously
- Immune system recognizes the large volume of cells (30-45 million) under the skin as potential foreign pathogens
- We believe Tcelna triggers an immune response specifically targeting circulating MRTC
- The irradiation of Tcelna prior to injection causes the injected cells to eventually die off, but only after they have primed the immune response

Tcelna Could Address the Root Cause of Multiple Sclerosis by Preventing Demyelination and Enabling Remyelination



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- Immune cells, including Tregs, have been primed, or sensitized, we believe, to specifically target the pathogenic MRTC for elimination or regulation
- Elimination of harmful MRTC may lead to:
 - Stabilization of disease by preventing further destruction of myelin
 - Improvement in condition by allowing Oligodendroglial cells to remyelinate axons (neuroprotection)

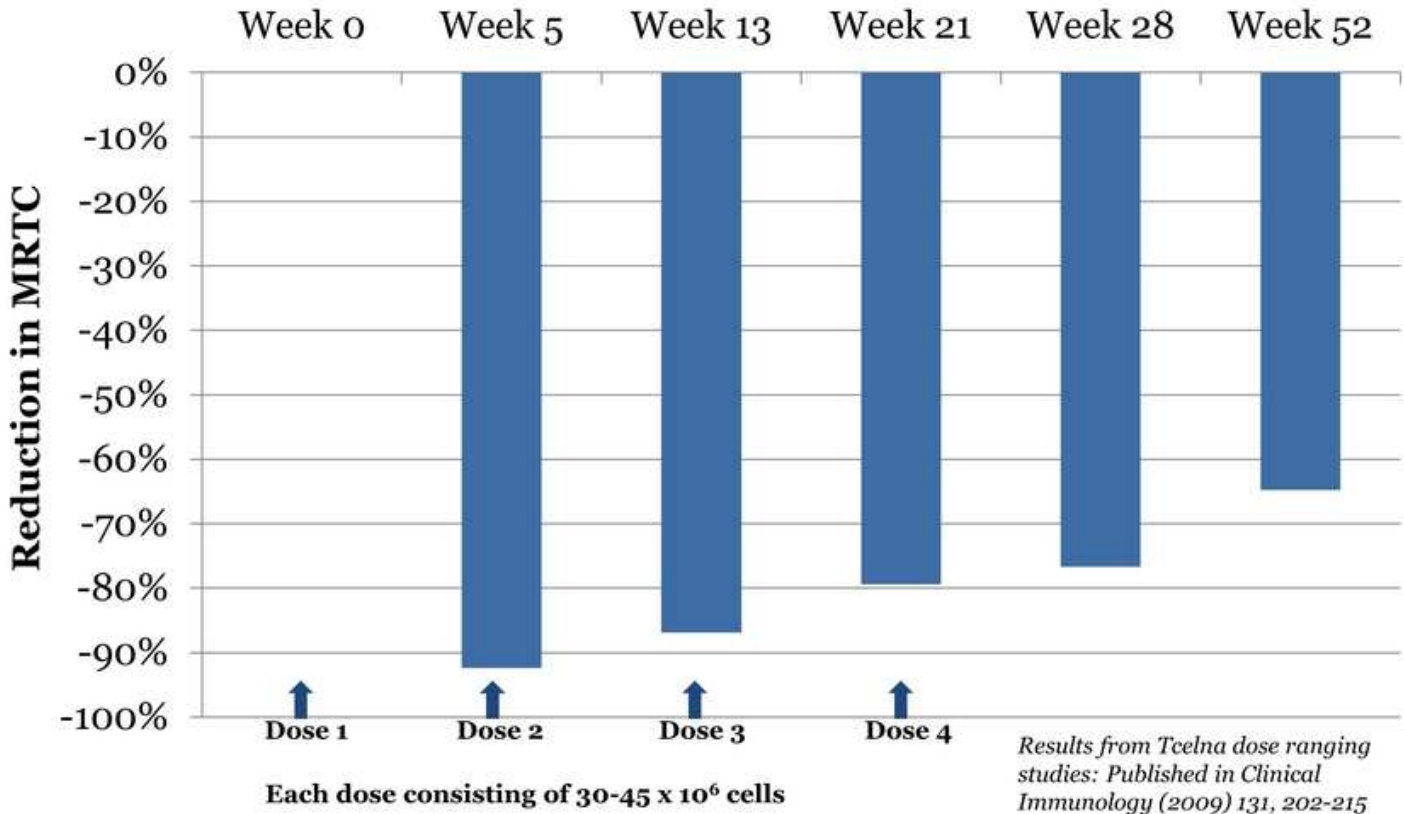
Opexa's Strategy

Tcelna programs the immune system to **specifically** recognize MRTC as pathogenic, thereby inhibiting further destruction of the myelin sheath and potentially enabling remyelination

Mechanism of Action

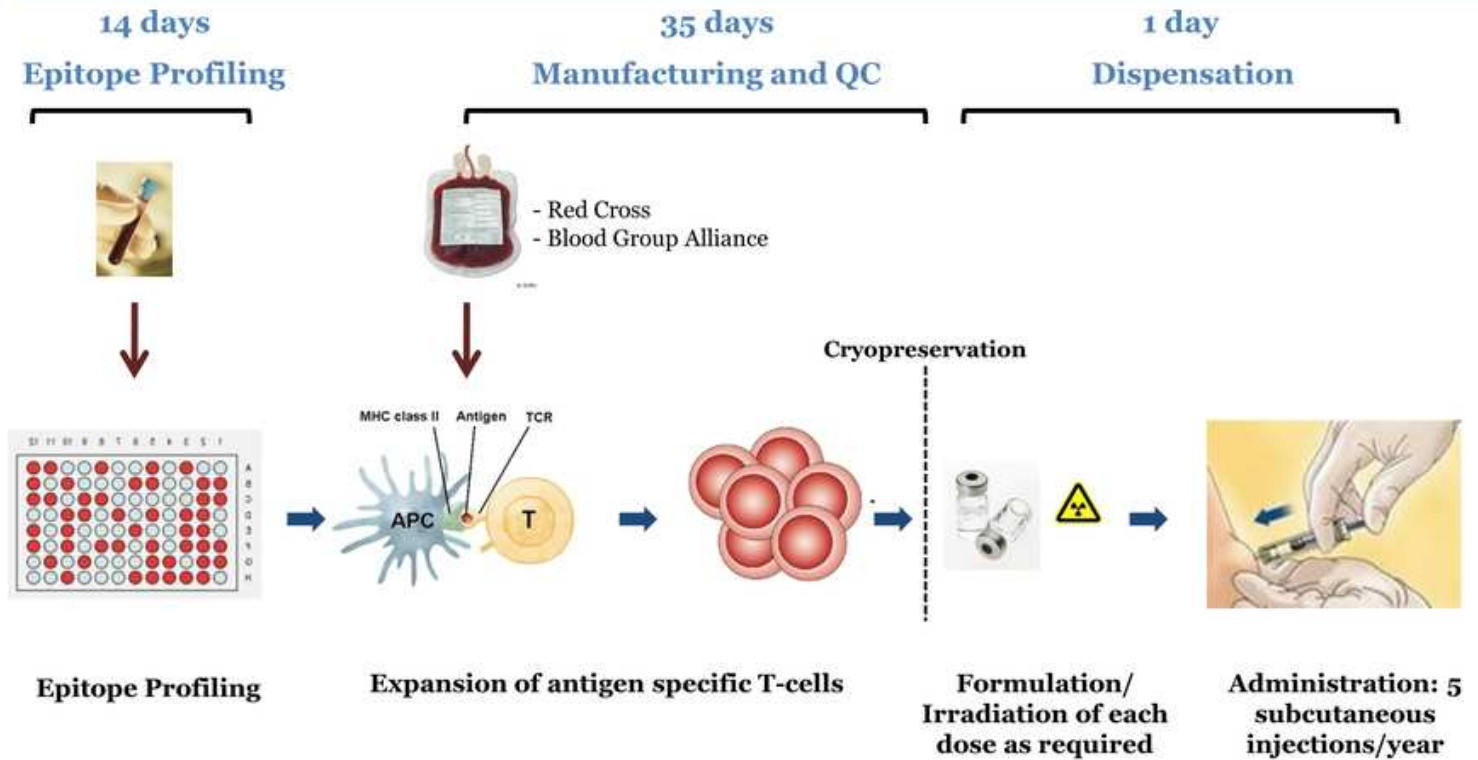
Reduction in Myelin Reactive T-Cells

Tcelna Demonstrated a Reduction in Myelin Reactive T-cells (MRTC)



Single Cycle Manufacturing Process:

Annual course of treatment (5 doses) from one blood draw



Merck Serono Agreement for MS indication

- **February 2013 option and license agreement with Merck Serono**
 - Up to \$220 million in additional payments
 - Option exercise \$25 million for starting Phase III/ or \$15 million if another Phase II
 - \$35 million FDA filing, approval and commercialized in US
 - \$30 million for EU filing, approval and commercialization in at least three countries
 - Relapsing Remitting MS development and commercialization of up to \$40 million
 - One time commercial milestones of up to \$85 million
- **Royalties ranging from 8% to 15% of annual net sales with step-ups occurring when net sales exceed \$500 million, \$1 B & \$2 B**
- **Opexa maintains key rights:**
 - Development and commercialization rights to Tcelna in Japan
 - Certain manufacturing rights
 - Co-development funding option in exchange for increased royalties
 - Rights to all other disease indications

Tcelna Development Program

Broad Spectrum of MS patients treated

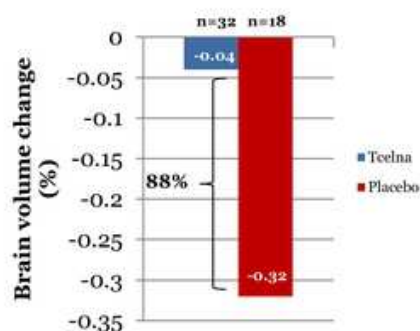
Phase	Completion Dates	Population	Total N	Treatment Duration (months)	Tcelna	Placebo
Baylor	1998	RRMS, PPMS, SPMS (26)	114	Up to 24 months	114	
Phase I dose escalation	2006	RRMS (5) SPMS (6)	16	12	16	-
Phase I/II Open label retreatment	2007	RRMS (9) SPMS (4)	13	12	13	-
Phase IIb TERMS	2008	RRMS, CIS	150	12	100	50
Phase IIb extension OLTERMS	2008	RRMS, CIS	38	At least one dose post TERMS	15 from placebo arm	
Phase IIb Abili-T	Mid 2016*	SPMS	180*	24*	90*	90*

* Expected upon completion of ongoing SPMS Abili-T trial

TERMS Study - Prospective Analysis in More Active or Progressive Patients

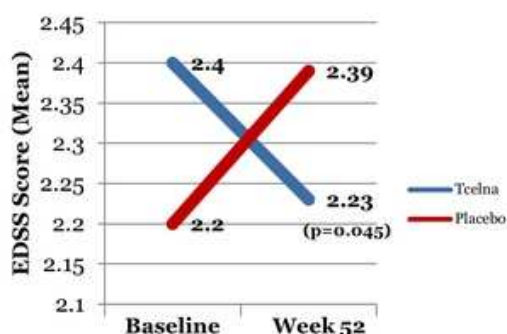
Sub-population of patients (n=50) with more progressed/active disease profile (baseline ARR >1)

Percent Brain Volume Change at Week 52



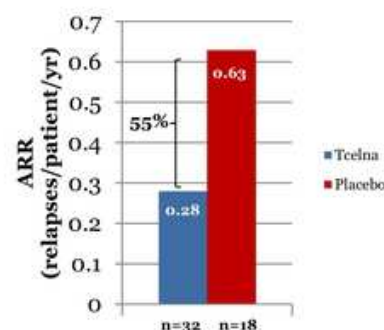
88% Reduction in Brain Atrophy

Change in Disability (EDSS) at Week 52



Statistically Significant Improvement in Disability (p=0.045)

Annualized Relapse Rate (ARR) at Week 52

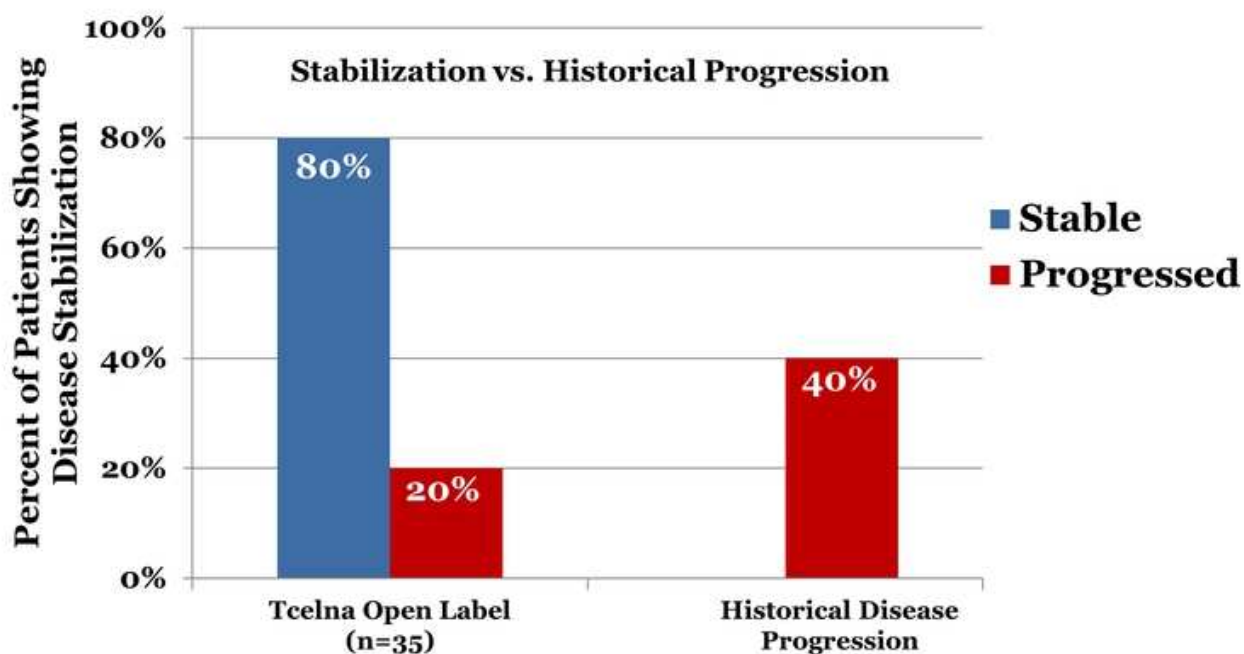


55% Reduction in ARR

These Data Support Phase IIb Program in SPMS

Tcelna Stabilizes Disease in SPMS at 2 Years

80% of subjects treated with Tcelna showed no further disease progression by EDSS at 2 years



*A small percentage of patients in pooled analysis showed an improvement (i.e. decrease in progression)

**Historical control: ESIMS Study, published Hommes Lancet 2004

Abili-T : Landmark trial in SPMS

- **Abili-T Phase IIb clinical trial in SPMS is ongoing**
 - Double-blind, 1:1 randomized, placebo-controlled
 - Inclusion criteria: Secondary Progressive MS with EDSS of 3 to 6
 - Immune Monitoring program conducted on a blinded basis
- **Fast Track designation granted by FDA for Tcelna in SPMS**
- **180 Patients expected to be enrolled**
 - SPMS population
 - Approximately 35 sites in USA and Canada
- **2 annual courses of personalized therapy**

Efficacy Assessments

- **Primary Endpoint**
 - Whole-brain atrophy
- **Secondary Endpoints**
 - Sustained progression measured by EDSS
 - Time to sustained progression
 - T2 lesions progressing to hypointense lesions (black holes)
 - Change in EDSS
 - Annualized Relapse Rate (ARR)
 - Change in MSFC Assessment of disability
 - Change in Symbol Digit Modality Test (SDMT)
- **Exploratory Endpoints**
 - Quality of life assessment by MSQLI
 - Gd-enhancing lesion volume with increasing MTR
 - Gd-enhancing lesion volume with decreasing MTR
 - Change in MTR in normal-appearing white matter
 - Changes in T-regulatory cell repertoire and function



Immune Monitoring Program

Trial initiation

40 patients at dose 5

90 patients at dose 5

180 patients at 10 doses

End of Study

2012

2013

2014

2015

2016

Immuno vigilance

Whole blood analysis:
Absolute frequency of T-cells, B-cells, Dendritic cells and Monocytes

- Goal is to show no systemic impact on immune response, i.e. Tcelna is a Precision Immunotherapy
- Tcelna differentiates by not depleting a broad spectrum of T-cells

Phenotypical Analysis (CD4 and CD8)

Pro-inflammatory Anti-inflammatory

TH1	Treg
TH17	Tr1
	TH2
IL-2	IL-4
IL-6	IL-5
IL-12	IL-10
IL-17E, IL-17F	
IL-23	IL-27
TNF α	TGF β
IFN γ	BDNF

Plausible indicators of Tcelna efficacy

- Reduction in Th1/TH17
- Increase in Treg/Tr1 cells
- Reduction in proinflammatory cytokines (IL-12, IL-23, IFN γ , TNF α)
- Increase in anti-inflammatory cytokines (IL-10, IL-27)
- Loss of proinflammatory monocyte markers (CD16/HLA-DR, CCR5)
- Gain in anti-inflammatory monocyte markers (PDL-1, HLA-G, ICOS)

Financials

Cash and Cash Equivalents (MM) as of December 31, 2013	\$23.6
Shares outstanding (MM) as of March 1, 2014	~27.7
Warrants (MM) ⁽¹⁾	~3.1
Stock Options (MM) ⁽²⁾	~2.2

(1) Weighted average exercise price = \$4.12 as of December 31, 2013

(2) Weighted average exercise price = \$3.06 as of March 1, 2014

Experienced Management Team and Board of Directors

Neil Warma, President & CEO, Director

- › 19+ years international healthcare experience with large Pharma and emerging biotechnology companies
- › Former Senior Management, Novartis Pharmaceuticals, Basel, Switzerland
- › Former CEO, Viron Therapeutics, Inc.
- › Co-founder and President of MedExact Inc., a company subsequently acquired

Karthik Radhakrishnan, Chief Financial Officer

- › 10+ years of health care capital markets experience
- › Formerly, Vice President at ING Investment Management
- › MBA, MS in Engineering, CFA charter holder

Don Healey, Ph.D., Chief Scientific Officer

- › 25+ years of experience in cellular immunology and immune regulation
- › Former Director of Immunology, Argos Therapeutics

Donna Rill, Chief Development Officer

- › 30 years in cell and gene therapy research and clinical application
- › Designed and validated cGMP Cell & Gene Therapy Laboratories, Vector Production facilities, and Translational Research Labs

Kenny Frazier, VP of Clinical Dev. and Regulatory Affairs

- › 24 years of extensive clinical and regulatory experience
- › Formerly, Head of Clinical Operations, Lexicon Pharmaceuticals and Tanox, Inc.

Board of Directors

Timothy Barabe

Board member of Arqule, Inc.; Former CFO of Affymetrix, Human Genome Sciences, Inc., Regent Medical UK and Sandoz GmbH

Dr. Hans-Peter Hartung

Chair of Neurology at Heinrich-Heine University, Germany; Executive Board member of ECTRIMS

Gail J. Maderis

CEO, BayBio, Former CEO of Five Prime Therapeutics, Founder of Genzyme Molecular Oncology

Michael S. Richman

CEO, Amplimmune

Scott B. Seaman

Executive Director, Alkek Foundation

Neil K. Warma

President & CEO, Opexa

SPMS Scientific Advisory Board

➤ **Dawn McGuire, M.D., FAAN (Chair)**

- Advisory Council of the Gill Heart Institute
- Former Vice President of Clinical Research at Elan Pharmaceuticals

➤ **Hans-Peter Hartung, M.D**

- Chair of Neurology at Heinrich-Heine University, Düsseldorf
- Executive Board member ofECTRIMS, World Health Organization Advisory Board on MS

➤ **Mark S. Freedman, M.D.**

- Director of the Multiple Sclerosis Research Unit at Ottawa Hospital
- Multiple Sclerosis Society of Canada, National MS Society (USA)
- ACTRIMS committee member

➤ **Clyde Markowitz, M.D.**

- Director of MS Center at the University of Pennsylvania

➤ **Doug Arnold, M.D.**

- James McGill Professor Neurology and Neurosurgery at the Montreal Neurological Institute

➤ **Edward Fox, M.D., Ph.D.**

- Director of Multiple Sclerosis Clinic of Central Texas
- Advisory Committee, Lone Star Chapter of the National Multiple Sclerosis Society

Investment Thesis

- T-cell platform company with Fast Track designation in SPMS
- Strong Intellectual property with 50 issued patents (domestic and international)
- Esteemed Scientific Advisory Board
- Precision Immunotherapy potentially optimizes benefit-risk profile
- Targeting an unmet medical need in a potentially substantial market
- Option Agreement with Merck Serono, a strong potential commercial partner
- Replacement value of company is multiples of present market cap
- Attractive potential risk-reward profile for long term/value investors
- Goal-oriented management team focused on value creation



APPENDIX

Tcelna[®] Highlights

- Clinical studies conducted in Relapsing Remitting and Secondary Progressive MS
- Progress made on manufacturing with focus on commercially viable process
 - Over 850 Tcelna preparations have been successfully manufactured, reproducible and consistent
- Safety demonstrated and trends in clinical efficacy across broad spectrum of patients for Relapsing Remitting and Secondary Progressive MS
- Dose and regimen for ongoing clinical development has been selected based on dose ranging studies
- Commercial opportunities in MS:
 - Secondary Progressive MS
 - Abili-T Phase II SPMS trial ongoing with 180 patients expected in U.S. and Canada
 - Fast track designation
 - Relapsing Remitting MS
 - Formal *End of Phase II* meetings have been conducted
 - FDA feedback obtained for potential Phase III studies

Tcelna Manufacturing: Personalization followed by Expansion Step

The Epitope Profiling Assay (EPA)

- Screen peripheral blood for Myelin-Reactive T-cells (MRTCs), and mapping of immunodominant epitopes to MBP, MOG and PLP
 - 109 overlapping peptides encompassing MBP, MOG and PLP
 - Interferon gamma response to individual peptide pools defines positive response in 7 day assay

ImmPath™ Process

- Procure unit of blood from which up to six T-cell lines reactive with immunodominant myelin peptides are generated and pooled as a patient-specific Tcelna product
 - Manufacturing performed under GMP/GTPs in functionally closed system
 - Process generates a year of Tcelna doses from a single unit of blood

Tcelna Manufacturing: Precision Medicine

Proprietary Assay Enables Annual Personalized Treatments

Year 1

Conduct analysis of 109 peptides from all three key myelin proteins (MBP, MOG, PLP)



Patient XX	Peptide 1	Peptide 2	Peptide 3	Peptide 4	Peptide 5	Peptide 6	Peptide 7	Peptide 8	Peptide 9	Peptide 10	Peptide 11	Peptide 104	Peptide 105	Peptide 106	Peptide 107	Peptide 108	Peptide 109
MBP																	
MOG																	
PLP																	

Year 2



Patient XX	Peptide 1	Peptide 2	Peptide 3	Peptide 4	Peptide 5	Peptide 6	Peptide 7	Peptide 8	Peptide 9	Peptide 10	Peptide 11	Peptide 104	Peptide 105	Peptide 106	Peptide 107	Peptide 108	Peptide 109
MBP																	
MOG																	
PLP																	

- Re-assess epitope profile annually to identify epitope shift
- Develop newly personalized formulation annually based on evolved epitope profile

Year 3

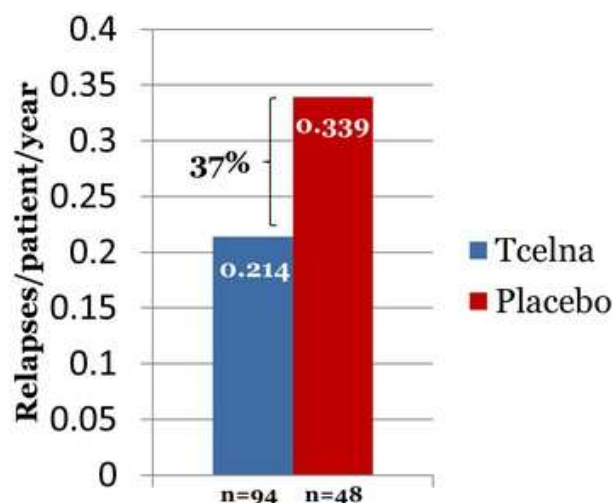


Patient XX	Peptide 1	Peptide 2	Peptide 3	Peptide 4	Peptide 5	Peptide 6	Peptide 7	Peptide 8	Peptide 9	Peptide 10	Peptide 11	Peptide 104	Peptide 105	Peptide 106	Peptide 107	Peptide 108	Peptide 109
MBP																	
MOG																	
PLP																	

TERMS Study

A Completed Phase IIb Clinical Trial in RRMS

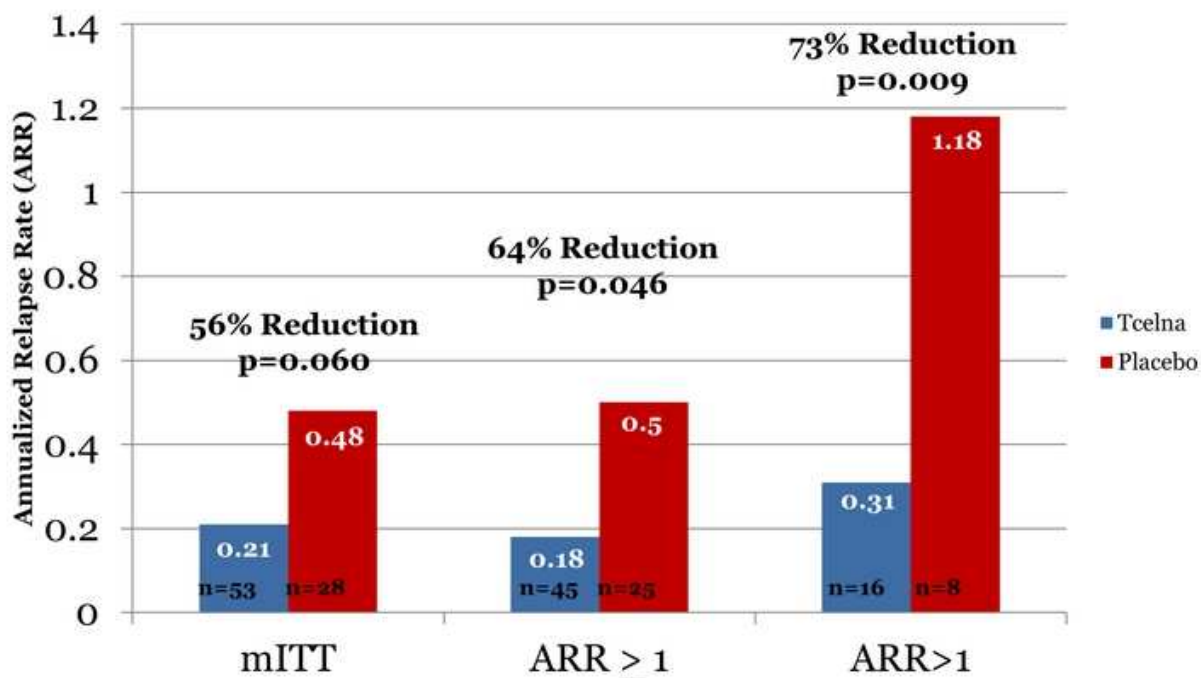
- Completed Phase IIb clinical trial in 150 RRMS patients; 33 sites in U.S.
- mITT population (n=142)
 - 37% reduction in ARR vs. placebo
 - ARR 0.214 vs. 0.339
- Superior safety and promising efficacy trend demonstrated
- Two *End-of-Phase II* meetings with FDA successfully completed



TERMS Study: Safety Overview

Safety Summary	
Deaths	• No deaths occurred
Serious Adverse Events (SAEs)	• No treatment-related SAEs
Most common adverse events	• Mild to moderate injection site reaction

TERMS Study - Subgroup Analysis in Patients Naïve to DMT



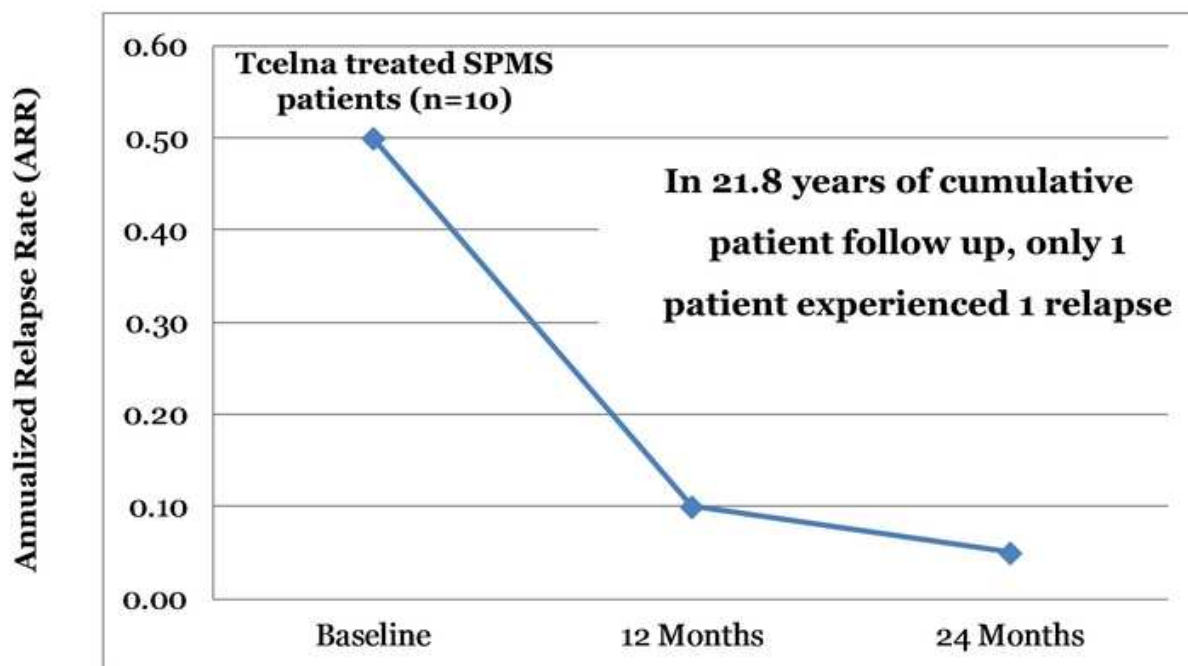
Annualized relapse rate in DMT naïve populations. ARR in placebo subjects without previous disease modifying treatment (DMT) experience reflects relapse rates commonly seen in other placebo controlled trials in MS. In this subpopulation, treatment with Tcelna resulted in a 56–73% reduction in ARR compared with placebo.

Secondary Progressive MS:

Overview of Phase I/II Patients treated with Tcelna

- **36 SPMS patients treated in three clinical studies**
 - 35 of these patients were treated with Tcelna for two years
 - 26 patients treated at Baylor; 10 patients treated by Opexa
- **Promising efficacy observed**
 - Disease stabilization as measured by EDSS was observed in 80% of patients at two years (compared to a historical control data that shows progression rate of 40%)
 - 10 patients in Opexa sponsored study showed significant reduction in relapse rates from a baseline ARR of 0.5 to an ARR of 0.1 at two years
 - No worsening in key Quality of Life Indicators (physical and psychological condition) at two years
- **Well-tolerated with a favorable safety profile**
 - No Serious Adverse Events

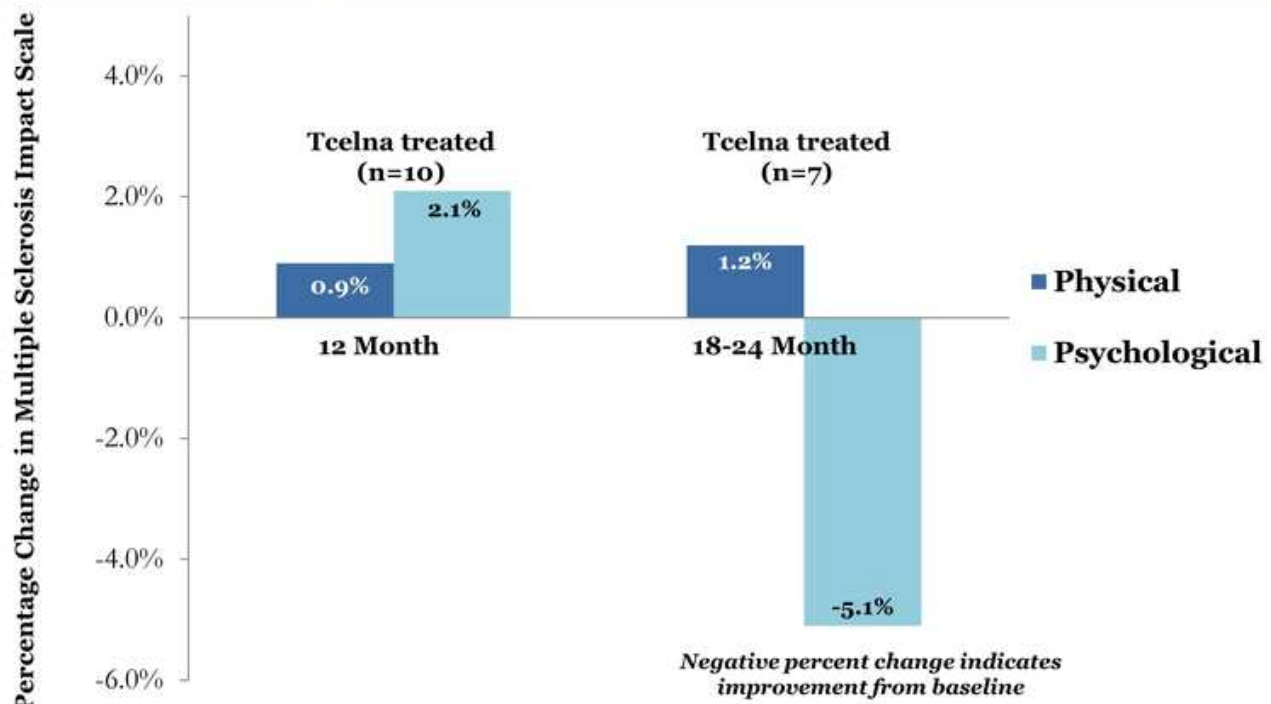
Tcelna Reduces Annualized Relapse Rate (ARR) in SPMS at 2 years



One relapse observed in 21 years of cumulative patient follow up

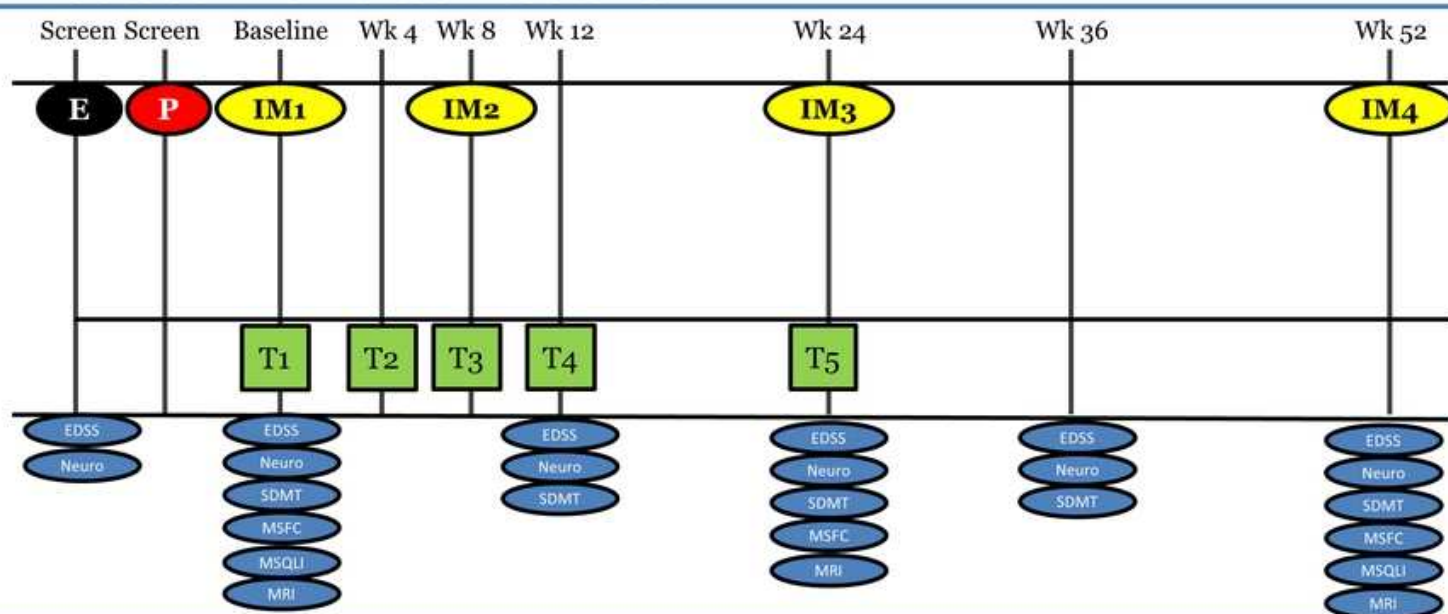


Tcelna Stabilizes Quality of Life Scores in SPMS at 2 years



Following two years of treatment, no worsening of physical condition and improvement in psychological condition

Abili-T Annual Treatment and Efficacy Assessment Schedule



Efficacy Assessments

EDSS: Expanded Disability Status Scale
 NEURO: Neurological Examination
 SDMT: Symbol Digit Modalities Test
 MSFC: MS Functional Composite
 MSQLI: MS Quality of Life Indicator
 MRI: Magnetic Resonance Imaging



Tcelna dose



Epitope
Profile Assay



Immune
Monitoring



500 mL
Procurement

Mechanism of Action

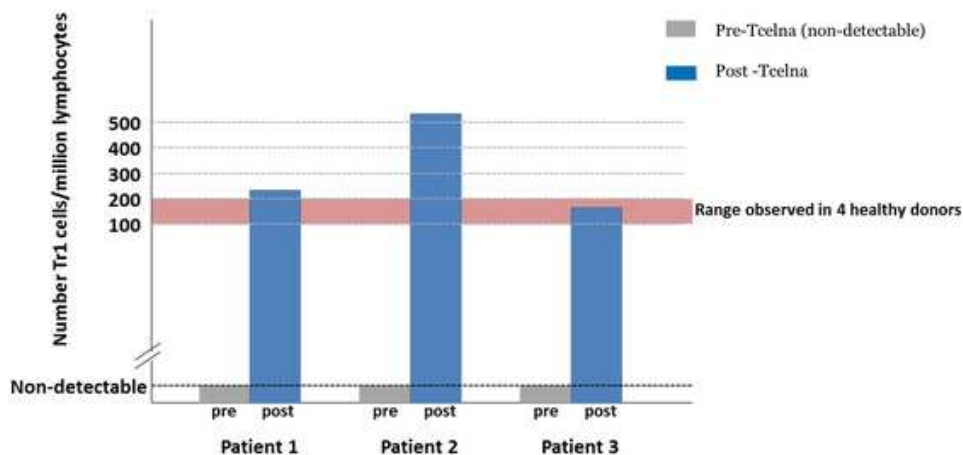
- **Attenuated, patient-specific (autologous) myelin reactive T-cells (MRTC)**
 - MRTC expanded *ex vivo* in response to immunodominant peptides of MBP, MOG and PLP
- **Therapeutic sc dosing ($30-45 \times 10^6$ cells) stimulates host reactivity to the ‘over-represented’ MRTC inducing a dominant negative ‘regulatory T-cell’ response leading to:**
 - Down-regulation of similar endogenous disease-causing myelin reactive T-cells
 - Potential to induce up-regulation of regulatory cells (Foxp3+ and Tr1 cells) to reduce inflammation and provide possible neuroprotection, should these gain entry to the CNS
- **Phase I/II studies conducted with Tcelna in RRMS and SPMS showed a substantial reduction in MRTC, and improved clinical outcomes**
 - lower relapse rates and stabilization of disease as defined by EDSS

Mechanism of Action

Tcelna increases Tr1 cells in SPMS Patients

Observations

- Increase in Tr1 cells from non-detectable to detectable levels in Tcelna treated patients (n=3)
- Increase in Tr1 cells to a level similar to those observed in healthy controls (n=4)
- $p=0.971$ (i.e. no statistical difference between healthy donor and post-treatment TR1 dose levels)



Clinical findings in Tcelna treated patients

- All three patients (who had experienced relapse in preceding 12-24 month) remained relapse free during the 52-week assessment
- Showed stabilization of disease progression
- Showed a 57%-67% reduction in myelin reactive T-cell counts from baseline

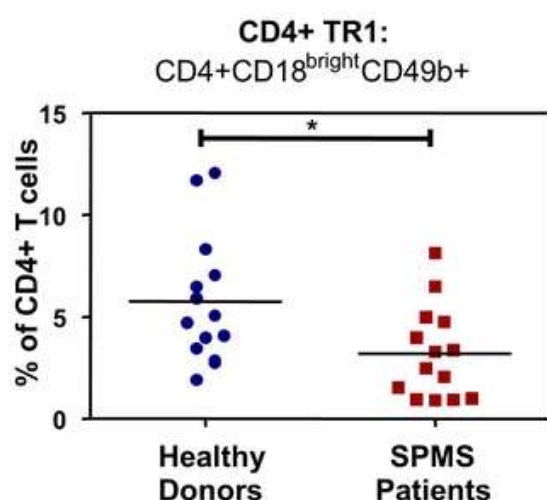
Mechanism of Action

The Immunopathology of SPMS

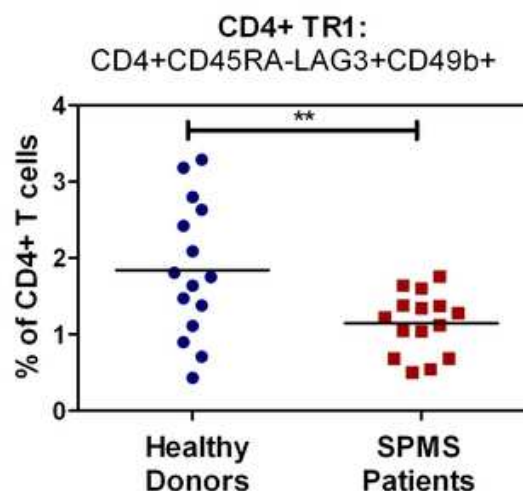
- **SPMS is associated with compartmentalized CNS inflammatory cells**
 - Microglia activation suggests ongoing chronic innate immune responses
- **SPMS is associated with inflammatory processes localized within the central nervous system**
 - Mechanisms responsible for continued neurodegeneration in SPMS are distinct from those of RRMS
 - In SPMS, it is believed that the Blood Brain Barrier (BBB) remains closed enabling only those products that are able to cross the BBB to be potentially effective
 - SPMS is characterized by a chronic inflammatory process (vs. acute episodes for RRMS)
- **Immunological defects associated with progression to SPMS**
 - Levels of the anti-inflammatory cytokine IL-10 are reduced in patients with SPMS
 - A therapeutic that has the potential to restore local production of IL-10 would be expected to alleviate chronic inflammation, and thereby reduce neurodegeneration

Baseline Abili-T patients versus Healthy Individuals

SPMS subjects have a reduced frequency of IL-10 secreting TR1 cells



* (p=0.02)

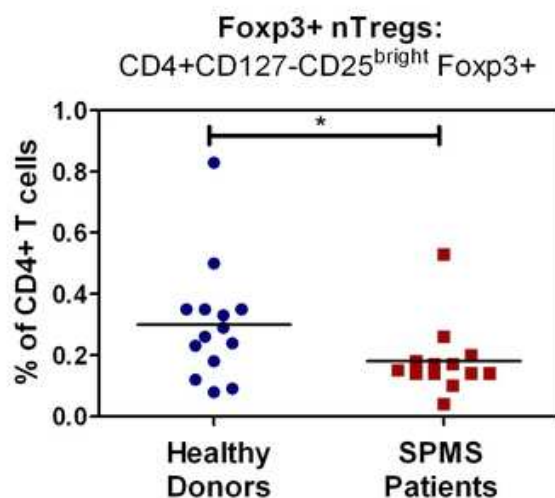


** (p=0.01)

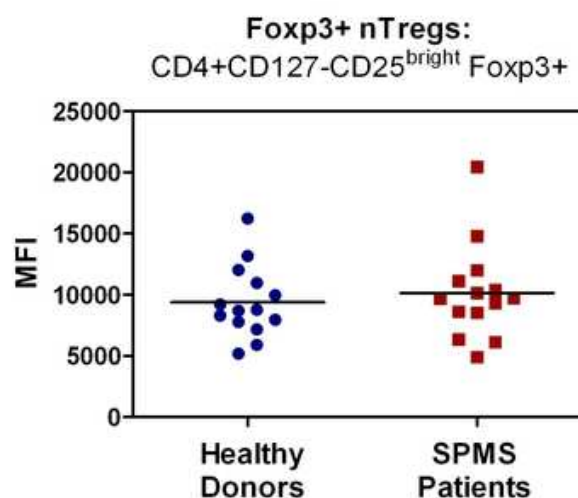
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SPMS subjects have reduced nTReg cells (another type of CD4 cells)

Frequency of nTregs may be reduced in SPMS, although the level of Foxp3 expression is equivalent to that of healthy donors. Therefore, function of Tregs cells is equivalent between the populations, unlike in RRMS where reduction in Tregs may play a greater role in the persistence of autoimmunity.



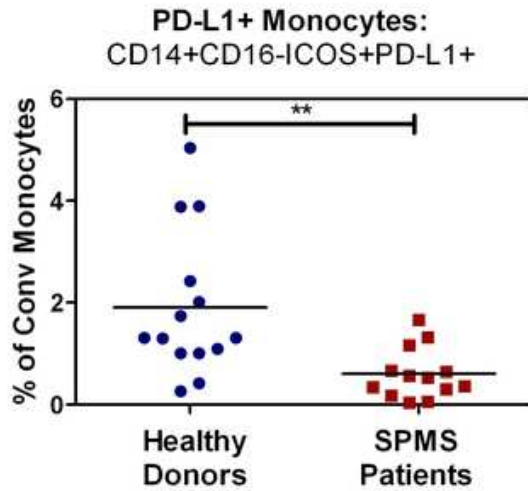
* (p=0.06)



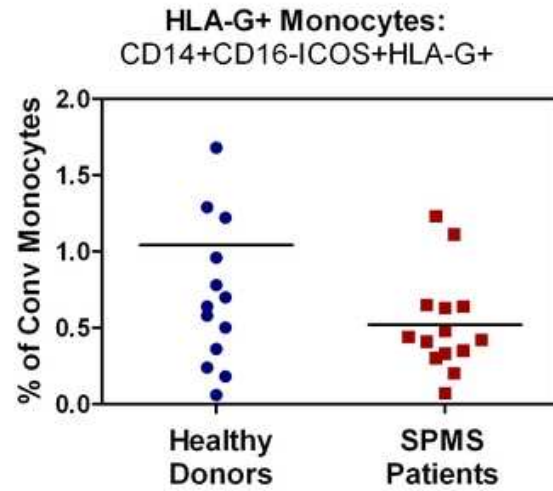
(p=0.56)

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SPMS patients have fewer Anti-inflammatory monocytes (PDL1 and HLA-G)



** (p=0.004)



(p=0.164)

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