

Stem Cell Medicine

THERAPIES FOR NEUROLOGICAL
INDICATIONS

Corporate Overview

October 2021

Investment Highlights



Developing products and treatments for neurological indications including combination products with pharmaceuticals and antibodies



Two lead products:

- a) naïve exosomes for treating Autism (ASD)
- b) an anti-BMP small molecule (SM1) for remyelination in multiple sclerosis (MS)



Strong IP position for all products including licensed technologies from leading research institutes and hospitals



Integrated R&D and GMP approved Manufacturing facility



Raised \$40 million to date, 2021 revenue from CMO and product sales \$1.5 million, Gov't of Israel-approved biotechnology company status providing tax benefits, received grants for investments in facilities

Pipeline

Program	Indication	Research	Pre-Clinical	Clinical	Licensing
Exosomes (Naive)	Autism / Schizophrenia				Tel Aviv University 
Anti-BMP (SM1)	Relapsing Remitting MS				Tel Aviv Sourasky Medical Center 
SCM-010	SPMS		 IND		
Gene Therapy	Neuropathic Pain / PNI				Tel Aviv University 
Exosomes (Loaded)	PD / ALZ / MS / GBM				
Protein Skin Care	Skin Rejuvenation				

PNI: Peripheral Nerve Injury
 PD: Parkinson's Disease
 ALZ: Alzheimer's Disease
 MS: Multiple Sclerosis
 GBM: Glioblastoma



Our Way to the Market



Fast Track approval via smaller scale clinical studies demonstrating safety and implying efficacy allowing marketing authorization (saves 5 years of developing programs)

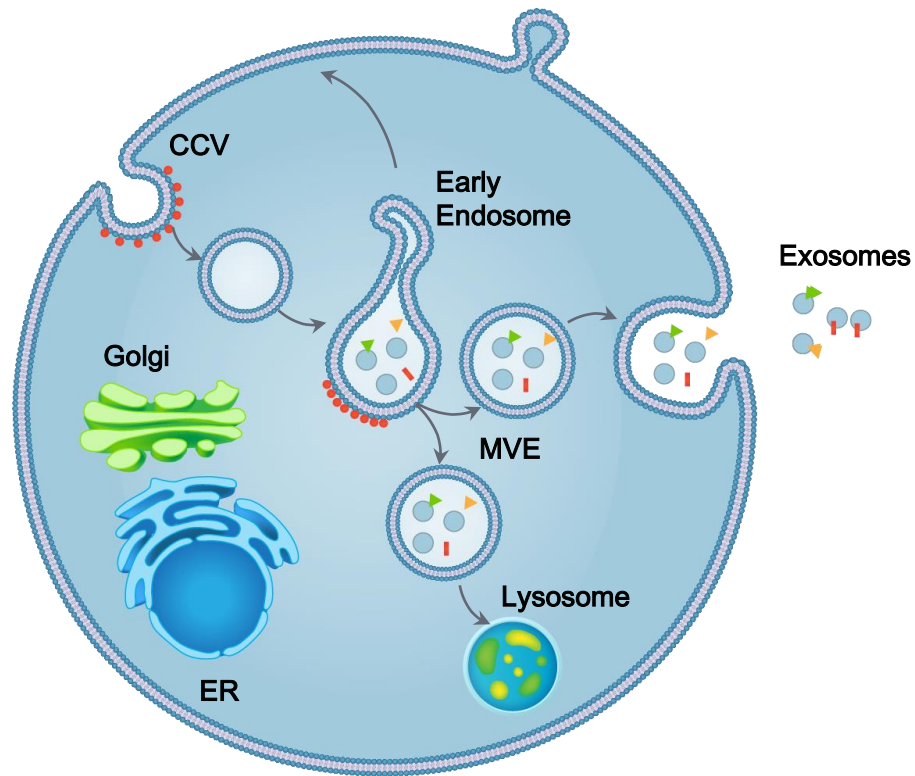


Ongoing revenue from CMO services



Products based on mesenchymal stem cells, which are reliably produced and a readily available source (adipose from Liposuction procedures), with excellent efficacy and safety for both autologous and allogeneic treatments

Exosomes - Role and Flexibility



Exosomes are:

Small extracellular vesicles (30-100nm) that can penetrate the Blood Brain Barrier (BBB) with a good safety profile

Representative of the originator's cell, containing the same molecules, proteins and DNA and mRNA that are present in the parent cell membrane

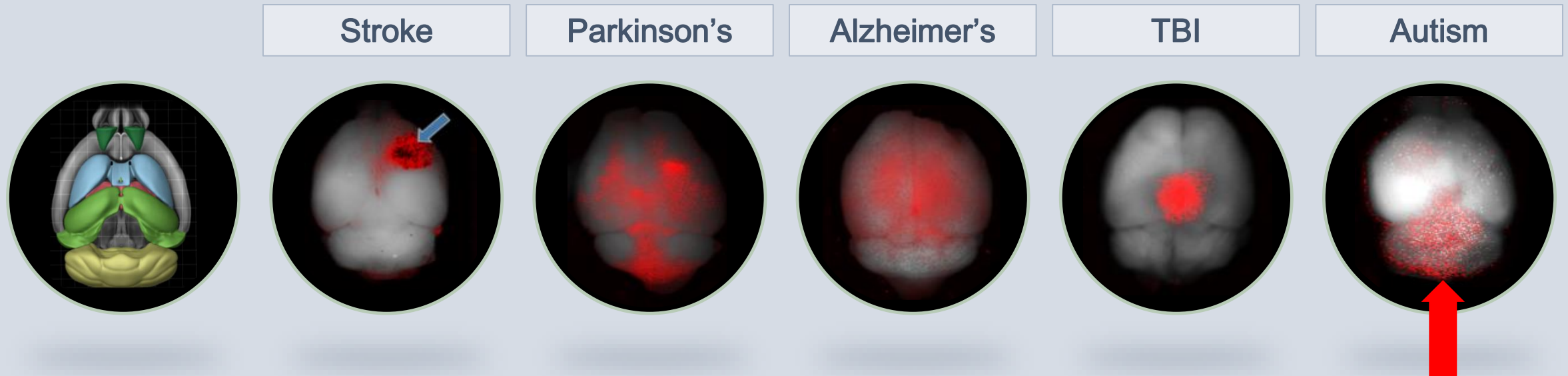
Once the exosome has left the cell, its primary function is to transport and deliver protein and nucleic acid cargo to target cells

Exosomes promote regeneration and immunomodulation processes in damaged tissue

Have an important cell-to-cell communication role in both physiological and pathophysiological conditions, including the regulation of immune responses, inflammation, tumor growth, coagulation and infection

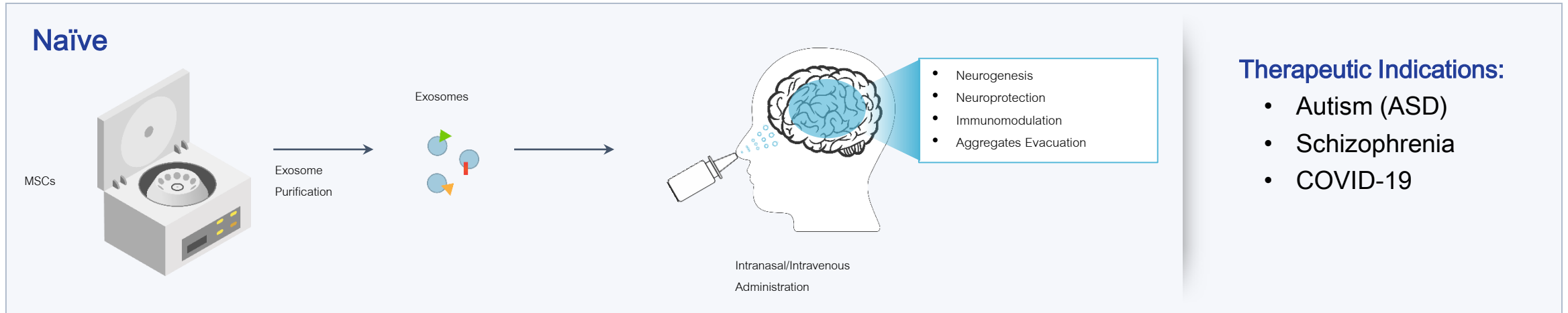
Exosomes Brain Penetration & Homering

Intranasal Administration of Stem Cell Medicine's MSC-exosomes effectively cross the BBB and specifically migrate to distinct pathological areas in the brain



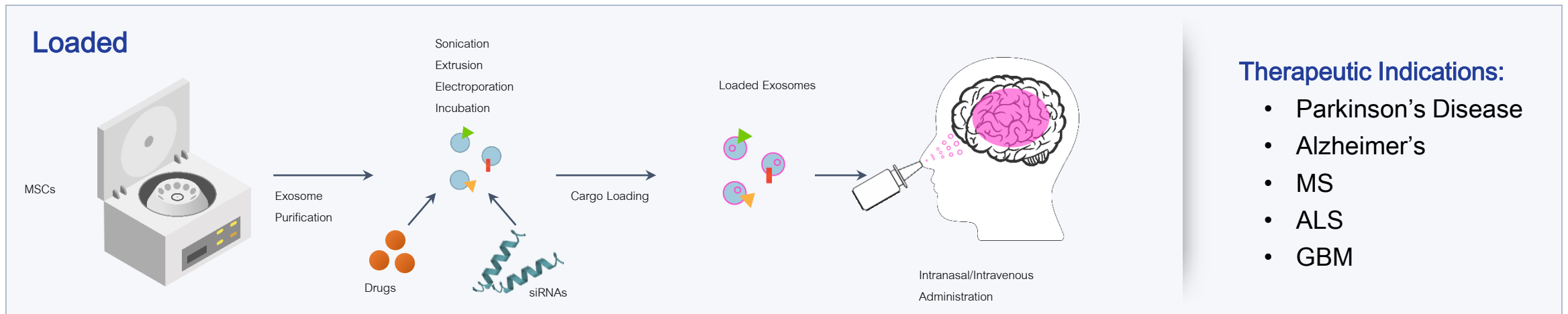
The cerebellum is linked to ASD by controlling movement, cognition, emotion, social skills

Naïve and Loaded Exosomes



Therapeutic Indications:

- Autism (ASD)
- Schizophrenia
- COVID-19



Therapeutic Indications:

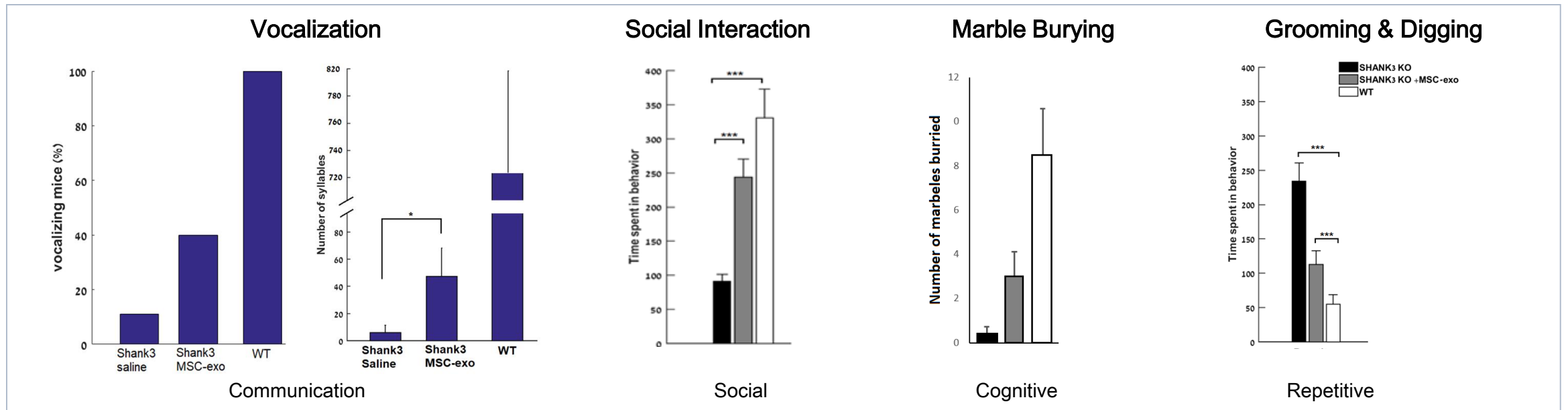
- Parkinson's Disease
- Alzheimer's
- MS
- ALS
- GBM

Autism



Autism: Pre-Clinical Impact of Naïve Exosomes

- Intranasal administration of MSC-exosomes specifically ameliorates autistic like behaviors in two benchmark mice models:
 - Idiopathic (multifactorial) model (BTBR)
 - Phelan-McDermid model (SHNAK3 KO/mutated)
- Significant behavioral progress in communication, social interaction, cognition and repeated behaviors



Autism: Phase I/II Clinical Trial Outline

Naïve exosomes for treating Autism Spectrum Disorder (ASD):

A prospective, single center, open label, dose escalation Phase I/IIa study to assess the safety and efficacy of a single intranasal administered exosomes for the treatment of SHANK3-derived ASD

Target Population:

Phelan-McDermid syndrome patients (PMS) have a rare genetic condition caused by a deletion or other structural change of the terminal end of chromosome 22 in the 22q13 location or a disease-causing variant of the SHANK3 gene.

Study Design:

- Single intranasal administered exosomes with dose escalation of two groups: first group of 4 subjects with dose of 10^8 exosomes and second group of 4 subjects with dose of 2×10^8 exosomes, to be continued with additional 8 subjects with selected MTD dose
- Subjects will be evaluated during screening, at baseline, 48 hours visit, week 4, week 12, and at week 24 (end of study)

Preliminary Phase I/IIa trial design determined after early discussion with Dr. Joseph Buxbaum, Mount Sinai (NY), a KOL in that area. This will be further discussed with the regulatory authorities.

Endpoints

Primary:

Safety and tolerability, Maximum Tolerated Dose (MTD)

Secondary:

1. Change in ABC-SW subscale--Reciprocal Social Behavior [Time Frame: 6 months]. The primary outcome is reciprocal social behaviors, which will be assessed using two co-primary measures. The first measure is the ABC-SW subscale, which is being used in other clinical trials focusing on the core social and communication symptoms of autism.
2. Change in SRS-Social Motivation Subscale [Time Frame: 6 months]. The Social Responsiveness Scale (SRS)-Social Motivation subscale, was developed to provide a quantitative measure of social impairments typically observed in ASD in children 3-18 years.

Multiple Sclerosis

Remyelination



SM1 for Remyelination in MS

- Current therapeutics for MS target the immune pathophysiology of MS. There is no approved remyelination therapy that may reverse disability, which is a major unmet medical need
- Mode of action: Small molecules that act through a novel mechanism of action of Anti-Bone Morphogenic Protein (anti-BMP). Anti-BMP agents promote remyelination by directing neural stem cells to differentiate into oligodendrocytes that induce myelination and differentiate into neurons. SM1 has the **potential to reduce disability and be a disease modifying treatment and cure.**

Market opportunity:

Can be used as standalone or on top of other available therapies

\$1-\$2 billion annual market opportunity for treating MS



SM1: The Product



Orally available
small molecule



Next Step:
Determine
appropriate dose
level for the clinical
program



Target Treatment:
Add-on treatment
during relapses



Suggested Course:
Treatment course
of 30 days on top of
the patients'
benchmark
treatment for MS

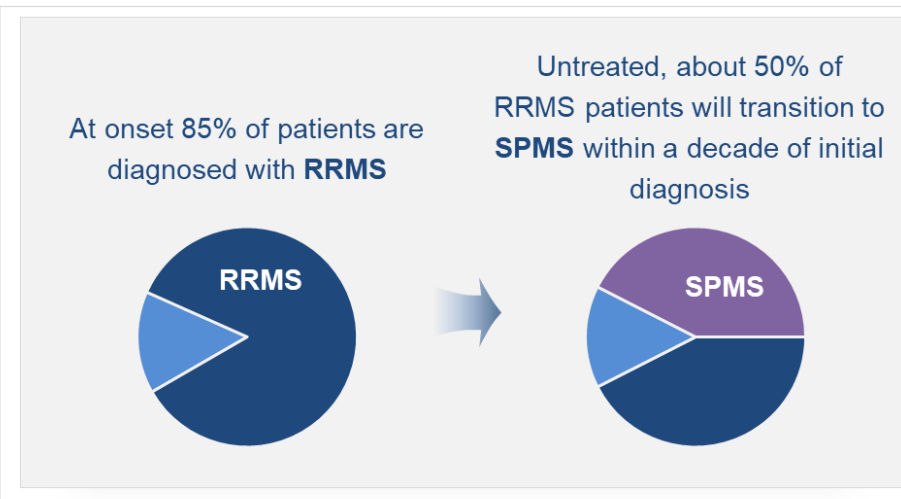
SCM-010 for Secondary Progressive MS

- SPMS is a major unmet medical need with only Novantrone® (cytotoxic), is approved for SPMS, and is still prescribed despite its severe safety profile (cardiac events) which limits its use.
- SCM-010 is an autologous, adipose-derived Mesenchymal Stem Cell (ADSCs) that effects SPMS by:
 - Immunomodulation of chronic inflammation
 - Neuroprotection by secretion of neurotrophic factors, such as VEGF, promoting neuronal cell survival growth
 - To be used as monotherapy or in combination with GA Depot
 - Animal POC and IRB approval for clinical study

Market opportunity:

RRMS is \$22 Billion annual market

SPMS patients constitute 40%-50% of RRMS patient population, therefore it may be assumed that the SPMS market potential may be estimated at up to \$10 billion annually



Gene Therapy for Neuropathic Pain

- Genetically modified progenitor muscle cells for the treatment of neuromuscular injuries, including Myogenic Modified Cells (addition of four different neurotrophic factors genes: BDNF, GDNF, IGF-1 and VEGF (MPCs-NTFs). Ex-vivo gene therapy
- **Mode of action:** Constant production and secretion of higher concentration of NTFs into the host muscle aimed to affect the adjacent motor neurons
- Allogeneic MPCs-NTFs showed a beneficial therapeutic effect in a model of acute motor neuron injury

Market opportunity:

Despite recent advances, functional recovery following repair of (Peripheral Nerve Injury) PNI remains disappointing, often leaving patients with impaired muscle control and sensation, pain and decreased function. Cell therapy is a promising treatment for PNI and nerve regeneration.



Anti-BMP: A Novel MOA and Novel Concept of Remyelination

Remyelination
in MS MOA

- RRMS is characterized by a demyelinating process that leads to loss of motoric functions
- There are 15 approved therapies for RRMS that target the immune pathophysiology of MS, by various mechanisms, these slow progression of the disease, but there is no cure
- Introducing a Novel Mechanism of Action that promotes remyelination by directing neural stem cells to differentiate into neurons and oligodendrocytes that induce myelination, hence, **has the potential to change the course of the disability and offer a chance of motoric improvement**
- This remyelination treatment is to be administered:
 - RRMS: only at the onset of a relapse, for short terms, on top of currently approved Disease Modifying Therapies
 - Progressive MS: As a continuous, stand-alone treatment

Production Facility



Location

Har Hotzvim, Bio Park, Jerusalem

Status

- 15,000 SQF cleanroom facility equipped with state-of-the-art cell and exosomes manufacturing equipment
- Built in 2013-2014 with the support of governmental grants
- Developing and manufacturing of pharmaceutical products
- Approved as a Biotechnology company by the Israeli Ministry of Economy with privileged conditions
- GMP facility approval by Israeli Ministry of Health (MOH) since March 2016
- ISO 22716 certification for cosmetics manufacturing obtained in July 2018

2021-2022 Business Plan Highlights

Goal:

- Raise \$10 million for the exosomes for autism and anti-BMP for MS clinical studies
- Raise additional \$20 million to advance other programs

Follow the market dynamics where once a Pre-IND stage is reached sign licensing agreements with pharmaceutical companies for milestone and royalties (**Codiak Biosciences** with Jazz Pharmaceuticals, Sarepta and the Ragon Institute, **Evox Therapeutics**: Takeda, Lilly)

Continue discussions with leading pharmaceutical companies who are showing interest, but will enter once Pre-IND stage is reached

Seeking pharmaceutical partners for the loaded Exosomes collaboration (loading their/our molecule)

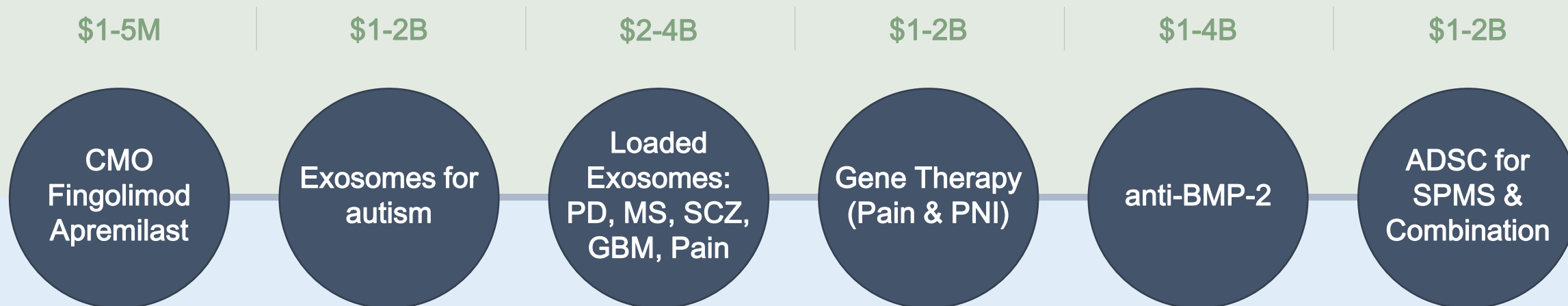
Seeking pharmaceutical partners to acquire the anti-BMP product

Discussion with Chinese companies regarding technology licensing for the Chinese market

Significant inflection point within 24 months

Value Drivers

Future Sales



Status

- | | | | | | |
|---|--|---|--|---|---|
| <ul style="list-style-type: none"> • Product launch in IS • Sales in East Europe and Latin America • Additional products in registration process | <ul style="list-style-type: none"> • Phase I/II in 2022 • Become leading company in therapeutic category | <ul style="list-style-type: none"> • Leading potential in neurological indications | <ul style="list-style-type: none"> • Approved GOI Grant for gene therapy facility • Global shortage in virus facilities • Pain & PNI programs | <ul style="list-style-type: none"> • High level interest from Big Pharma • Phase III and registration in 2025 | <ul style="list-style-type: none"> • Phase II IRB approved • Combination drug in 2026 |
|---|--|---|--|---|---|

Ehud Marom, Founder, CEO & Chairman

Founder of Stem Cell Medicine and has served as CEO and Chairman since inception

Over 40 years of senior management and operational experience in the life sciences industry

Vice President of two divisions at Teva Pharmaceutical Industries Ltd. (1992 to 1995)

Launched Copaxone® and was the head of the Copaxone global operation team and headed the global operations of Teva Pharmaceutical's chemical division

President of Peptor Ltd.(2000 to 2002), where he led the pharmaceutical development of the innovative diabetes product, DiaPep

CEO of Gamida-Cell Ltd. (2002 to 2004), a stem cell development company

CEO of Makhteshim, a company with annual sales of \$1 billion, and the world's leader in branded off-patent crop protection solutions. Acquired by ChemChina for \$2.4 billion in October 2011, the largest deal ever between a Chinese company and an Israeli company.

Currently serves on the BOD of Pharma Two B (is the founder and previously served as Chairman) and is CEO and Chairman of Mapi Pharma.

B.Sc. in chemical engineering with honors from the Technion, Israel



teva

ADAMA 

mapi
PHARMA LTD 

Pharma Two B
TO BE BETTER 

gamida  Cell