Company Presentation November 2018







Forward looking Statement

This presentation contains express or implied forward-looking statements within the Private Securities Litigation Reform Act of 1995 and other U.S. Federal securities laws. For example, we are using forward-looking statements when we discuss the expected timing of obtaining regulatory approval for our various patient trials and clinical data readout, proposed trials that may occur in the future, the timing and implementation of our collaborations with various partners and the execution of definitive agreements relating to such collaborations and the potential benefits and impact our products could have on improving patient health care. These forward-looking statements and their implications are based on the current expectations of our management only, and are subject to a number of factors and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. The following factors, among others, could cause actual results to differ materially from those described in the forward-looking statements: changes in technology and market requirements; we may encounter delays or obstacles in launching and/or successfully completing our clinical trials; our products may not be approved by regulatory agencies, our technology may not be validated as we progress further and our methods may not be accepted by the scientific community; we may be unable to retain or attract key employees whose knowledge is essential to the development of our products; unforeseen scientific difficulties may develop with our process; our products may wind up being more expensive than we anticipate; results in the laboratory may not translate to equally good results in real clinical settings; results of preclinical studies may not correlate with the results of human clinical trials; our patents may not be sufficient; our products may harm recipients; changes in legislation; inability to timely develop and introduce new technologies, products and applications; loss of market share and pressure on pricing resulting from competition, which could cause our actual results or performance to differ materially from those contemplated in such forward-looking statements. Except as otherwise required by law, we undertake no obligation to publicly release any revisions to these forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. For a more detailed description of the risks and uncertainties affecting us, reference is made to our reports filed from time to time with the Securities and Exchange Commission



Corporate Overview

- Regenerative medicine company developing off-theshelf placenta-derived cell products
- Entering late-stage trials in 3 indications
- Multifactorial therapy releasing a range of therapeutic proteins in response to signals from patient's body
- First in class 3D cell culturing technology allowing for efficient, controlled production of different cell products in commercial quantities
- Hundreds of patients treated worldwide



Pluristem _ Therapeutics

Regenerative medicine company committed to advancing placenta-derived cellbased therapeutics that transform patient outcomes

PSTI – NASDAQ / TASE	
Headquarters	Haifa, Israel
Shares outstanding	~115M
Market capitalization	~\$140M
Cash and cash equivalents, bank deposits and restricted deposits	\$22.5M (9/30/18)
Additional resources from approved non-dilutive grants	~\$8M
Full-time employees	175 (150 in research/ manufacturing/clinical)



Placenta



Next Generation of Biological Therapy



Disease Complexity

Complex diseases requires adaptive multifactorial treatments

The Need for Cell Therapy

Longer lifespans

Nearly 2 billion people across the world are expected to be over 60 years old by 2050 (World Health Organization)

The Human Impact

Aging is often associated with debilitating medical conditions, many of which are still **unmet needs**

The Economic Impact

Some of the world's largest economies are now facing subsequent **increase in healthcare costs**

Diseases Complexity

Innovative treatments needed to treat complex diseases





A Change In Regulatory Environment

"Cell therapies...hold significant promise for transformative and potentially curative treatments for some of humanity's most troubling and intractable maladies"

FDA COMMISSIONER SCOTT GOTTLIEB, M.D., AUGUST 2017













The PLX Platform Technology







Placenta Derived Cells

- Ethically accepted
- **Rich & Diverse**
- Highly potent Pro-angiogenic Immunoregulatory
- Young donors
- Unlimited source & Easy to collect
- Wastes and carbon dioxide are passed back from the baby to the mother for excretion. Oxygen nutrients, and hormones are Maternal portion **Fetal portion** of placenta

http://www.the-scientist.com/?articles.view/articleNo/43618/title/The-Prescient-Placenta/

of placenta

Ability to manufacture treatments for over 20,000 patients per placenta



The Placenta Project was Launched by the US National Institutes of Health (NIH) to further explore the role of the placenta in health and disease

Best In Class GMP Facility Commercial Scale Highest Quality Cell Products



- Tightly controlled, completely automated, efficient and scalable cell manufacturing technology
- State-of-the-art, proprietary bioreactor system which provides a 3D micro-environment for cells that mimics the human body condition
- Our cells expand rapidly and remain healthy and potent as we alter conditions within our bioreactors to transform them into unique, patented products
- Produce highest quality cell products on a commercial scale with batch-to-batch consistency

Manufacturing Process 11 Approved by:









PLX Products

PLX-IMMUNE



Inhibits Cancer Cell Growth

PLX-R18



Stimulates regeneration of damaged bone marrow to produce blood cells (white, red and platelets) PLX-PAD



Reduces inflammation Stimulates growth of collateral blood vessels

Stimulates repair of damaged muscle

Phase II - Intermittent Claudication (IC) Phase III – Critical Limb Ischemia (CLI) Phase III- Hip Fracture



Next step- apply for IND approval of clinical trials

Phase III - Radiation Exposure Damage Phase I - Bone Marrow Deficiencies

Company Pipeline





* One Multinational trial- U.S- phase 3, Europe- via adaptive pathway allowing early marketing approval



regenerative hyperplasia

VEGF Angiogenesis 1 Angiogenin HGF Osteopontin Immunomodulation: SDF1 reduction of • GDF15 inflammation • MIF Decorin MMP1 Muscle • HGF regeneration TGFB Galectin1

Reduces inflammation Stimulates growth of collateral blood vessels Stimulates repair of damaged muscle

Peripheral Arterial Disease

Peripheral Arterial Disease (PAD) is caused by fatty deposits in leg arteries that obstruct blood flow. Risk factors include smoking, diabetes, heavy weight, cardiovascular problems and hypertension

Critical limb ischemia (CLI)

severe pain at rest, skin wounds, tissue necrosis and poor quality of life **High risk of leg amputation and death**

- Up to 40% of patients are unsuitable for revascularization
- 5-6 million patients in U.S. and Europe suffer from CLI. Estimated cost of treatment in U.S. alone is over \$25 billion per year
- Annual health care costs during 4 years of follow-up of CLI patients in U.S. are ~\$50,000 for endovascular revascularization, surgical revascularization, and amputation



Phase II Intermittent Claudication Study

(N= 172 - U.S., Germany, South Korea and Israel)



Study Data

- ✓ Demonstrate efficacy of PLX-PAD in the treatment of IC
 - Patients treated with 2 administration of 300 million PLX-PAD cells originating from different placentas, showed statistically significant improvement in MWD at 52 weeks as compared to placebo
 - Reduced revascularization risk by 49% in the main efficacy group at week 65. Patients receiving 2 administrations of cells originating from different placentas had no revascularization events at week 65
- ✓ Validate the design of pivotal Phase III study in CLI
 - <u>Dose confirmation</u>- Study results demonstrated dose of 300 million PLX-PAD cells as the optimal dose for treatment of PAD
 - <u>Dose regimen-</u> Two administrations of 300 million cells demonstrated a statistically significant superior effect (p=0.0331) compared to a single administration of 300 million cells in MWD at week 52
- ✓ Validate the company's proprietary Bio-Therapeutic approach of giving two doses, several months apart, each dose originating from different placenta
- Confirm safety- IM administration of PLX-PAD cells was safe and well tolerated





PACE Ongoing CLI Phase III Study - Overview

Design	Phase III, randomized, Double-Blind, Placebo-controlled (2:1)
Study population	CLI subjects with minor tissue loss, unsuitable for revascularization
Countries	Germany, UK, U.S., Poland, Hungary, Czech republic, Bulgaria, Macedonia, Israel
Sample size	246 patients
Doses tested	300M cells vs. Placebo (randomization ratio 2:1)
Administration	IM injections in the affected leg, 2 treatments at 8-week interval
Primary efficacy endpoint	Time to occurrence of major amputation of leg or death (AFS)
Main Secondary & exploratory efficacy endpoints	Composite efficacy endpoint; Pain; Complete wound healing; Quality-of-life; Adjudicated amputations; TcPO2; cytokine levels
Follow Up length	12-36 months





CLI Expanded Access Program (EAP)

- CLI Expanded Access Program cleared by FDA to enroll patients unsuitable for inclusion in the ongoing Phase 3 clinical trial
- Program to enroll an initial 100 CLI Rutherford Category 5 patients
- FDA approved cost recovery for the treatment

EAP allows for the collection of real-world data while the Phase 3 trial is ongoing





Muscle Regeneration- Overview

- Hip fracture often results in serious long-term complications, including pain, functional decline and disability
- Femoral neck fracture, the most common form of hip fracture, has mortality rates of up to 36%
- Annual treatment costs in the U.S. are between \$10 to \$15 billion, and are expected to rise due to aging population
- Incidence of hip fracture expected to increase markedly as the global population ages

There are currently no approved treatments for the post-operative regeneration of injured or weak skeletal muscle







Muscle Regeneration

Phase I/II Study of PLX-PAD for Muscle Injury Following Total Hip Replacement (N=20)



- PLX-PAD demonstrated a significant increase in muscle strength & volume compared to placebo
- First study to show efficacy of cell therapy in skeletal muscle injury





Ongoing Hip Fracture Phase III Study



Design	Phase III, randomized, Double-Blind, Placebo-controlled
Study population	Patients suffering from muscle injury following arthroplasty for hip fracture
Countries	U.S., Germany, UK, Denmark, Israel
Sample size	240 patients
Doses tested	150M cells vs. Placebo (randomization ratio 1:1)
Administration	IM injections in the operated leg on the day of surgery
Primary efficacy endpoint	Short Physical Performance Battery (SPPB) score at week 26
Main Secondary & exploratory efficacy endpoints	Muscle strength, muscle mass & volume, hospitalization time, lower extremity measure
Follow Up length	52 weeks



\$8.7 million grant from the EU Horizon 2020 program to support Phase III study Pluristem

CELL PRODUCT II - PLX-R18

Bone Marrow Deficiencies

Following or in support of a transplant of hematopoietic stem cells (HCT), Autoimmune diseases, Genetic disorders, Chemotherapy, Radiation therapy, Acute Radiation Syndrome (ARS), Side effects from treatments

Phase III: Acute Radiation Syndrome (ARS)

Phase I: Incomplete Hematopoietic Recovery Following Hematopoietic Cell Transplantation (HCT) Stimulates regeneration of damaged bone marrow to produce blood cells (white, red and platelets)



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PLX-R18 Programs

Acute Radiation Syndrome

- Phase III-equivalent pivotal trial is expected to begin during 2019, program funded by U.S. government
- The FDA has cleared Pluristem's Investigational New Drug (IND) application for PLX-R18 in the treatment of ARS in case of nuclear events
- FDA Orphan Drug Designation
- Hematological Program

Ongoing Phase I clinical trial of R18 for the treatment of **insufficient hematopoietic recovery following bone marrow transplantation**

- N= 24
- Open-label trial allows for interim data analysis
- Clinical sites in U.S and Israel
- FDA Orphan Drug Designation



Bone Marrow Recovery Data (via the FDA Animal Rule, ARS program)



Acute Radiation Syndrome (ARS)

Collaboration with U.S. Government



- Phase I and II-equivalent studies were conducted and funded by U.S. government (NIAID), to evaluate PLX-R18 as a treatment for exposure to radiation
- Pluristem has 2 ongoing projects with the U.S. Department of Defense (DOD) to examine PLX-R18 as a treatment for exposure to radiation and for the treatment of mustard gas injuries

PLX-R18 advantages for government stockpiling

- Allogeneic, off-the-shelf product with long shelf life
- Easy IM administration
- No need for prescreening no effect if injected to those who were not exposed to radiation
- Supports recovery of all three blood lineages (red and white blood cells and platelets)
- ✓ Beneficial even when administered 48 hrs. following exposure to radiation
- Multifactorial secretion profile may treat other injuries to tissues potential for use in a broad spectrum of indications



Collaboration with Fukushima Medical University



Evaluating PLX-R18 cells as a treatment for radiation damage to the gastrointestinal (GI) tract and bone marrow

- 50% Increase in survival rate
- preserve GI stem cells activity to enhance recovery of the GI system and prevent severe damage to the intestinal lining
- Significantly reduced weight loss
- Increased white blood cell and platelet counts

Suggesting PLX-R18 potential as a multi-organ therapy for radiation exposure



Significant increase in Ki-67+ cells in the crypt base with PLX No OLFM-4 on CBC cells at the Crypt bottom with PLX Red arrow - losing crypts structure

Commercialization Strategy

- Direct sales to specialty centers, post-pivotal-data out-licensing deals
- 2. Direct sales for indications with small patients population & high market price
- 3. Direct sales of PLX-R18 product for Acute Radiation Syndrome (governments)







Management Team



Zami Aberman Chairman & Co-CEO







Erez Egozi <mark>CFO</mark>



Racheli Ofir, Ph.D. VP Research & Intellectual Property



Karine Kleinhaus, M.D., MPH Divisional VP, North America



Yaky Yanay President & Co-CEO



Dan Peres VP Medical & Clinical Affairs



Lior Raviv VP Development



Boaz Leshem VP Operations & Manufacturing



Orly Amiran VP Quality Assurance





Investor.relations@Pluristem.com



www.Pluristem.com



