מפגש פלוריסטם מאי 2015

הישגיים רגולטורים משמעותיים וקיצור זמן הגעה לשוק

המפגש יתקיים ביום שני ה-25 במאי, 2015
בשעה 8:30 במרכז הכנסים
הבורסה לניירות ערך
רחוב אחוזת בית 2, תל אביב

לו"ז הכנס

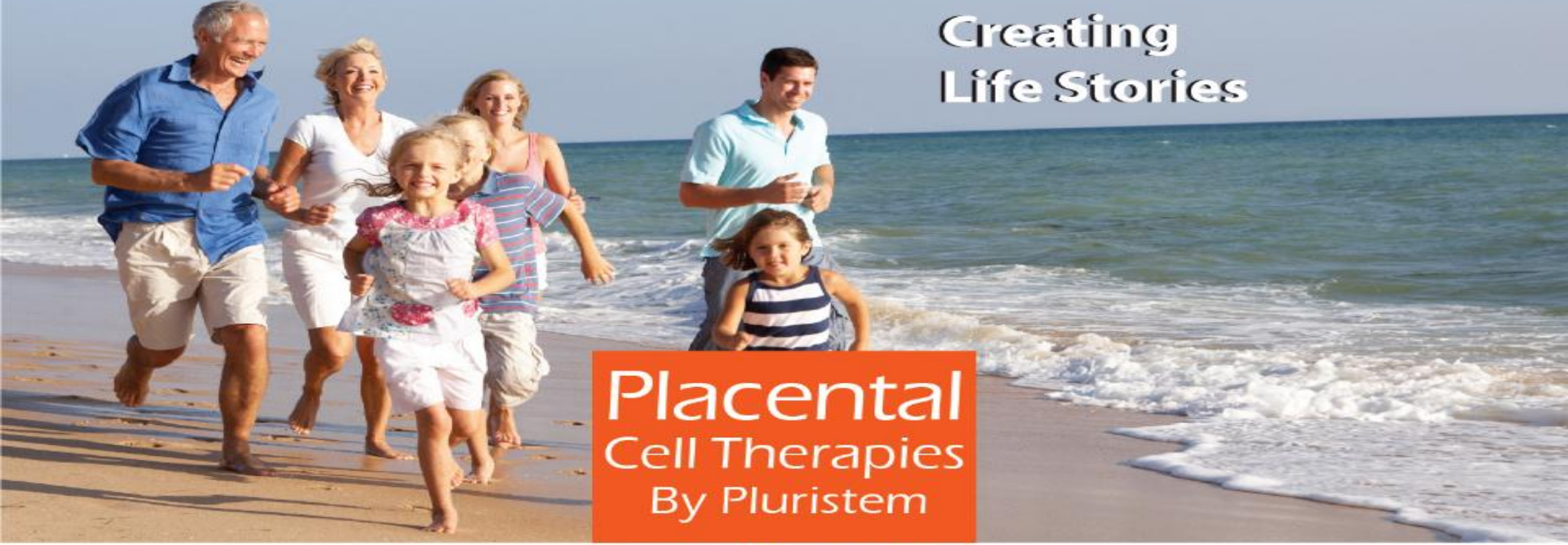
8:30 התכנסות וכיבוד

9:00 זמי אברמן, מנכ"ל ויו"ר פלוריסטם
עולם הטיפול התאי- סקירה והתפתחויות

9:30 ד"ר אסתר לוסקביץ-חגי, סמנכ"ל קליניקה ורגולציה פלוריסטם
מנגנונים רגולטוריים חדשים ומשמעותם הקלינית

10:00 יקי ינאי, נשיא פלוריסטם
אז מה עכשיו? אבני דרך, אסטרטגיה וחזון

מספר המקומות מוגבל, הרשמה למפגש זה הינה חובה
אנא אשר השתתפותך ב efratk@pluristem.com
או בטלפון 074-7108600/721



Advancing cell therapeutic products for clinical use

- Placenta-Derived Cell Therapy
- Clinical Studies EMA & FDA
- In-House Manufacturing
- Traceable 3D-Grown Cells
- Specific PLX products
- Patent Protected
- Out-Licensing per Indication or Field

Pluristem Therapeutics Inc.

Forward Looking Statement

This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995 and federal securities laws. For example, we are using forward-looking statements when we discuss moving closer to reaching our objective to bring innovative, effective treatments to patients, when we discuss the timing of receiving marketing approval for our product candidates, if at all, and the forecasted worldwide sales of our product candidates, when we discuss the potential and timing of achieving regulatory approval for our product candidates via the EU Adaptive Pathway or other expedited regulatory pathways, regarding future collaboration with other pharmaceutical companies, when we discuss anticipated milestones regarding our regulatory approach and the development of current and future product candidates, including the timing and design of future clinical trials, and whether such trials will be conducted at all. These forward-looking statements and their implications are based on the current expectations of the management of Pluristem 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 surgical 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 the actual results or performance of Pluristem to differ materially from those contemplated in such forward-looking statements. In addition, historic results of scientific research do not guarantee that the conclusions of future research would not suggest different conclusions or that historic results referred to in this presentation would not be interpreted differently in light of additional research or otherwise. Also, while the company's program was selected for the European Medicines Agency's Adaptive Pathways pilot project, as well as recognized by the PMDA, these agencies are not bound by these communications and accordingly may change their position in the future due to reasons within or outside the control of Pluristem. Except as otherwise required by law, Pluristem undertakes 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 Pluristem, reference is made to Pluristem's reports filed from time to time with the Securities and Exchange Commission.

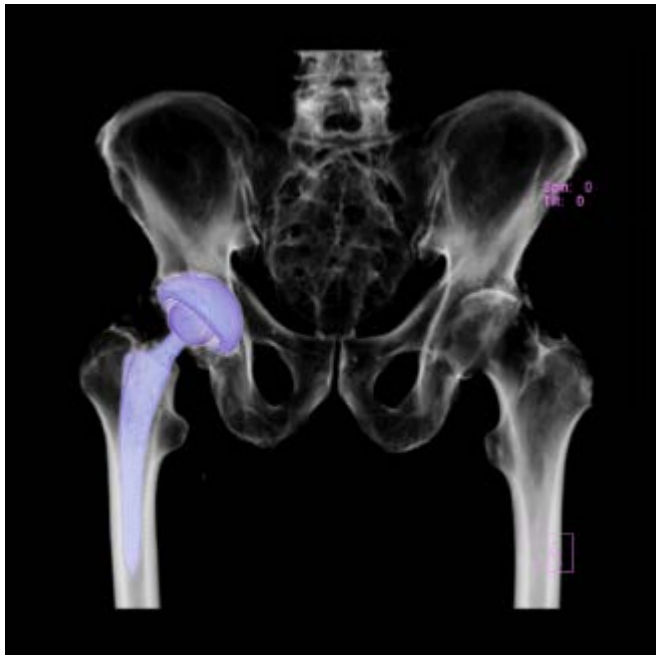
Corporate Overview

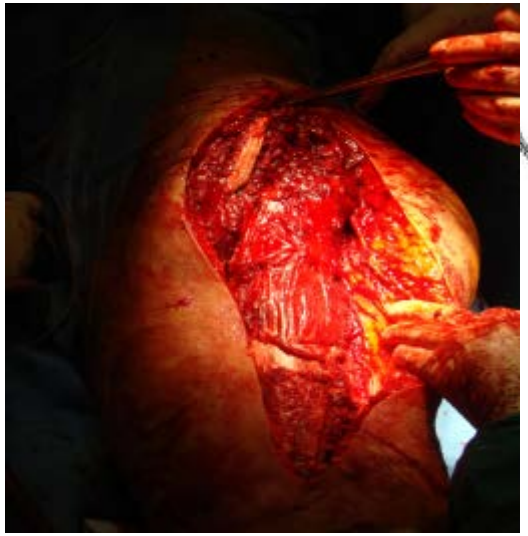
- Cell therapy company (NasdaqCM: PSTI, TASE: PLTR)
- Using off-the-shelf placental expanded cells to achieve both local and systemic therapeutic effects
- First in class 3D cell culturing technology allowing for efficient, controlled production of different cell products in commercial quantities – “the process is the product”
- Active with regulators in the U.S., EU, Japan, Korea, Australia and Israel

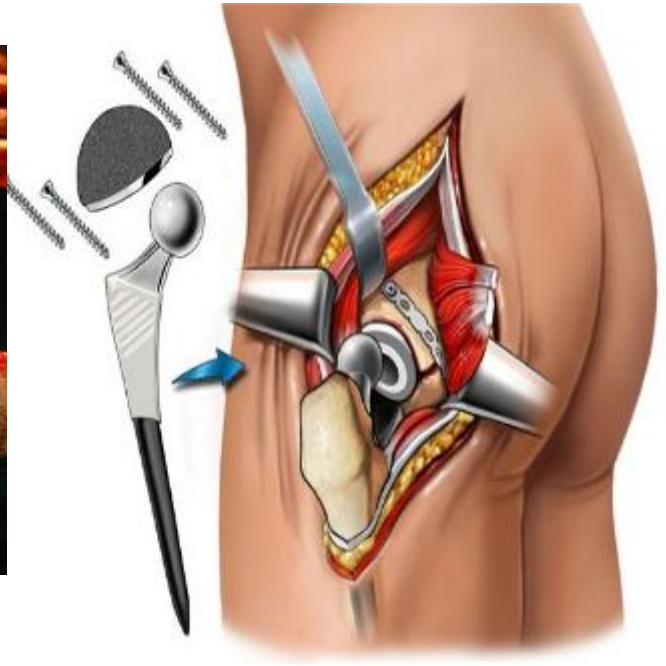
- **Demonstrated clinical safety and significant efficacy in 3 clinical studies (Two Phase I and one Phase I/II study)**

Strong Clinical Data

Muscle Injury following Total Hip Replacement N=20





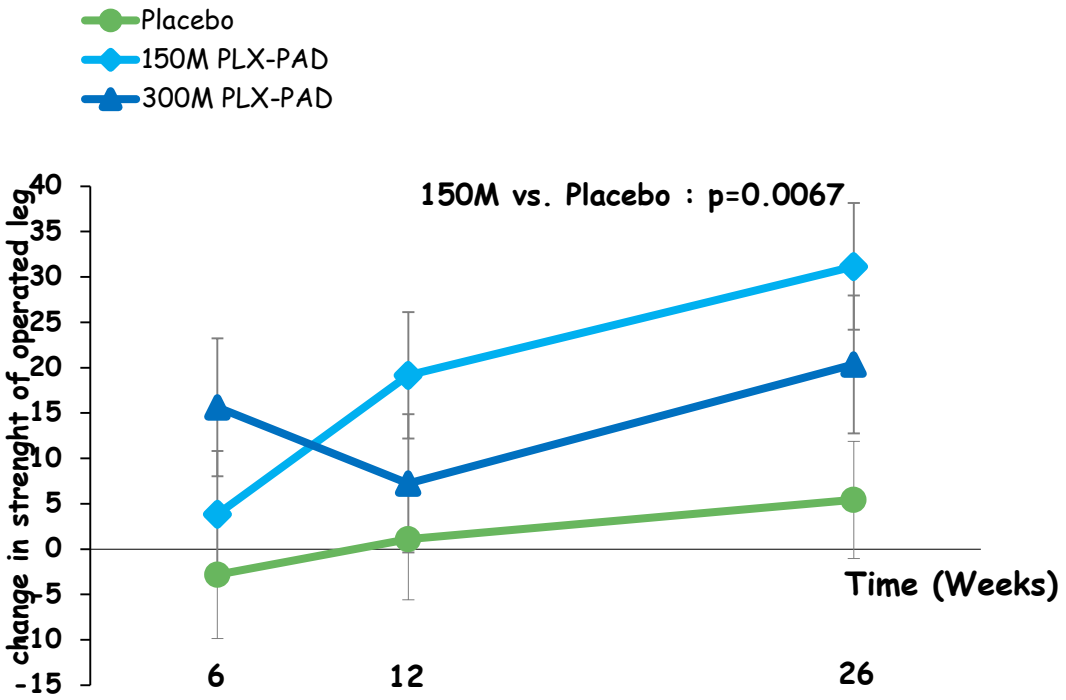


CHARITÉ

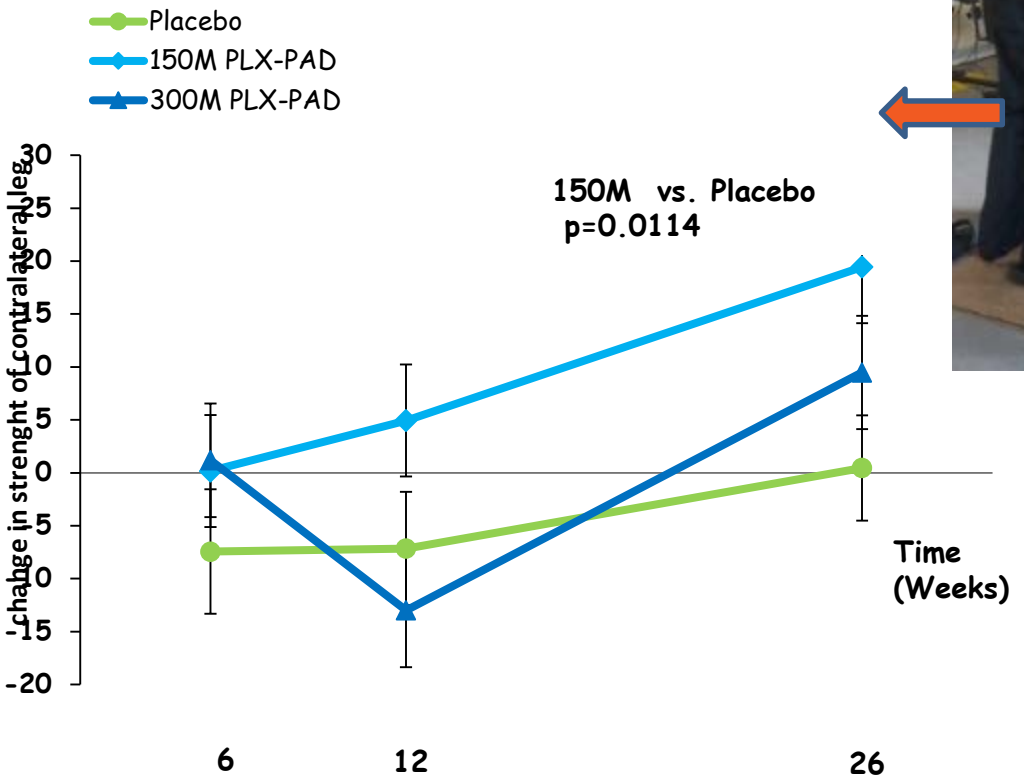
JULIUS WOLFF INSTITUT

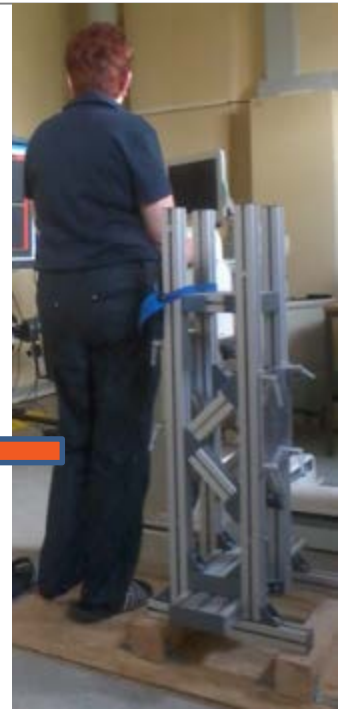
Correlation Between Improvement in the Muscle Force of Injured and Contralateral Leg

Injured (operated)



Contralateral (non–operated)





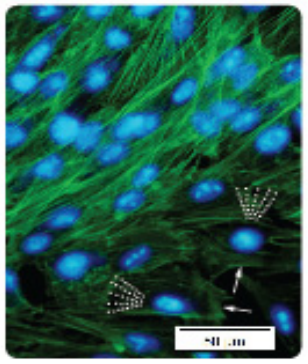
PLX Technology

Following child-birth, cells are extracted from the Placenta

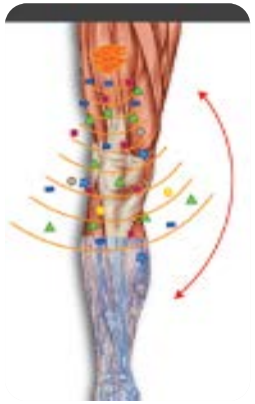
Cell growth in a proprietary platform in a State-of-the-art GMP manufacturing facility

PLX cells are frozen & stored, readily available for use

Point of care thawing device, to assure cells' quality, prior to administration



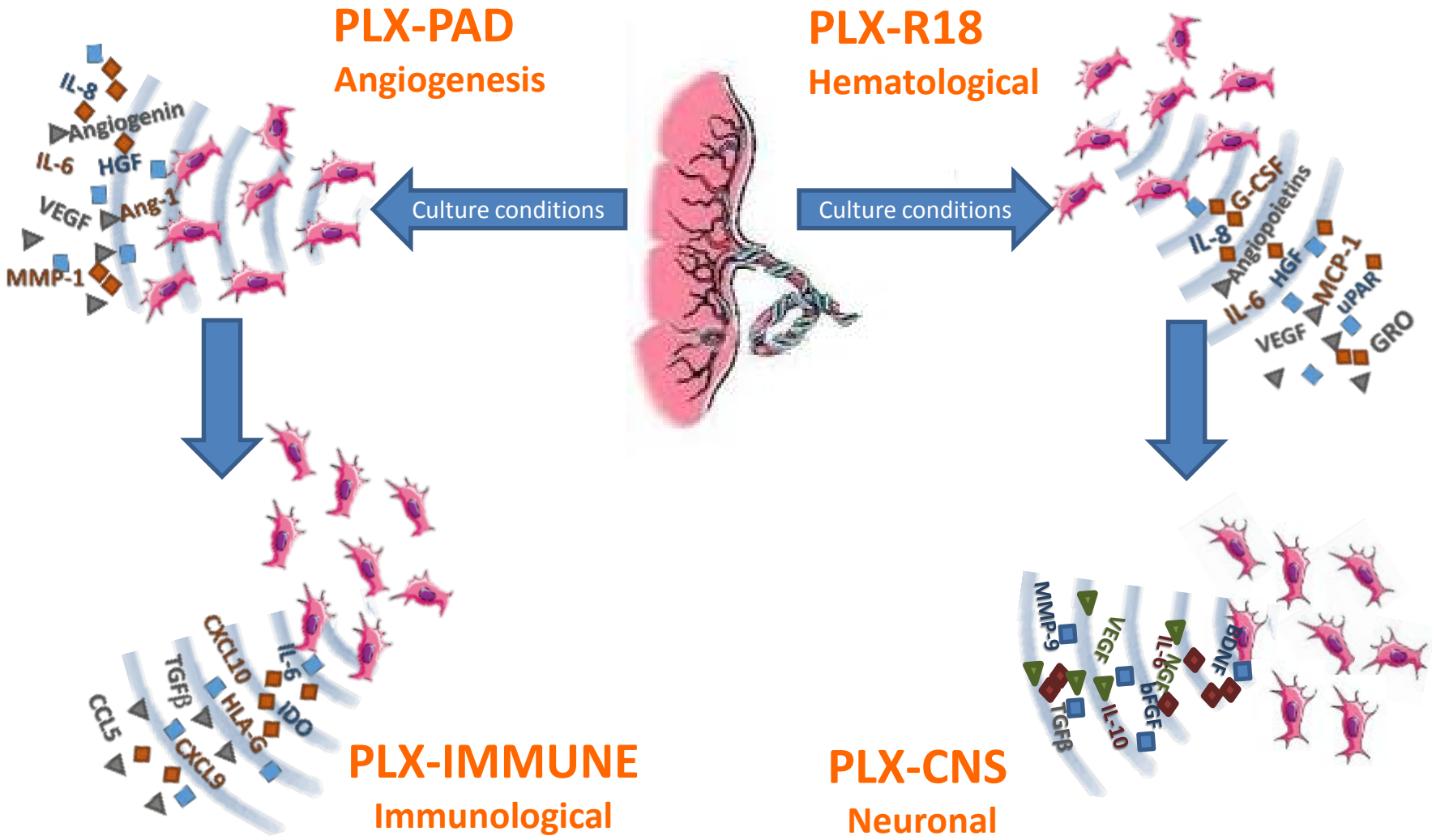
PLX cells release therapeutic proteins in response to signals within the patient's body



The proteins released by the PLX cells help the body heal itself, creating life stories

Human Placenta- A platform for distinct cell products

Four Distinct Products Derived from Placenta

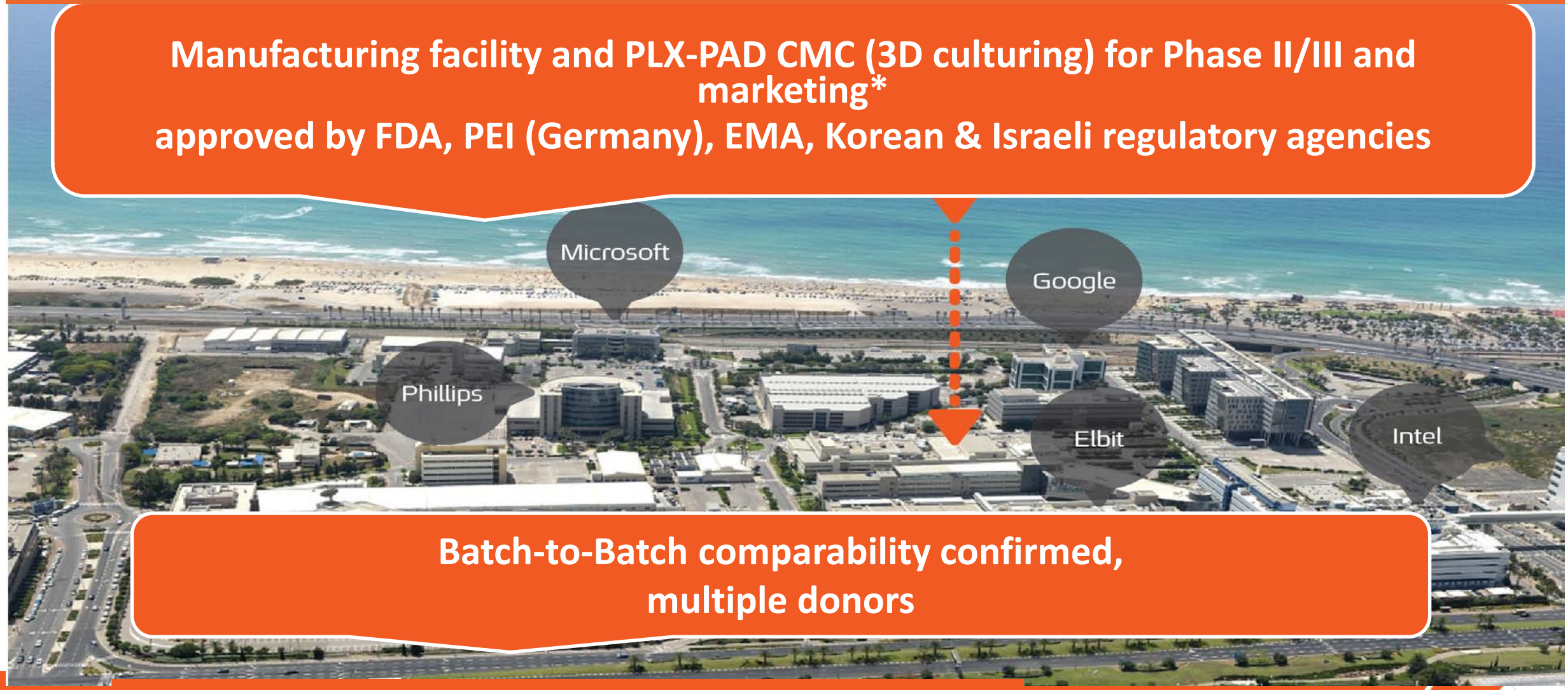


PLX-PAD CMC approved by 5 Regulatory agencies

Powered by Pluristem

Manufacturing facility and PLX-PAD CMC (3D culturing) for Phase II/III and marketing*

approved by FDA, PEI (Germany), EMA, Korean & Israeli regulatory agencies



Batch-to-Batch comparability confirmed, multiple donors

* Subject to supplier approval

Pluristem's Pipeline

Indication	Pre-Clinical	Phase 1	Phase 2	Phase 3	Market	Partner
PLX-PAD						
Critical Limb Ischemia (CLI)	→	→				CHA Biotech [1]
Intermittent Claudication (IC)	→	→	→			CHA Biotech [1]
Muscle Injury	→	→	→	→		
Pulmonary Arterial Hypertension	→	→	→			United Therapeutics [2]
Preeclampsia[3]	→	→				
PLX-R18						
Bone Marrow Transplant Failure[4]	→	→				
Acute Radiation Syndrome[5]	→	→				
Support for Hematopoietic Cell Transplantation[6]	→	→				

[1]CLI/IC license for the South Korean market only
[2]Worldwide PAH license
[3]Currently addressing FDA request for additional preclinical studies before Phase I
[4]Compassionate use treatment (with PLX-PAD)
[5]Supported by the NIH (NIAID). Animal Rule pathway
[6]Umbilical cord blood transplantation, peripheral blood cell transplantation, bone marrow transplantation

Pluristem's Pipeline

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PLX-PAD						
Critical Limb Ischemia (CLI)	→	→	→			
Intermittent Claudication (IC)	→	→	→			
Muscle Injury	→	→	→			
Pulmonary Arterial Hypertension	→	→				
Preeclampsia[3]	→					
PLX-R18						
Bone Marrow Transplant Failure[4]	→	→				
Acute Radiation Syndrome[5]	→	→				
Support for Hematopoietic Cell Transplantation[6]	→	→				

Selected for EU Adaptive Pathway – potential for marketing approval in 2018

[1]CLI/IC license for the South Korean market only
[2]Worldwide PAH license
[3]Currently addressing FDA request for additional preclinical studies before Phase I
[4]Compassionate use treatment (with PLX-PAD)
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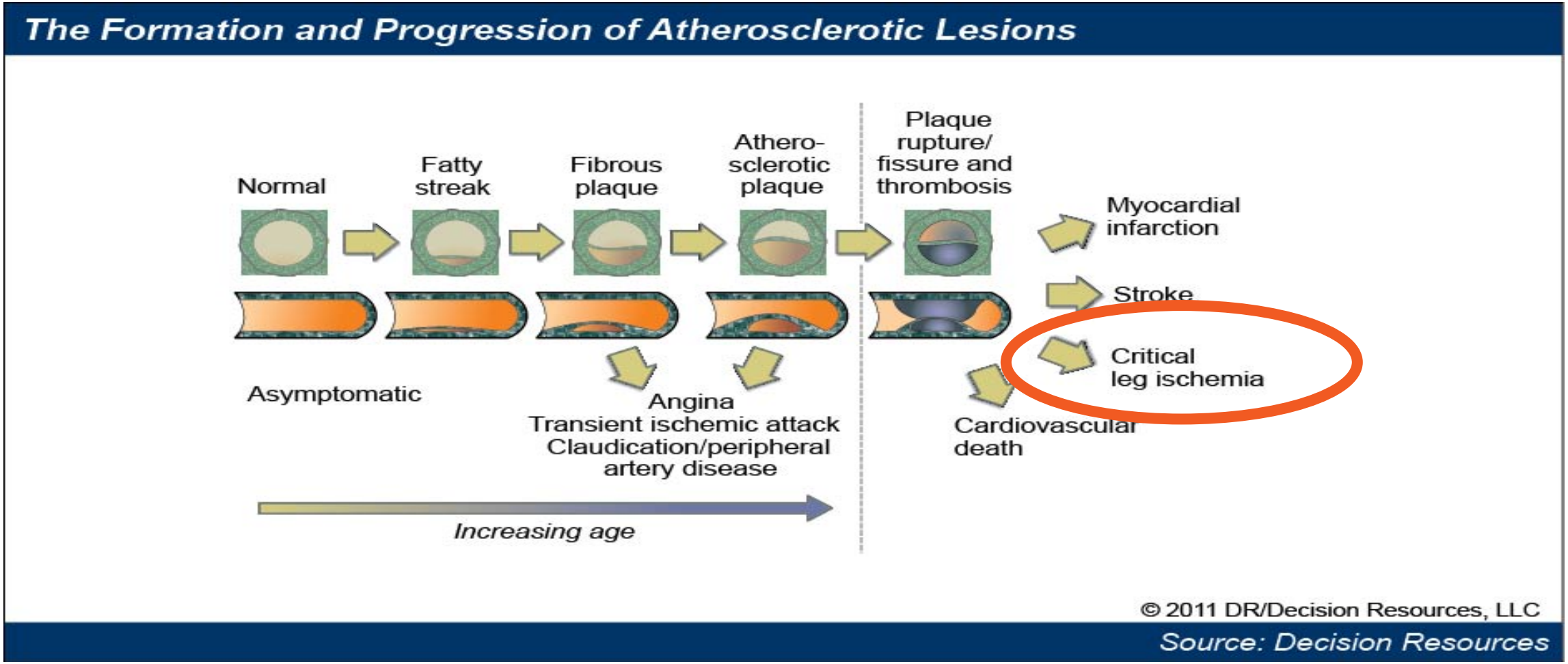
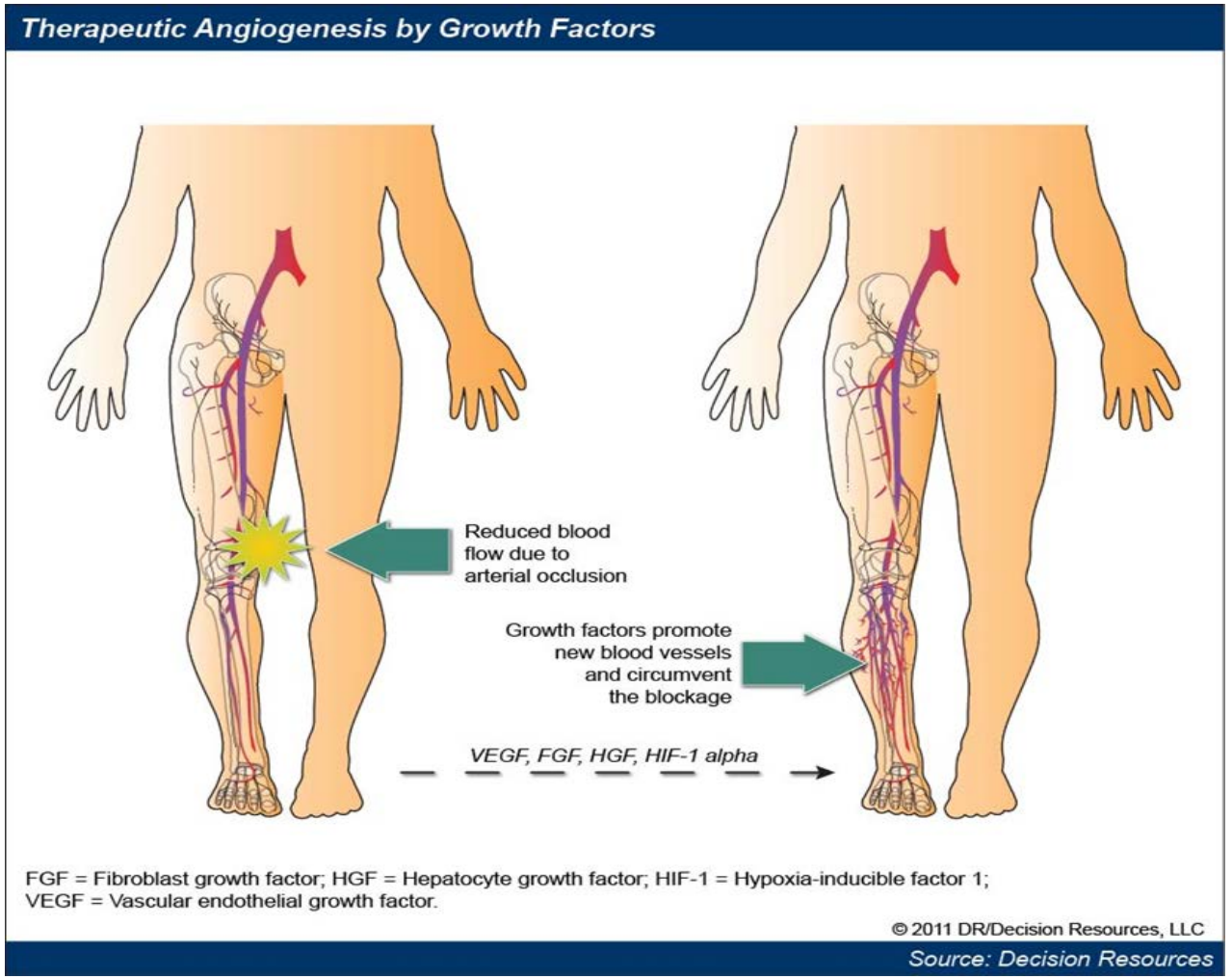
Progression of Atherosclerotic Lesions



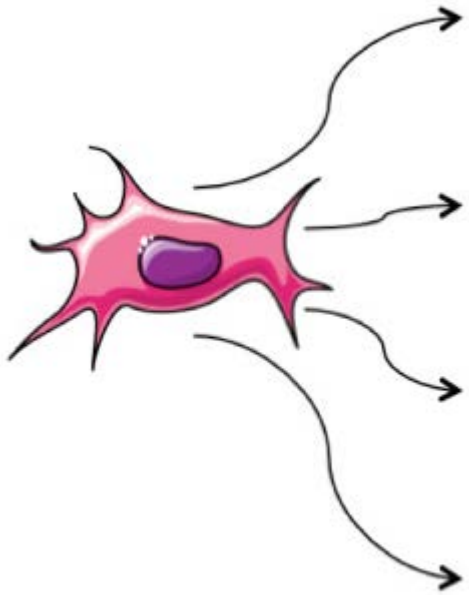
From: Peripheral Arterial Disease. Source: Decision Resources
Created for Hillit Mannor Shachar, Pluristem Therapeutics. IP Address: (Unknown)

Therapeutic Angiogenesis by Growth Factors



From: Peripheral Arterial Disease. Source: Decision Resources
Created for Hillit Mannor Shachar, Pluristem Therapeutics. IP Address: (Unknown)

PLX-PAD secretion profile



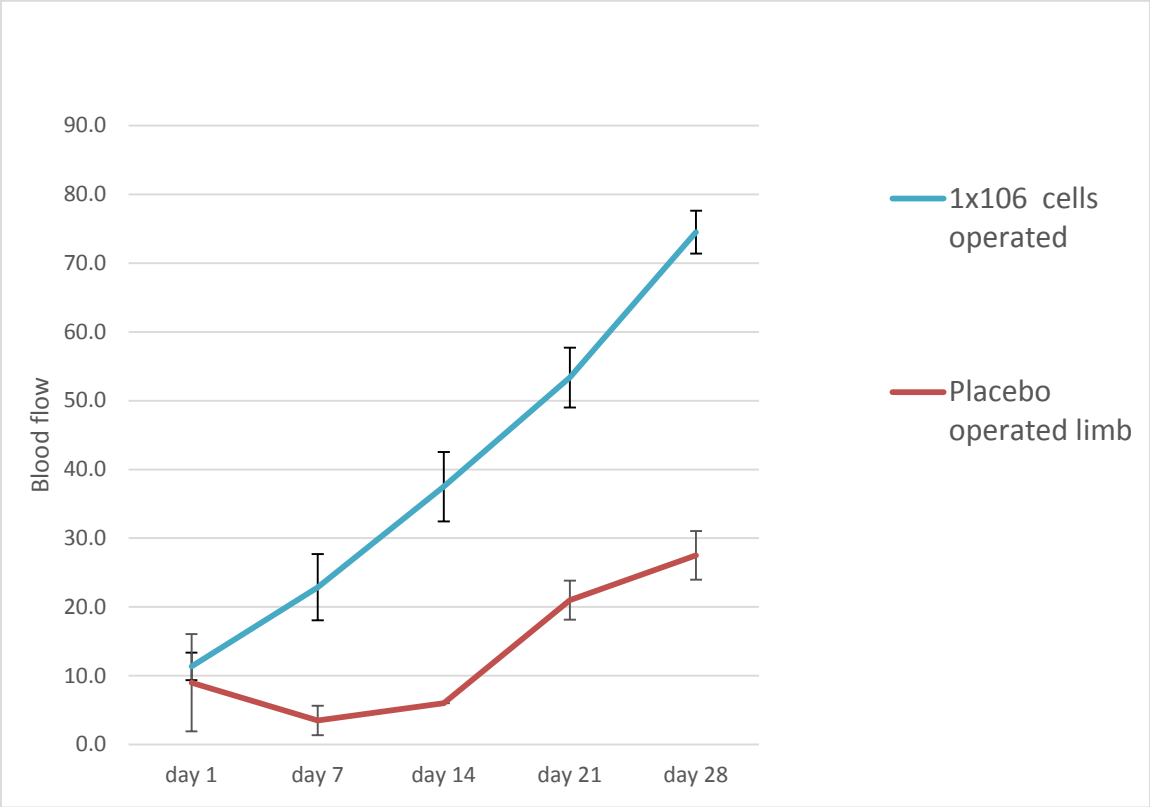
Proangiogenic VEGF, HGF, TGFβ, Angiogenin, IL-8, Angiopoietin, IL-6, MMP-1, TIMP-1, PAI-1, IGFBPs,

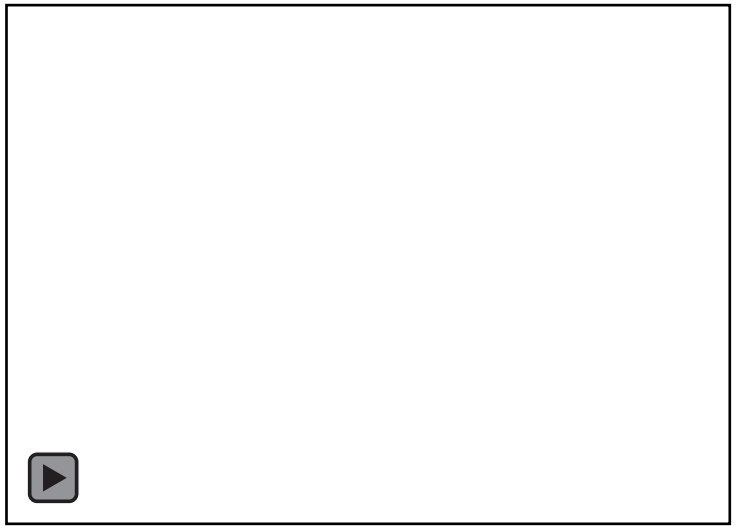
Immunomodulatory HGF, IDO, IL-28, IL-22, IL-10RA,

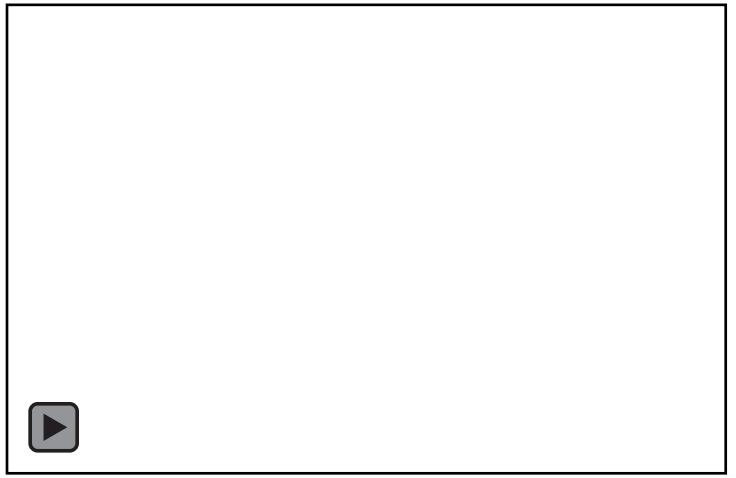
Antifibrotic HGF, Decorin

Protrophic- LIF, Angiopoietin, b-NGF

PLX-PAD increased blood flow in the tibia





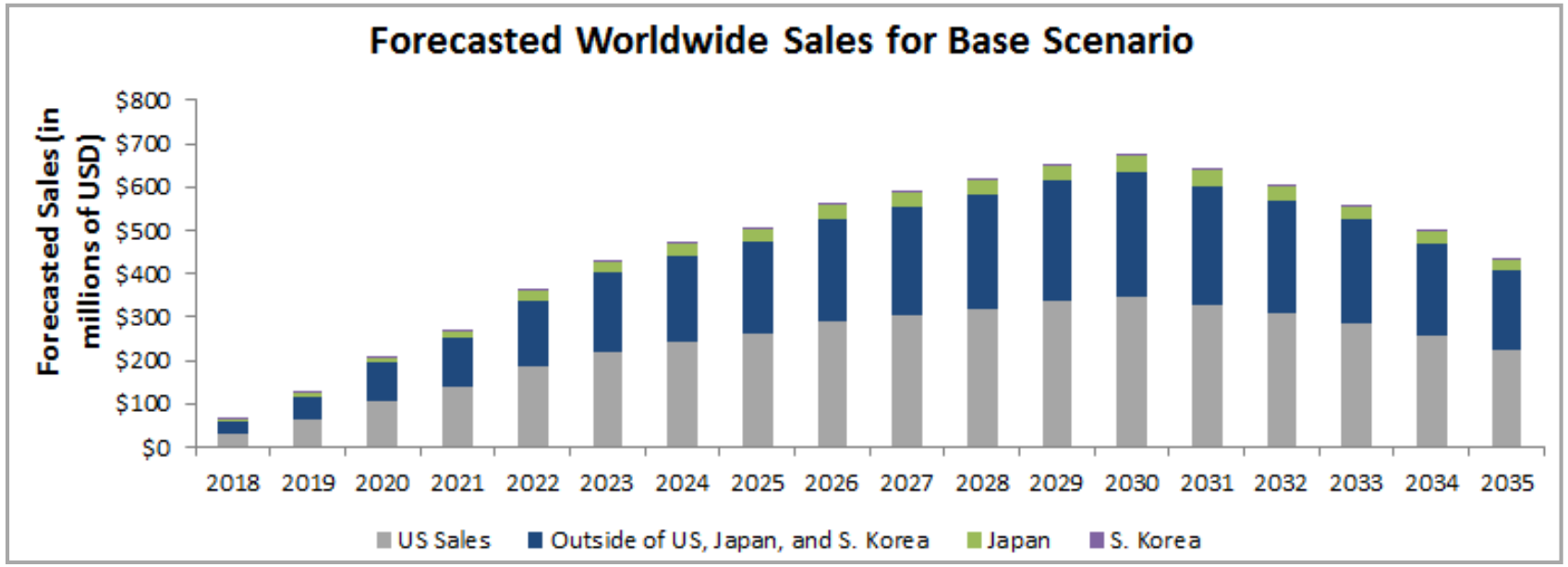


Live Cellvizio imaging following IV administration of FITC labeled Dextran

PLX-PAD in Peripheral Artery Disease

- **July 2009 – First CLI patient injected in Berlin (N=15)**
- October 2010 – last CLI Patient injected in US (N=12)
- April 2012 – EMA declaration - Adaptive Pathways program
- May 2012 – End of 2 years patients safety follow-up in Europe
- **April 2012 – EMA initiated the Adaptive Pathways program**
- December 2012 – Initiation of IC Phase II clinical study (N=150)
- March 2014 - Pilot project launched by EMA
- **May 2014 – Approval of the new facility, ready for Phase III and marketing**
- **May 2015 - PLX-PAD cells have been selected for the Adaptive Pathways pilot project**

NPV - Base Scenario Peak sales in 2030



Peak worldwide sales: ~$700M

Peak US sales: ~$350M

Peak Europe sales: ~ $290M

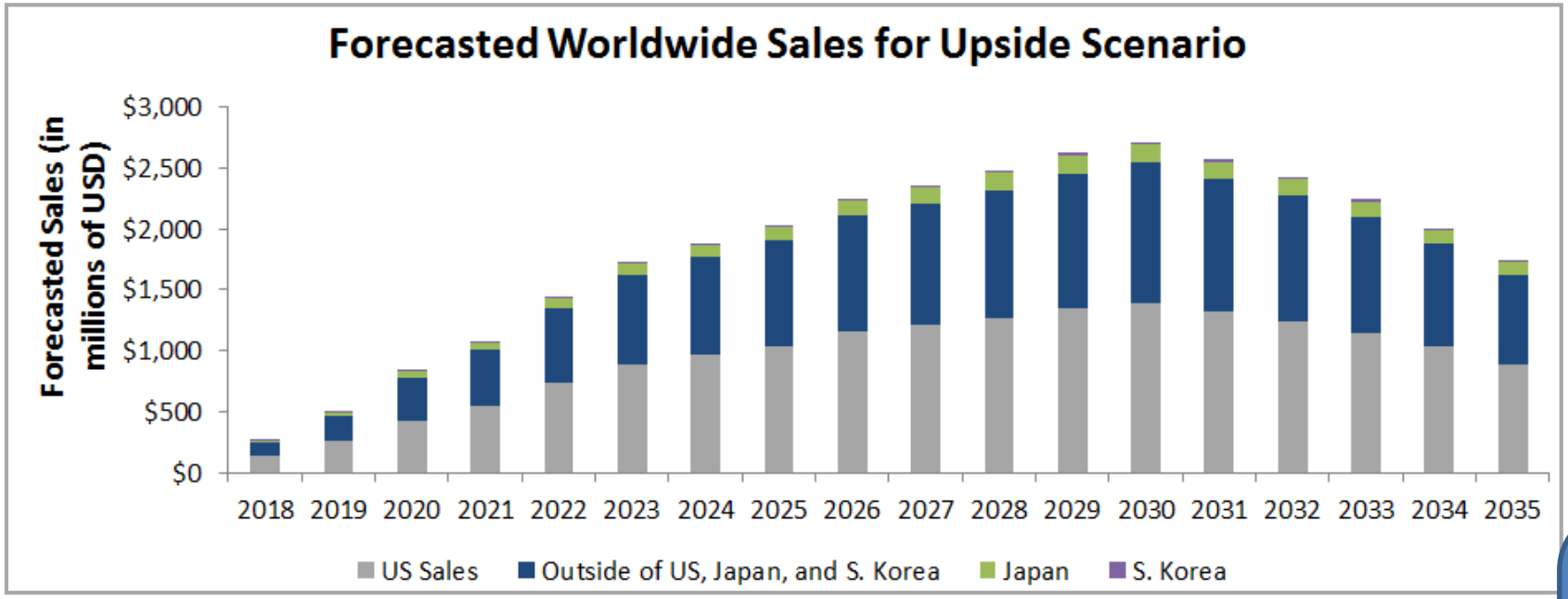
NPV for CLI WW sales is: $2,100M

NPV for CLI Sales in Europe : $850M

Without the EMA approval, Peak sales in 2033. Reduce the NPV by $200M (~25%)

In the base scenario, PLX-PAD has the potential to achieve peak sales of ~$350M in the US And ~ $290M in Europe

NPV Upside Scenario Peak sales in 2030



Peak worldwide sales: ~$2.7B

Peak US sales: ~$1,400M

Peak Europe sales: ~ $1,000M

NPV for CLI WW sales is: $8,300M

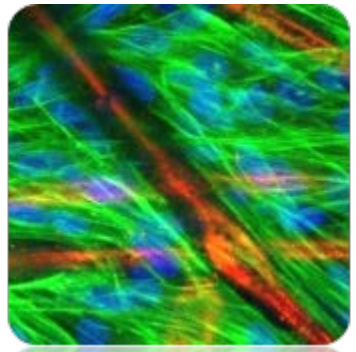
NPV for CLI Sales in Europe : $3,100M

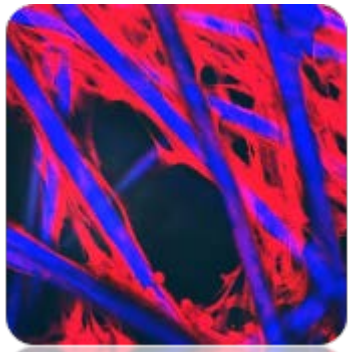
Without the EMA approval, Peak sales in 2033. Reduce the NPV by $700M (~ 25%)

In the upside scenario, PLX-PAD has the potential to achieve peak sales of ~$1.4B in the US and ~$1B in Europe

PLX-PAD CLI program status in Europe

- **3-4 years earlier in a multi-billion market**
- Manufacturing facility approved and inspected by European Qualified Person for Phase III and marketing
- Granted European patent for the use of PLX in ischemic disease
- Higher probability for a large pharma deal
- **EMA new approach to expand the use of PLX-PAD to additional indications within PAD and other ischemic indications**





Cell therapy – the next generation of biological therapeutic products

Celgene
Committed to improving the lives of patients worldwide®

Genentech
IN BUSINESS FOR LIFE

AMGEN®

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Divisional VP, North America

Yaky Yanay
President & COO

Hillit Mannor Shachar, M.D., M.B.A.
VP Business Development

Ohad Karnieli, Ph.D., M.B.A.
VP Technology & Manufacturing

Esther Lukasiewicz Hagai, M.D., Ph.D.
VP Clinical & Medical Affairs

Orly Amiran
VP Quality Assurance

New Regulatory Approaches for Accelerated Approval of PLX-PAD in Critical Limb Ischemia

Dr Esther Lukasiewicz-Hagai, MD, PhD

VP Medical and Clinical Affairs

Introduction

- **Pluristem is highly committed to provide early access of PLX-PAD to Critical limb ischemia (CLI) patients all over the world**

- **Pluristem is taking advantage of each new regulatory opportunity to achieve this goal:**

  - **In Europe**: New Adaptive Pathways pilot project of EMA

    May 2015: PLX-PAD cells have been selected for the Adaptive Pathways pilot project

  - **In Japan**: Accelerated Pathway for Regenerative Medicine

    April 2015: PLX-PAD quality and manufacturing processes agreed with PMDA for use in clinical studies

Completed, ongoing and planned studies in PAOD

- 2 completed Phase I studies in Critical Limb Ischemia (n= 27)
- 1 ongoing Phase 2 study in Intermittent claudication (n=150)
- 2 planned studies in CLI:
  - ✓ 1 Phase II/III in Europe via Adaptive Pathways
  - ✓ 1 Phase I/II in Japan through Expedited Approval for Regenerative Therapy

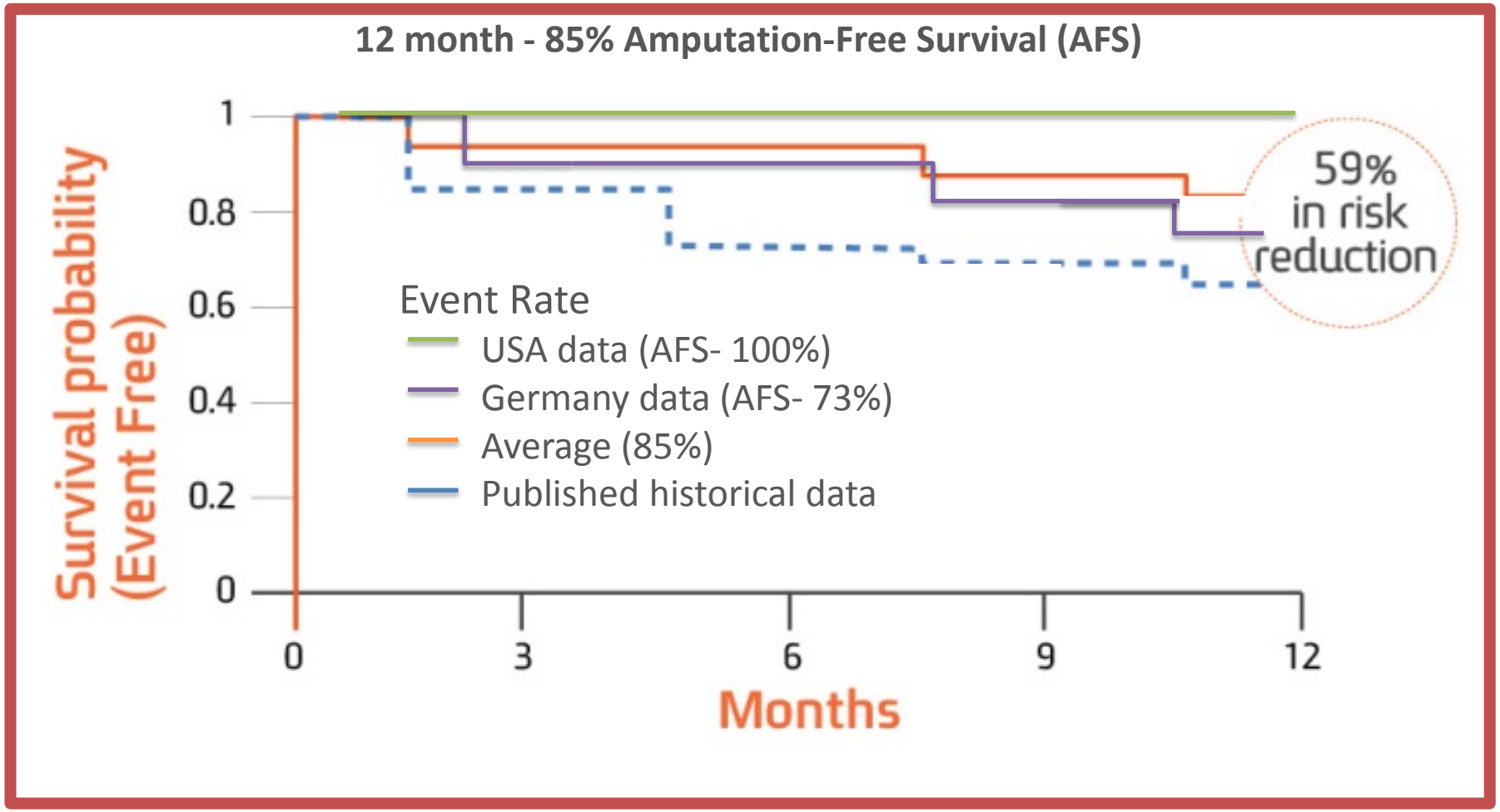
Completed Phase I Studies in CLI

- Two open label, dose-escalation, Phase I studies in patients with CLI Rutherford category 4 (pain at rest) or 5 (minor tissue loss)

PLX-PAD dose	U.S. study n=12 (8 Ruth 4/4 Ruth 5)	German study n=15 (9 Ruth 4/6 Ruth 5)
200x 10^6	-	Single course 50 injections (n=3)
300x 10^6	Single course 30 injections (n=5)	Single course 50 injections (n=6)
600x 10^6	2 courses of 300 10^6 at 2 weeks apart (30 injections per course) (n=7)	Single course 50 injections (n=6)

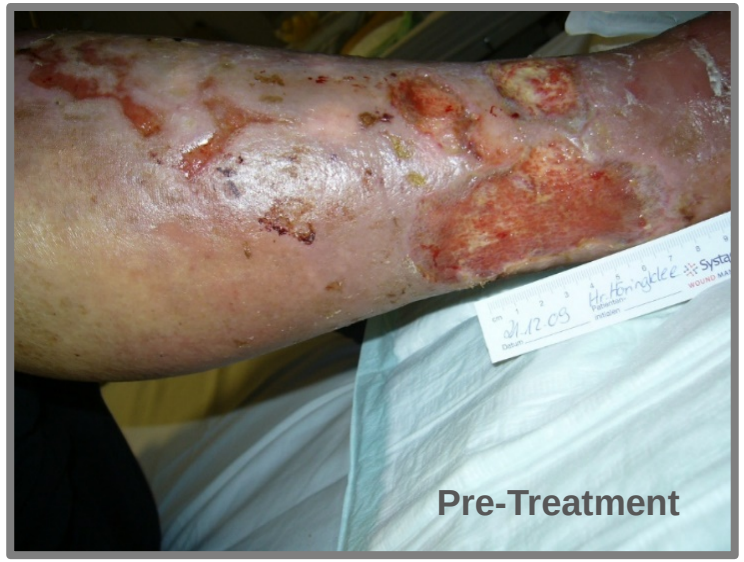
- 12 months FU in US study and 24 months FU in German study

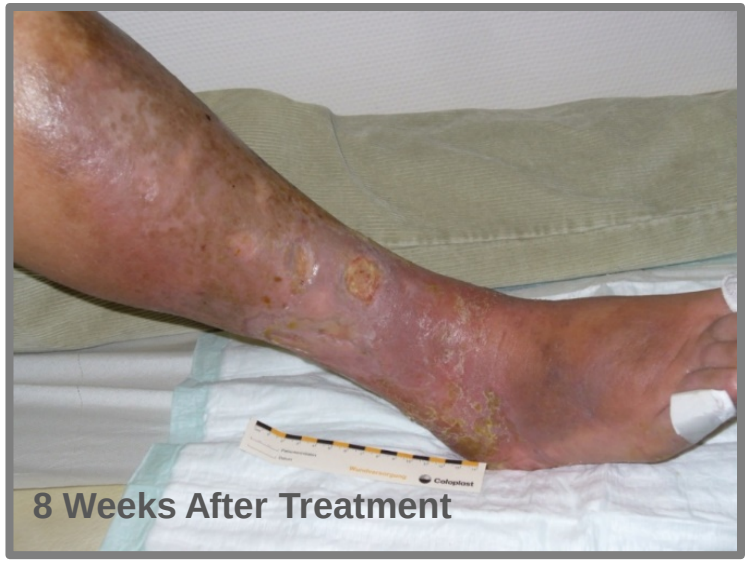
Strong Clinical Data from 2 Phase I/II Critical Limb Ischemia Trials (N=27)



Main studies results

- Good Safety profile
- Trends in efficacy with improvement from baseline in:
  - Transcutaneous Oxygen Pressure (limb perfusion)
  - Quality of Life
  - Pain score





EMA Adaptive Pathways

EMA Adaptive Pathways - Background

Pilot project launched by EMA on March 19th, 2014 :

- European initiative intended to grant earlier access to drugs meant to treat **debilitating and/or life-threatening** diseases with **unmet medical need**
- Only for Product at an **early stage of clinical development** (during or prior to Phase II)

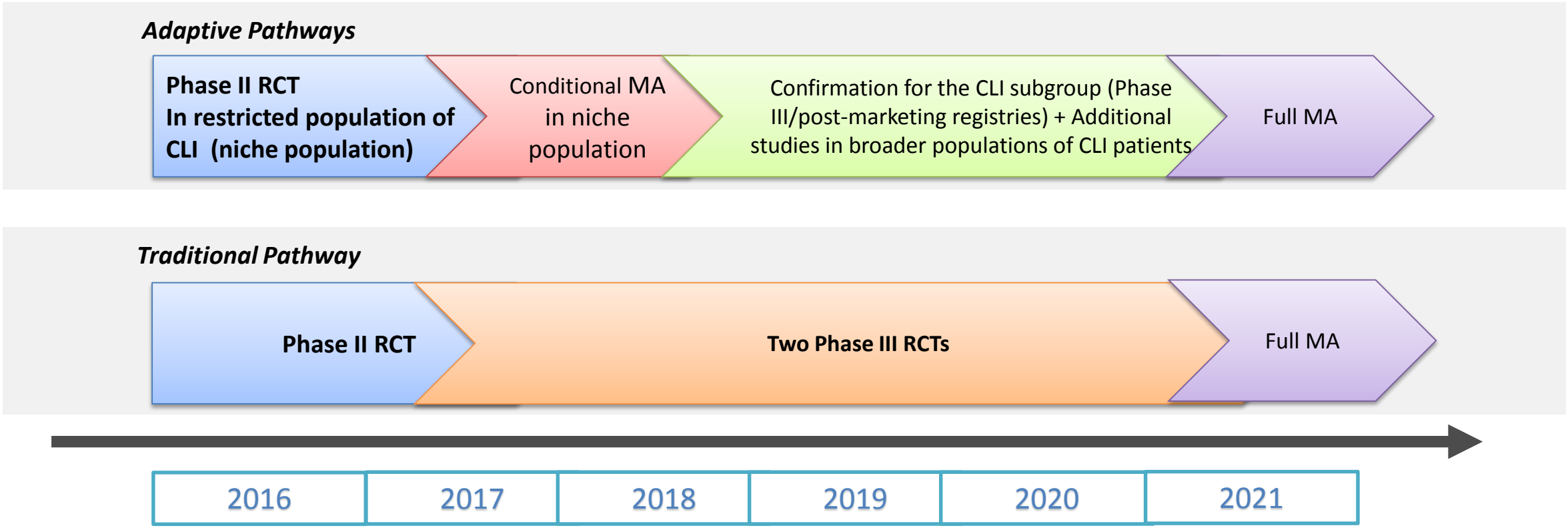
EMA Adaptive Pathways - General principles:

- **Early approval of a drug for a restricted patient population** followed by progressive adaptations of the marketing authorization to expand access to the drug to broader patient populations based on data gathered from its use and additional studies

AND/OR

- **Early regulatory approval** (e.g. conditional approval) with collection of post-approval confirmatory data on the drug's use in patients
- Involves balancing the importance of **timely patient access** with the need for adequate, evolving evidence on a drugs' **risks and benefits**
- Builds on **regulatory processes already in place** within the existing European Union legal framework
- Early discussion between a **wide range of stakeholders** to explore ways of optimizing development pathways: HTA bodies, payers, patients' organizations, physicians' organizations, academic and researchers

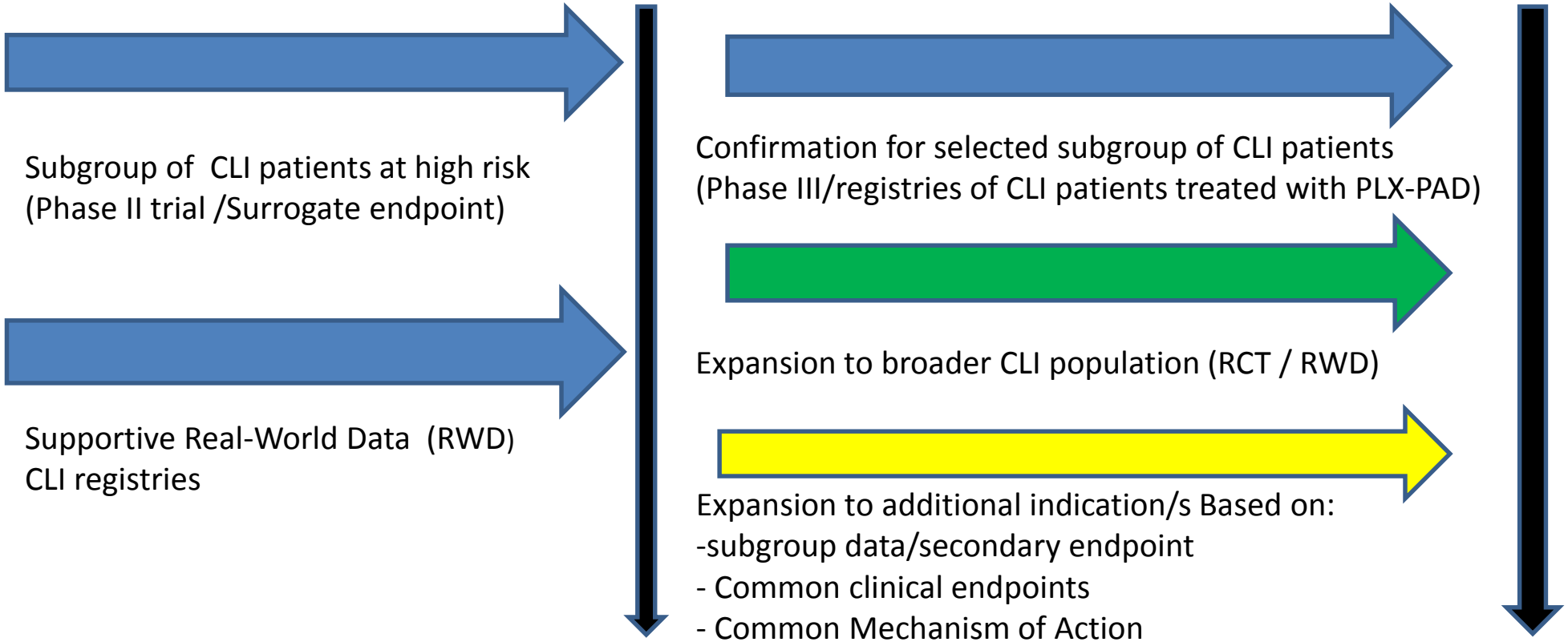
Adaptive vs. traditional Pathway to Market



Adaptive Pathways for PLX-PAD in CLI

- **Severely debilitating and life-threatening disease**: overall 30% of CLI patients have amputations and 25% die by 1 year after diagnosis (higher rates in CLI patients that cannot undergo revascularization)
- **Unmet medical need**: CLI patients who are not eligible for revascularization or have failed revascularization have no treatment option
- Phase I data with PLX-PAD in CLI patients with no option for revascularization showing good safety profile and trends of efficacy
- Safety data from 150 patients enrolled into IC study to support initial approval in CLI
- **Initial Phase II study to get conditional approval in a selected population of CLI patients with high unmet medical need , then post-marketing extension to more CLI patients**
- A surrogate endpoint will most probably be accepted for initial approval (reducing length of the study)

Clinical development of PLX-PAD



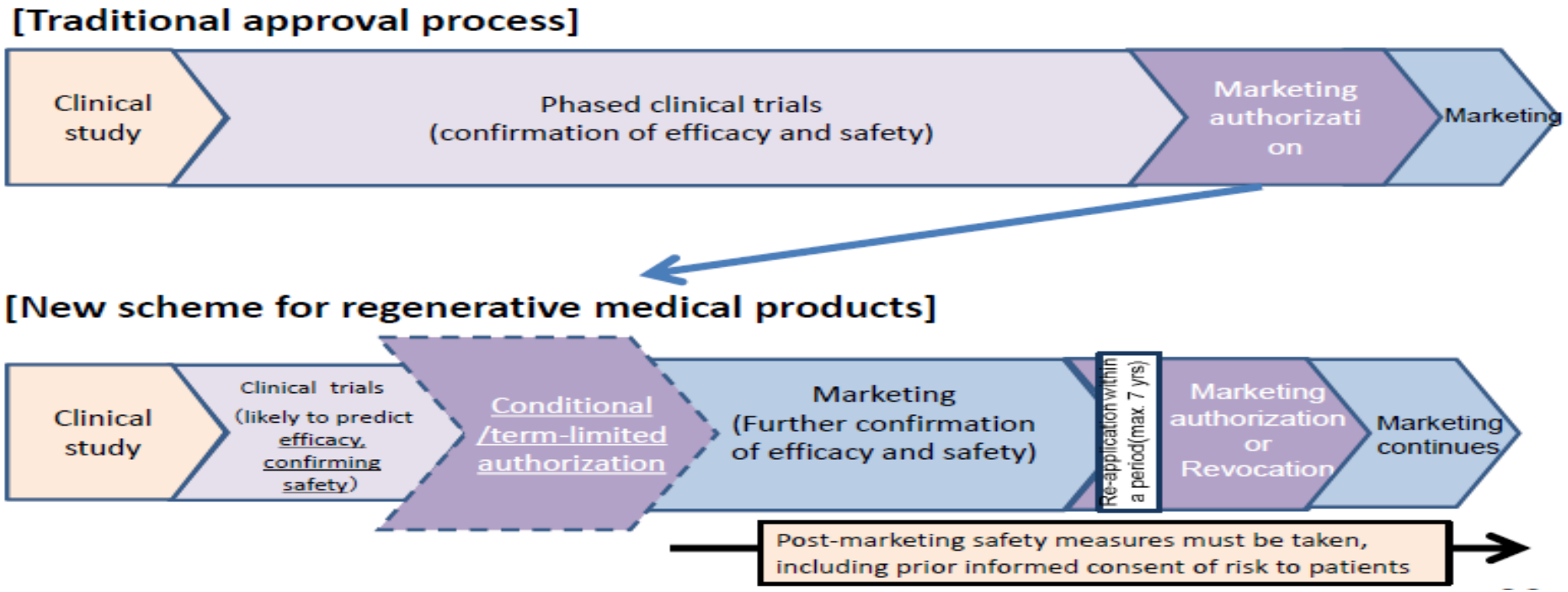
Expedited approval for regenerative therapy in Japan

Background

New Japanese regulations from Nov 2014 to accelerate development of drugs in the field of regenerative therapy:

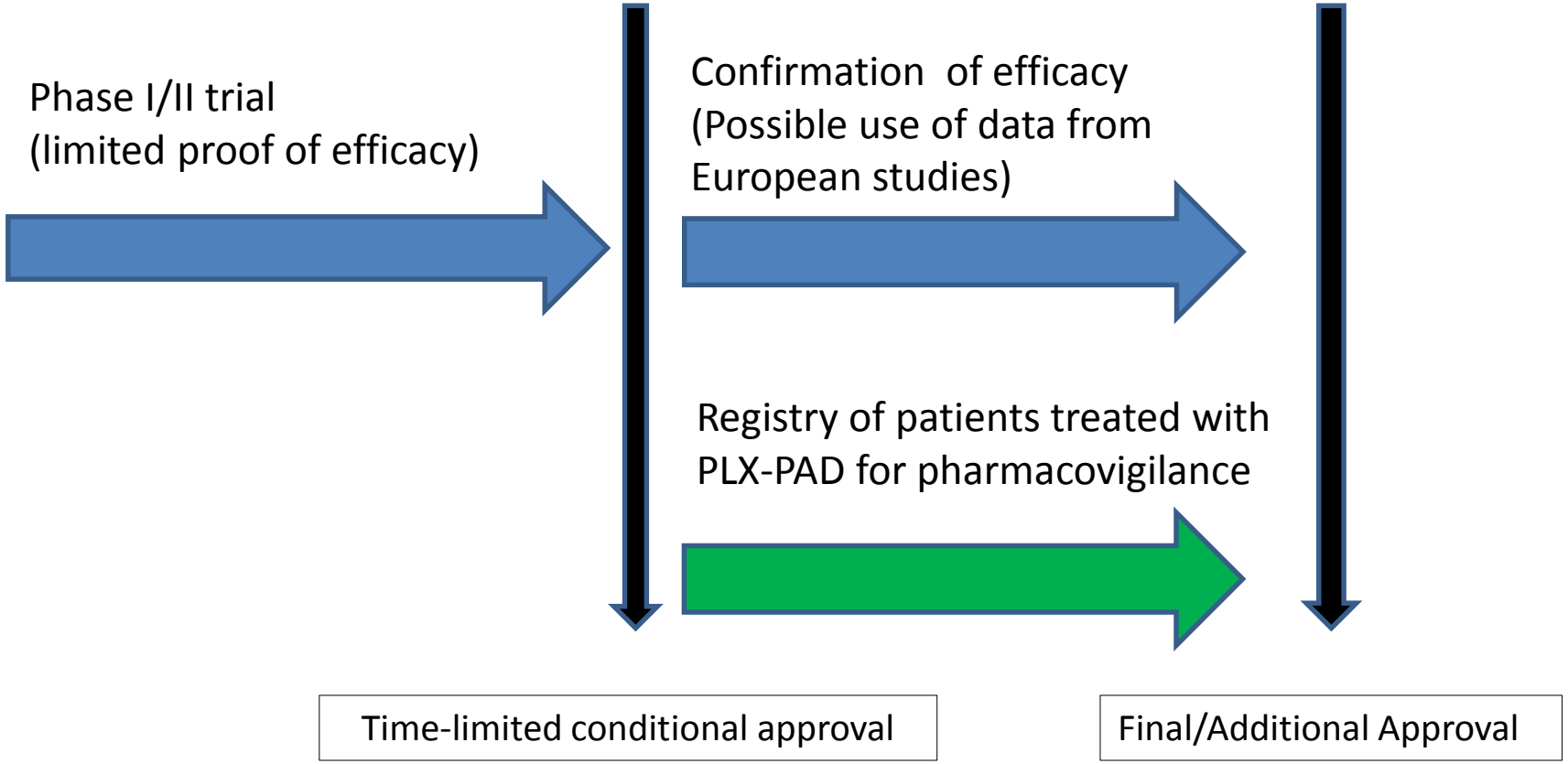
- Only for **Regenerative therapy**
- **Seriously-debilitating / Life-threatening** indication
- **Unmet medical need**

Accelerated vs. traditional approval process



- Conditional time-limited approval can be obtained based on proof of safety and "**limited proof of efficacy**" (Phase I/II, surrogate endpoint)
- Up to 7 years to confirm efficacy post conditional approval
- Condition to have patients treated post conditional approval signed an ICF and registered in a post marketing registry for pharmacovigilance

Clinical development of PLX-PAD for CLI



	2015		2016		2017		2018		2019		2020		2021	
EMA initiation	PIP Waiver													
	ATMP Class.													
	SA on CMC	SA with EMA/HTA												
Phase II/III (EU)		CTA Subm.	Phase II				Phase III/Long term follow up Registry of patients treated with PLX-PAD							
MA (EMA)							CMA				Presub. meeting	MAA subm.	MA Approval	
PMDA initiation	R&D meeting	Pre Phase I/II meeting												
Phase I/II (Japan)		CTN submission	Phase I/II			Safety follow up	Confirmation of efficacy Registry of Patients treated with PLX-PAD							
Conditional Time-Limited Authorization Application (PMDA)					Pre-NDA meetings	CAA subm.	CAA Approval							
Marketing Authorization Application (PMDA)											Pre-NDA Meeting	NDA Subm.	NDA Approv.	

Conclusion

In the framework of the 2 new regulatory approaches that exist in Europe and in Japan , Pluristem plan to initiate 2 clinical studies in CLI in 2016 with the aim of obtaining initial approval already in 2018

So, what's next?

- Time to Market (TTM)- we will be focus on adaptive pathways
  - Europe
  - Japan
  - Our goal is to file early/conditional approval by the end of 2017/early 2018
- Launching PLX-R18 studies for hematology and ARS
- Building platform for new products- serum free based
- Entering into Life changing indication
- Entering into licensing deal

Pluristem's Pipeline

Indication	Pre-Clinical	Phase 1	Phase 2	Phase 3	Market	Partner
PLX-PAD						
Critical Limb Ischemia (CLI)	→	→	→			CHA Biotech [1]
Intermittent Claudication (IC)	→	→	→			CHA Biotech [1]
Muscle Injury	→	→	→	→		
Pulmonary Arterial Hypertension	→	→	→			United Therapeutics [2]
Preeclampsia[3]	→	→				
PLX-R18						
Bone Marrow Transplant Failure[4]	→	→				
Acute Radiation Syndrome[5]	→	→				
Support for Hematopoietic Cell Transplantation[6]	→	→				

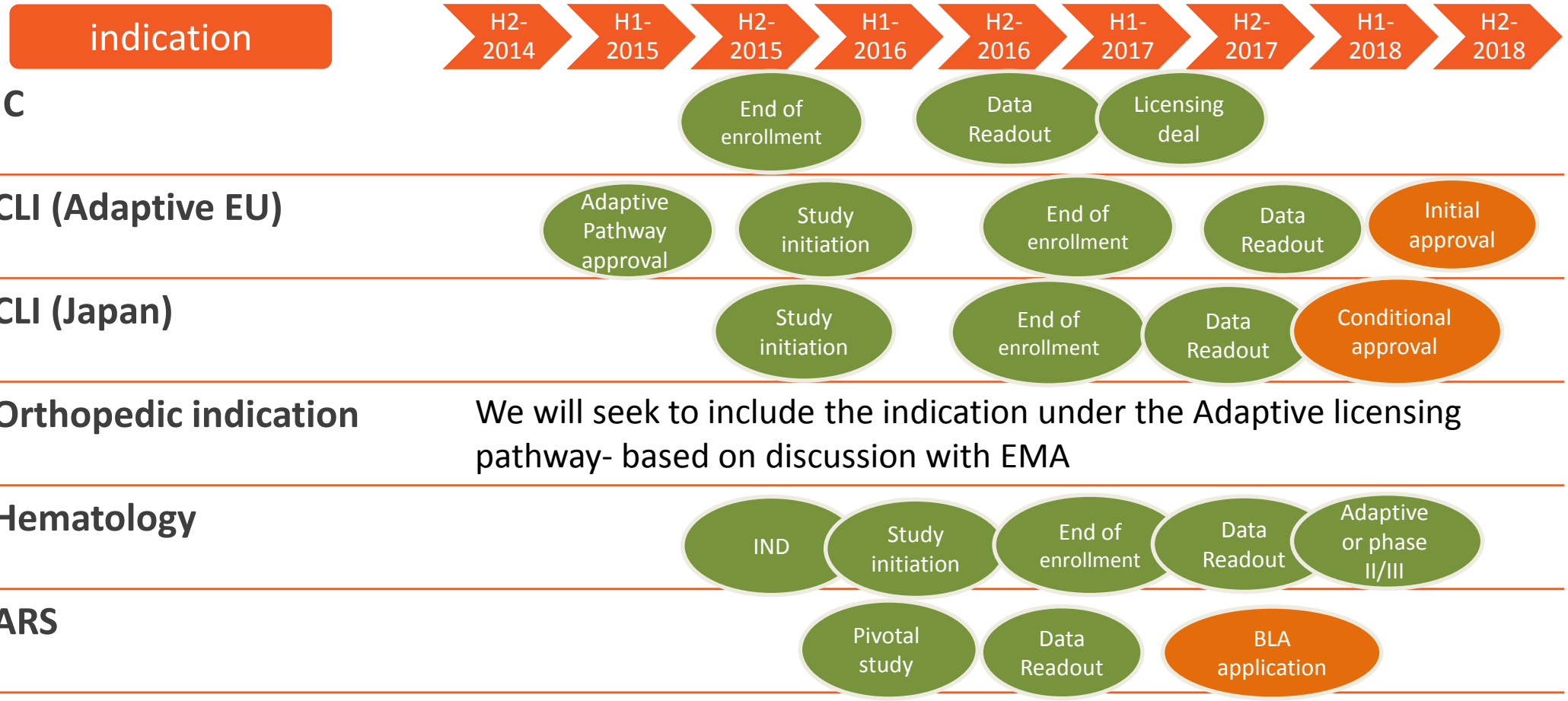
[1]CLI/IC license for the South Korean market only
[2]Worldwide PAH license
[3]Currently addressing FDA request for additional preclinical studies before Phase I
[4]Compassionate use treatment (with PLX-PAD)
[5]Supported by the NIH (NIAID). Animal Rule pathway
[6]Umbilical cord blood transplantation, peripheral blood cell transplantation, bone marrow transplantation

Collaborations

Partner	Indication	Deal structure
United Therapeutics CORPORATION	Pulmonary Arterial Hypertension Worldwide license 	Upfront payment of $7M, additional $48M in milestones, cells supply (cost +) and royalties in gross margin
CHA Biotech	IC, CLI South Korea only	JV following marketing authorization of the Korean authorities
NIH National Institute of Allergy and Infectious Diseases	Acute Radiation Syndrome 	U.S. National Institutes of Health to support development of Pluristem's PLX-R18

Pluristem keeps IP and manufacturing rights in all collaborations

Company milestones



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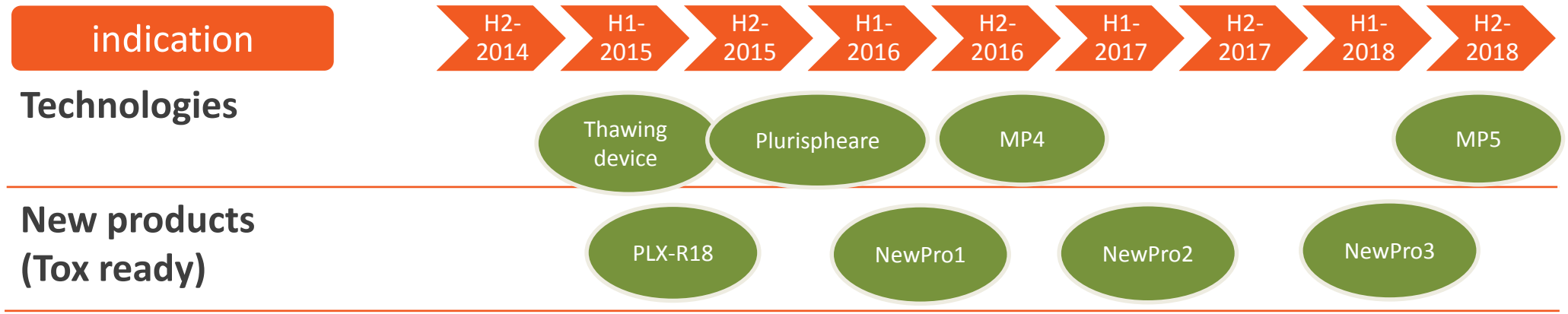
Proprietary data of Pluristem Therapeutics Inc.

Company milestones

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could help people
all over the world?