

#### **ASX ANNOUNCEMENT**

**26 November 2013** 

# Eminent stem cell scientist and Cynata co-founder to speak at local stem cell conference

Cynata Therapeutics Limited (ASX:CYP) is pleased to announce that Cynata Inc's co-founder, Professor Igor Slukvin, will be a keynote speaker at the NSW Stem Cell Network Conference to be held in Sydney on November 29.

Professor Slukvin, from the University of Wisconsin – Madison, has an outstanding international reputation having published more than 70 scientific papers and being an inventor on a range of patents in the fields of regenerative medicine and human pluripotent stem cell biology.

CEO of Cynata Therapeutics, Dr Ross Macdonaldsaid "We are thrilled to have an inventor of our core stem cell technology, Cymerus<sup>TM</sup>, visit Australia to present at this conference and to join us for animportant milestone - the commencement of Cynata Therapeutics"

"Cynata's Cymerus<sup>™</sup> stem cell technology seeks to fill the critical gap in the process of taking stem cells from the laboratory into widespread therapeutic use— it potentially enables the manufacture of billions of human stem cells to facilitate commercial-scale production," said Dr Macdonald.

Professor Slukvin will be in Australia to share his in-depth knowledge of the Cymerus<sup>™</sup> stem cell technology platform and its potential in taking stem cells to market.

Professor Slukvin said "The promise of stem cell therapy has taken many different and exciting paths from that which scientists predicted over ten years ago. Today, there is great promise in human mesenchymal stem cells which work by stimulating the body's own healing and regenerative systems" he said.

The Cymerus<sup>™</sup> technology potentially enables mass production ofmesenchymal stem cells that, subject to further testing, may be used to remedy a broad range of diseases including cardiovascular disease, diabetes, diseases of the blood, lung, kidney and immune system diseases.



In addition to speaking at the NSW Stem Cell Workshop entitled, *Innovating the Marketplace with Stem Cells*, Professor Slukvin will also be participating in a series of investor briefings held by Cynata Therapeutics during his short visit to Australia. A copy of the investor briefing slidedeck is attached to this release.

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#### About Cynata Therapeutics (ASX:CYP)

Cynata Therapeutics Ltd (ASX: CYP) is an Australian stem cell and regenerative medicine company that is developing a therapeutic stem cell platform technology, Cymerus™, originating from the University of Wisconsin-Madison, a world leader in stem cell research. The proprietary Cymerus™ technology seeks to address a critical shortcoming in existing methods of production of mesenchymal stem cells (MSCs) for therapeutic use, which is the ability to achieve economic manufacture at commercial scale. Cymerus™ does so through the production of a particular type of MSC precursor, called a mesenchymoangioblast (MCA). The Cymerus™ MCA platform provides a source of MSCs that is independent of donor limitations and provides a potential "off-the-shelf" stem cell platform for therapeutic product use, with a pharmaceutical business model and economies of scale. This has the potential to create a new standard in the emergent arena of stem cell therapeutics and provides both a unique differentiator and an important competitive position



### A Next Generation Stem Cell Company

Professor Igor Slukvin MD PhD, Cynata Inc Co-founder and Scientific Advisor Dr Ross Macdonald, CEO, Cynata Therapeutics Ltd

November, 2013







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# Cynata's Science Leadership

Igor Slukvin, MD, PhD, Diplomate of ABP, Associate Professor of Pathology, Cell and Regenerative Biology University of Wisconsin-Madison

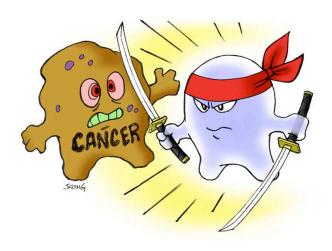
- Expertise in hematopoietic (blood) and mesoderm (soft tissue) development from human pluripotent stem cells
- Published more than 70 peer reviewed papers
- First to isolate MCAs (mesenchymoangioblasts; MCA)
- Scientific co-founder of CDI (Madison, WI, USA) and Cynata (Melbourne, Australia)
- Inventor of more than 12 key patents covering derivation of cells of mesodermal lineages from human PSCs (blood, endothelial and mesenchymal progenitors)



## **Small Molecules**

Kill strategy





 During the last century small molecules and protein-based drugs revolutionized medical treatment and led to significant improvement of quality of life and lengthened the life span

### The Major Challenges in Current Medical Practice

- Aging Population
- Chronic degenerative diseases
- Organ failure
- Strong need for novel therapies to regenerate the damaged tissues





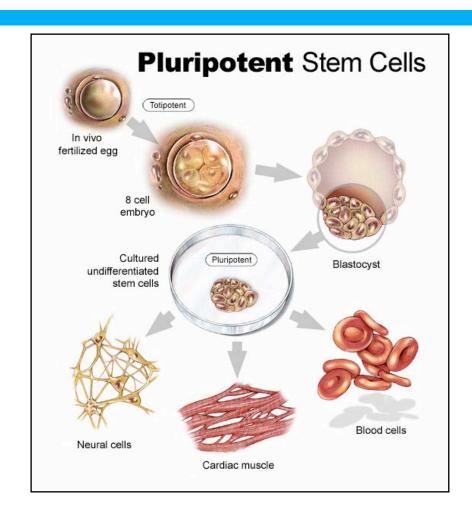
#### Stem Cells

- Potential to develop in multiple cell types in human bodies
- Divide without limit to replenish cells during lifetime





# Human Pluripotent Stem Cells





James Thomson (University of Wisconsin 1998)



Shinya Yamanaka (University of Kyoto 2006)

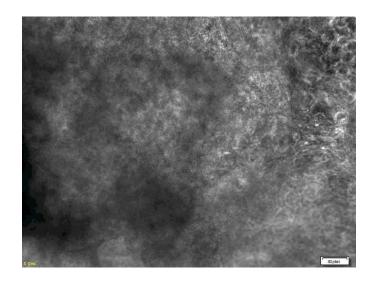
- Self-renewal and large-scale expansion
- Differentiation into all types of cells found in human body



# Pluripotent Stem Cells



**Red Blood Cells** 

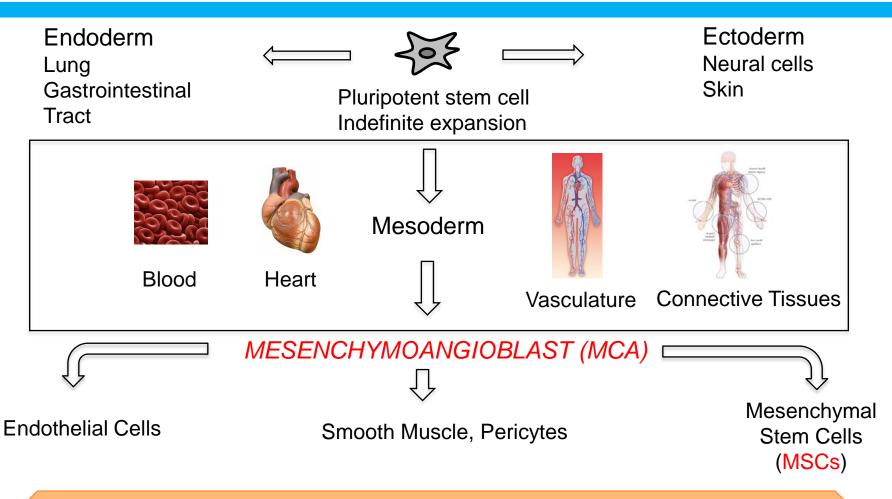


**Heart Cells** 



# Cynata's Cymerus™ Technology

# Mesenchymoangioblast: Multipotent Vasculogenic & Skeletogenic Progenitor



**Target Therapeutic Areas** 

Ischemic Heart Disease Peripheral Vascular Disease Bone/cartilage repair Immune modulation

# **MSC** Therapies

- Tissue Engineering and Soft Tissue Repair
  - Reconstruction of tendons, bone, cartilage, bladder, trachea
- Cardiovascular Therapies
  - Pro-angiogenic properties
- Inflammatory Diseases, Transplant Rejection
  - Immunomodulatory properties



# Clinical Translation of MSC Therapies

 191 open studies that use MSCs to treat variety of medical conditions are listed at www.clinicaltrials.gov



# MSCs in Orthopedics

- Osiris is evaluating Chondrogen, an injectable formulation of MSCs, for arthritis
- Cellular Biomedicine Group, Inc. received approval to conduct a Phase IIb clinical trial for ReJoin, a human adipose-derived MSC therapy for knee osteoarthritis



#### **MSCs** in Wound Care

 MSCs enhance healing of chronic diabetic foot ulcers, thermal and radiation burns

- Grafix® (Osiris)
  - Clinical trial demonstrated the safety and effectiveness of Grafix(R) in patients with chronic diabetic foot ulcers
  - Received Medicare Reimbursement Codes for Grafix®



#### MSCs For Graft-Versus-Host Disease (GvHD)

- GvHD is a major complication that occurs after bone marrow transplant to treat leukemia and lymphoma
- Prochymal® MSC preparations (Osiris/Mesoblast)
  - Approved for the management of acute steroid unresponsive GvHD in children (Canada and New Zealand)



#### MSCs For Cardiovascular Diseases

 Phase I/II clinical data reported a safety and beneficial effect of intravenous, intracoronary, or intramyocardial administration of MSCs in acute myocardial infarction and ischemic cardiomyopathy

#### Mesoblast

- Phase III clinical trial for using MSCs to treat chronic congestive heart failure
- Phase IIa/IIb clinical trial for using MSCs for myocardial infarction



#### MSCs for Critical Limb Ischaemia

 Dangerously diminished tissue perfusion due to vascular damage (atherosclerosis, diabetes)

#### Pluristem

 Phase II study using PLAX-PAD cells for the intermittent claudication has been approved in Korea







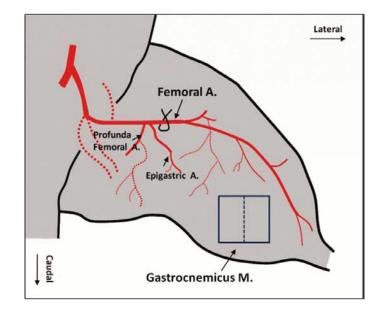
# Tissue Salvage in Mouse Ischemic Hind Limb with Cynata's MCA-Derived MSCs

 Excision of femoral artery in 20 NOD/SCID Mice

10 mice: 6x10<sup>6</sup> MCA-MSCs

10 mice: Saline

- Recovery Monitoring:
  - Laser Doppler Blood Flow
  - Hind Limb Function/Gross Appearance
  - Postmortem studies





# **Pre-clinical Study Conclusions**

- Recovery of animals in Cynata MSC treatment group was significantly better as measured by:
  - Recovery of hind-limb blood flow
  - Reduction of necrosis/loss
  - Prevention of hind-limb muscle atrophy
- Promising potential treatment using Cynata Cymerus<sup>™</sup>
   MSCs in a range of circulatory/vascular diseases including
   chronic limb ischemia



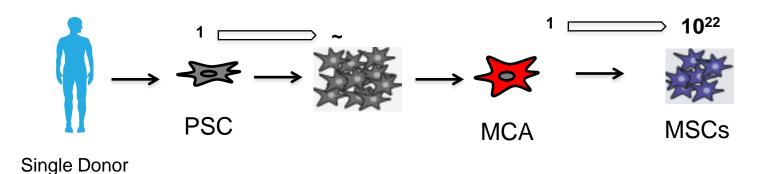
# Limitations in Manufacture of Current MSC-based Therapies

Commercial-scale manufacture of current MSC products is a major practical & regulatory challenge:

- The limited expansion potential
- Donor-to-donor and intra-population heterogeneity
- The difficulties of obtaining pure MSC populations/immunogenicity
- Negative effect of cryopreservation



### Cynata's Cymerus™ Technology Facilitates Commercial-Scale Manufacture



- Unlimited production of uniform, pharmaceutical grade MSCs lacking contaminating immune cells from a <u>single</u> donor
- Easier regulatory route
- Easier manufacturing
- Greater clinical predictability



# Summary

- Cynata will develop the proprietary Cymerus<sup>™</sup> MCA technology into:
  - a scalable manufacturing process, and
  - commercial allogeneic stem cell therapeutic products
- Cynata's Cymerus<sup>™</sup> MCAs are outstanding stem cell therapeutic candidates
  - Provide unlimited supply of well-defined drug-like quality cellular products for therapies
  - Easy to develop continuous manufacturing and quality control procedures to meet FDA criteria
  - High volume/low cost manufacturing
  - Downstream novel platforms therapeutic MCAs, endothelial cells, pericytes, and smooth muscles



# Cynata Therapeutics Ltd Key Facts

CYP - Daily Line Chart [Close]

ASX: CYP (prev ECQ)

Market Cap (25 Oct 13): \$15.5m

Shares on Issue: **54.9m** 

Options (31/12/14, \$0.2): 11.16m

Cash (25 Nov 13): \$6.52m

Number of

shareholders: 1,086

Business focus: Stem cells + regenerative medicine

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Major holders: Mr Ian Dixon 4.34%

Prof Igor Slukvin 4.34%

Celtic Capital Pte Ltd 3.64%

JK Nominees Pty Ltd 3.64%

<sup>2,500,000 27/9/18</sup> unlisted \$0.40 restricted options issued to each of RM and SW, vesting upon attainment of performance hurdles

# Stem Cell Field is Emerging

- Analogous to monoclonal antibody enabling technology: hybridoma technology developed in 1975; therapeutic market value now in excess of US\$44.6b<sup>1</sup>
- Commercial stem cell products are entering the market:
  - Prochymal (GvHD) Osiris/Mesoblast
  - Cartistem (Osteoarthritis) Medipost/Dong-A
- Most stem cell companies attractively priced based on forward estimates
- Short regulatory track in Japan: ground-breaking legislation
- Multiple products in Phase 2 and 3
  - Sector news flow
  - Creates opportunities for Cynata
- Big pharma partnering/M&A:
  - Teva/Mesoblast
  - Pfizer/Athersys
  - United Therapeutics/Pluristem
  - Novartis/Regenerex

CUNala therapeutics

# Stem Cell Company Market Valuations

Company	Mkt cap	Development stage	Partners	Cash <sup>+</sup>
Mesoblast (Aus)	\$1.8b	6 x Ph2 1 x Ph3	Teva (CHF)	\$292M
Medipost (S. Korea)	\$512m	Cartistem on sale 2 x Ph1	N/A	\$132M
Osiris (USA)	US\$539m*	Prochymal on sale# 3 x Ph3 3 x Ph2	N/A	\$35m
Biotime (USA)	US\$258m	1 x Ph1	Teva (AMD)	\$6.7M

<sup>\*</sup>Nearly trebled in Aug on news of overwhelming efficacy in diabetic foot ulcers. #pre-MSB acquisition of Prochymal assets

<sup>\*</sup>most recent filings

# Cynata's Cymerus™: Outstanding Pedigree

- Inventors include James Thomson who derived the first human embryonic stem (ES) cell line in 1998 and human induced pluripotent stem cells (iPSCs) in 2007
- WARF: US\$2 billion endowment built from licensing and investment
- In-licensed intellectual property includes several issued US patents as well as a broad estate of issued and pending patents



(12) United States Patent Vodyanyk et al.

(10) Patent No.: US 7,615,374 B2 (45) Date of Patent: Nov. 10, 2009

- (54) GENERATION OF CLONAL MESENCHYMAL PROGENITORS AND MESENCHYMAL STEM CELL LINES UNDER SERUM-FREE CONDITIONS
- (75) Inventors: Maksym A. Vodyanyk, Madison, WI
  (US); Junying Yu, Madison, WI (US);
  James A. Thomson, Madison, WI (US);
  Igor I. Slukvin, Verona, WI (US)
- (73) Assignee: Wisconsin Alumni Research Foundation, Madison, WI (US)

Olivier, Stem Cells, 2006, vol. 24, p. 1914-1922.\*
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Meuleman N, et al., "Human marrow mesenchymal stem cell culture: serum-free medium allows better expansion than classical alphaminimal essential medium (MEM)," Eur. J. Haematol. 76:309-316 (2006)

Meuleman N, et al., "Human marrow mesenchymal stem cell culture: serum-free medium allows better expansion than classical alphaminimal essential medium (MEM)," Eur. J. Haematol. 77:168 (2007).



# Cymerus™ Development Strategy

- REGULATORY: confirmation of regulatory strategy to define preclinical requirements and facilitate first-in-man Phase 1 study
- MANUFACTURE: manufacture of Cymerus<sup>™</sup> product for pre-clinical program; commence development of manufacturing scale-up
- PRE-CLINICAL: confirm product characteristics, safety, efficacy
- CLINICAL: aim to commence Phase 1 clinical study preparation during 2H14 (dependent upon regulatory path)
  - Selection of lead indication during 4Q13: short study, clear endpoints

Expect news flow and value inflection points coincident with this program and with partnering activity



# **Proposed Timeline**

Complete transaction

Regulatory engagement

Manufacturing

Safety (Animals)

Australian human trials

Further POC studies

Partner engagement and

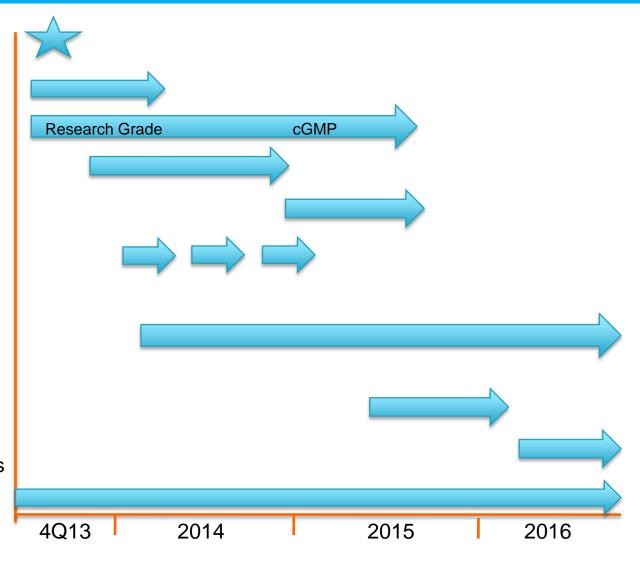
licensing

FDA pre IND meetings

and filing

IND Approval and US trials

IP Development



# Proposed Budget: 2013-15

Item	Amount
Development of the Company's biodegradable hygiene assets	\$200,000
Estimated cost of the Acquisition and Capital Raising and associated matters	\$512,635
Development of regulatory strategy	\$300,000
Pilot scale product manufacture	\$200,000
Manufacturing process development	\$1,500,000
Pre-clinical development	\$1,650,000
Clinical trial preparation	\$600,000
Contingency	\$400,000
Working capital and corporate administration	\$1,337,365
TOTAL	\$6,700,000



# Potential revenue from Cymerus™ Technology

- Two potential revenue sources:
  - Clinical need: specific "off the shelf" therapeutic products derived from the Cymerus<sup>™</sup> technology
  - Manufacturing scalability: Cymerus<sup>™</sup> proprietary (enabling) method of commercial-scale manufacture → platform technology for partnering/licensing
- Partnership-driven business strategy: business development activities will be initiated upon completion of roll-up



# Cynata Board and Management

Executive Chairman: Dr Stewart Washer

Managing Director & CEO: Dr Ross Macdonald

Non-Executive Director

and Company Secretary: Mr Peter Webse

Executive Director: Mr Howard Digby

- A tight team with extensive industry and public company experience plus a track record of commercialising therapeutic products
- Additional resources to be considered as product development progresses

# Why Invest in Cynata Therapeutics?

- Access to the vibrant and expanding field of stem cell medicine
- Innovative technology sourced from established and prestigious centre
- Cymerus<sup>™</sup> addresses a known shortcoming in the commercial model of existing stem cell companies
- Experienced management team
- Value-accretive news flow expected in near term
- Potential revenues from both specific therapeutic products and from enabling platform technology

### Thank you for your attention

