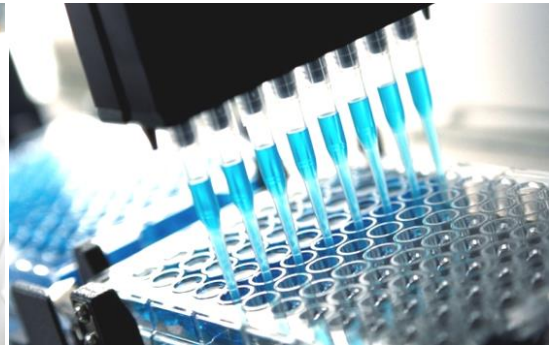
2015 Annual General Meeting: CEO Address

Dr Ross Macdonald, CEO, Cynata Therapeutics Limited

November, 2015

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Cynata Therapeutics Ltd: Our Business

- ASX-listed company (CYP): November 2013
- ~1900 shareholders; 72.7m shares
- Market cap: $32m (10 Nov ‘15)
- 52 week range: $0.32-$1.44

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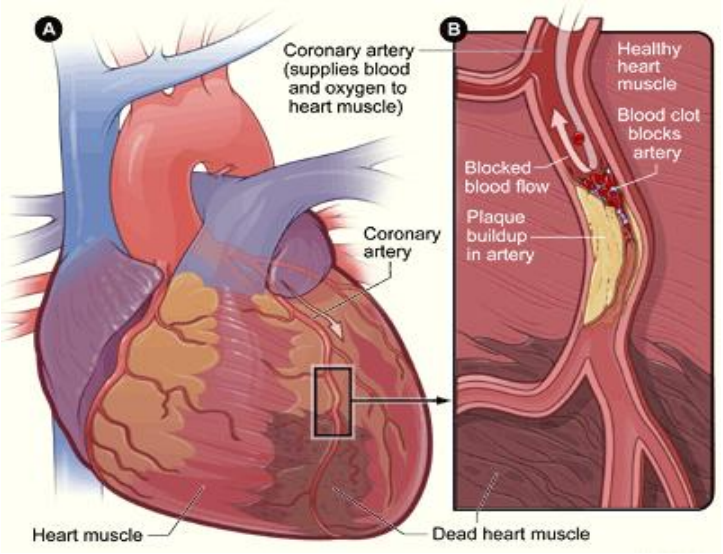
- <u>Focus: Stem cells and regenerative medicine</u>
  - Commercial development of mesenchymal stem cells (MSC) for therapeutic use
  - Cymerus™: unique product manufacturing platform
    - utilises induced Pluripotent Stem Cells (iPSCs)
    - “Off the Shelf” medicine
    - Not derived from embryos
    - Derived from a single donor for universal use (allogeneic)

Why are Mesenchymal Stem Cells (MSCs) Important?

- Regenerative medicine is a revolution: potential to resolve unmet medical needs by addressing the underlying causes of disease

- For example: heart attack (MI)
  - Sudden block of blood flow to a section of heart muscle
  - Most occur as a result of coronary heart disease (CHD): plaque build up inside the coronary arteries
  - Cholesterol lowering medicines ("statins") reduce CHD
  - BUT current medicines do NOT address the scar tissue that replaces healthy heart muscle after a heart attack
  - MSCs are being extensively investigated as a potential therapeutic approach for cardiac regeneration after MI, eg Cynata's University of Sydney collaboration

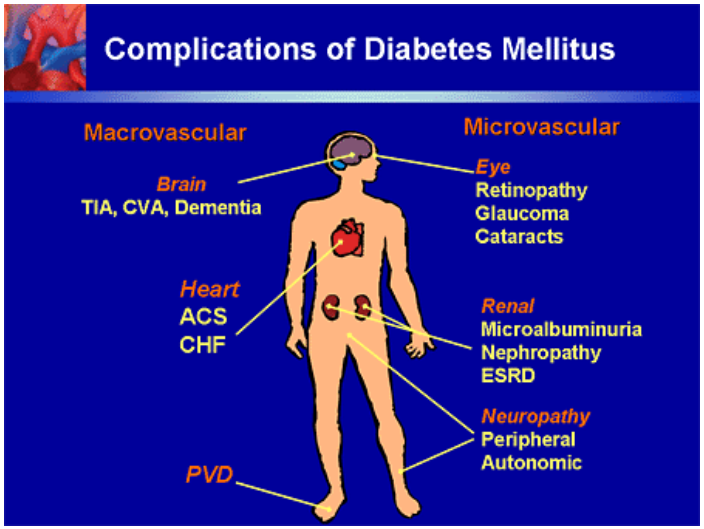


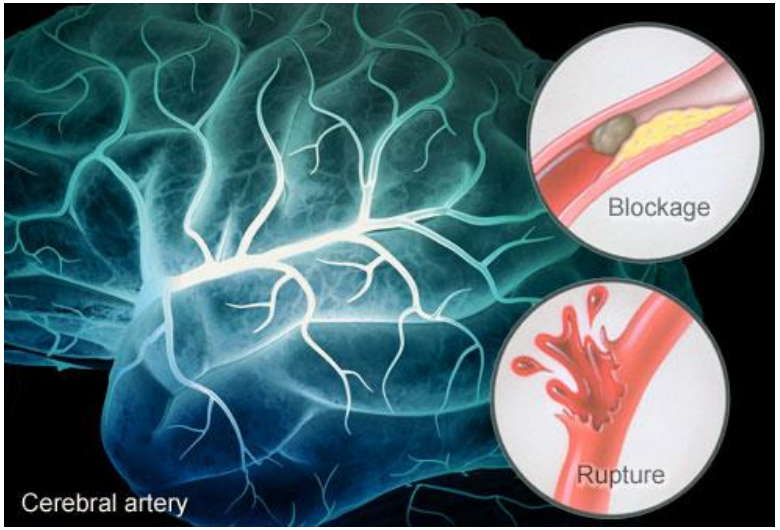
Heart disease facts

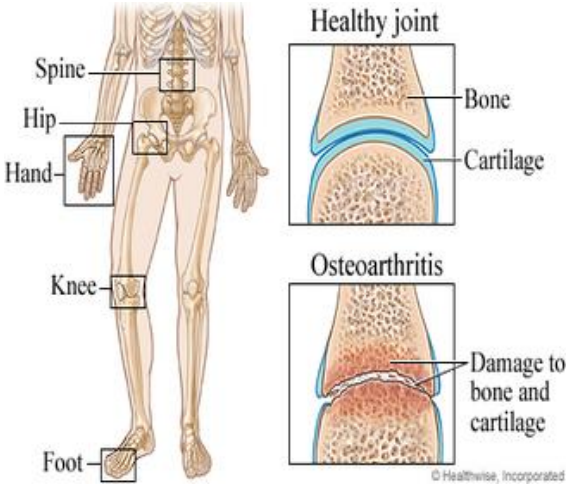
- Coronary heart disease is the biggest single cause of death in the UK
- It kills about 150,000 people every year, 21,000 of which are under 65
- About 300,000 people suffer heart attacks each year
- Two million people suffer angina
- It costs the UK economy about £10bn a year

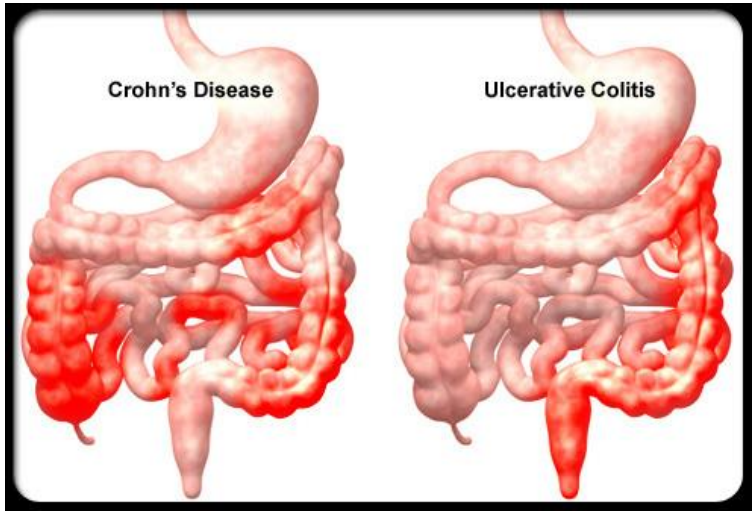
Why are Mesenchymal Stem Cells (MSCs) Important?

Around 300* clinical trials underway with MSC therapies:





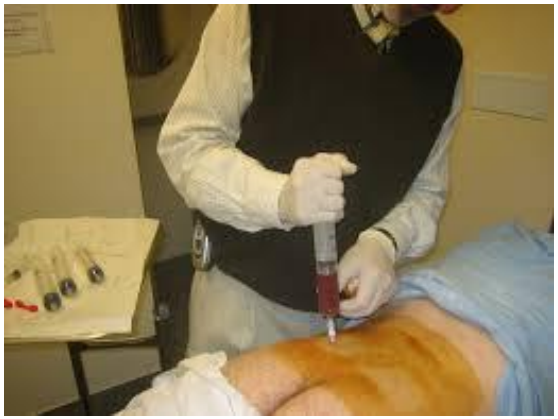




*www.clinicaltrials.gov

Cymerus Competitive Advantage

- All current MSC-based medicines require donor derived material
  - Bone marrow
  - Adipose tissue
  - Placenta



- Yield of MSCs is low, eg bone marrow harvest → ~20 **thousand** cells
- Typical dose is >100 **million** cells
- How can enough be produced?

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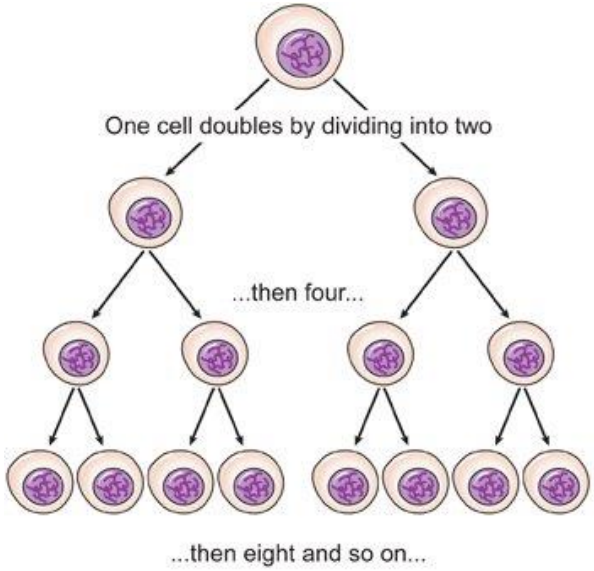
Cymerus Competitive Advantage

- Cell **expansion** is used to create the quantities needed

- Sounds simple?
- BUT, MSCs exhibit changes during expansion, including altered phenotype, differentiation potential, gene expression profile
- This occurs after as few as 13 population doublings, **equivalent to ~ 1.6 doses**
- Maybe lots of donors would suffice?



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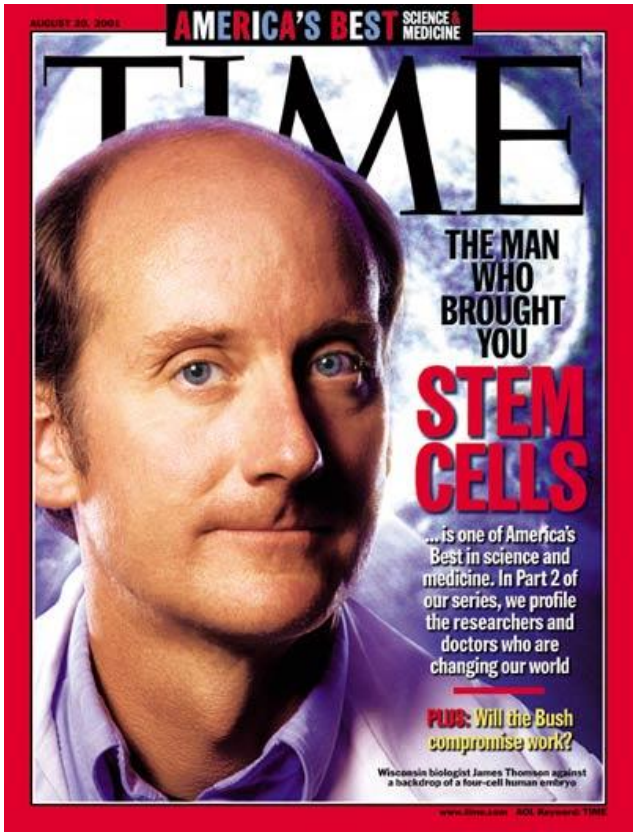
Cymerus Competitive Advantage

- Multiple donors are not a practical solution for scalable manufacture
- The solution lies in a different starting material to provide a virtually limitless source of MSCs without excessively expanding the MSCs in culture

Cynata's Cymerus™ technology



- Cymerus™ process uses iPSCs as starting material to **mass produce MSCs**
- iPSCs: adult-derived cells with embryonic-like properties – effectively limitless expansion potential; ability to differentiate into any cell type
- Inventors include:
  - Prof James Thomson – derived first human embryonic stem cell line in 1998 and human induced pluripotent stem cells (iPSCs) in 2007
  - Prof Igor Slukvin, co-founder of Cynata and author of >70 publications in the stem cell field

Cell PRESS

(Cell Stem Cell (2010) 7;718–729)

Cell Stem Cell
Article

A Mesoderm-Derived Precursor for Mesenchymal Stem and Endothelial Cells

Maxim A. Vodyanik,[1] Junying Yu,[1] Xin Zhang,[2] Shulan Tian,[3] Ron Stewart,[3] James A. Thomson,[1,3] and Igor I. Slukvin[1,4,*]

THE UNIVERSITY of WISCONSIN MADISON

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Business Strategy

- Cymerus technology is relevant to all potential therapeutic uses for MSCs
- Logical to seek to partner the technology: resources, expertise, cash and market access
- GMP manufacturing milestone in February facilitated commercial discussions
- Vibrant deal landscape
  - CDI and Fujifilm
  - Athersys and Chugai
  - MSB and Celgene
  - Gamida Cell and Novartis
  - Ocata and Astellas
- Goal to secure at least one commercial alliance in 2015

Cynata Therapeutics: The Past 12 Months

- Consolidating a commercial and clinical path:
  - December 2014 options exercised yielding $2.9m gross
  - Further validation through UWA, University of Sydney and Harvard/MGH collaborations
  - Validation of up-scaled manufacturing process in a GMP environment: major milestone
  - Engagement of US investor relations and PR firm
  - Invited presenter at major international regenerative medicine and investor conferences
  - Formal interaction with regulatory agencies
  - Research coverage by leading US-based independent equity research and corporate access firm: A$1.55 price target
  - Strengthened the balance sheet with a $5m (gross) placement to US investors
  - Engaged CRO to conduct the Phase 1 clinical trial
  - Appointment of John Chiplin to the Board

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Cynata: The Year Ahead

- Important Development Milestones and Value Drivers:
  - Continue our partnering activities
  - Commence Phase 1 clinical trial of CYP-001 in GvHD
  - Vigorous investor relations campaign
  - Assessment of off-shore listing opportunities
  - Data from pre-clinical program and PoC studies
  - Strengthen our patent portfolio

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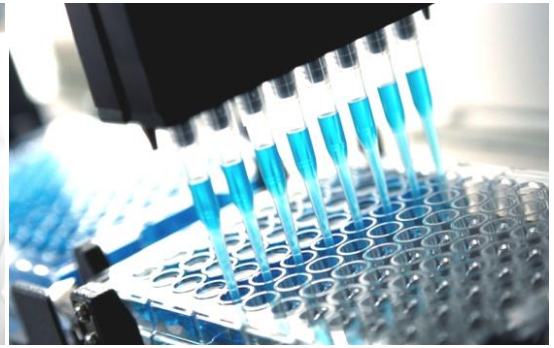
A Next Generation Stem Cell Company

Modified Stem Cells: The Future of Cancer Treatment

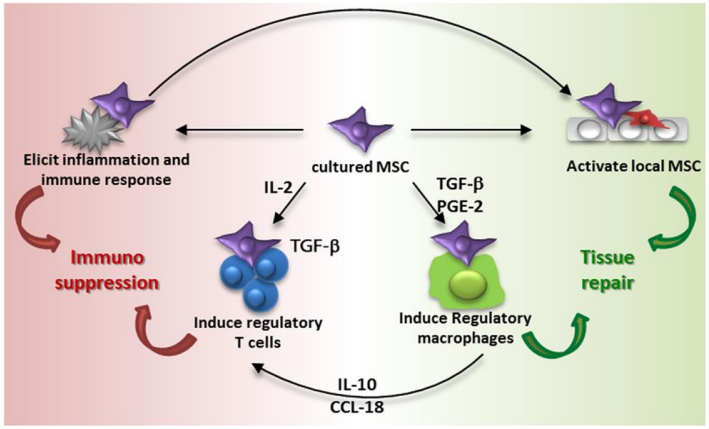
Kilian Kelly, PhD
Vice President, Product Development
November 2015

Unmodified MSCs

- MSCs have a natural ability to:
  - home to sites of inflammation/injury
  - modulate the immune system
  - secrete bioactive molecules
- Potentially effective for a wide range of conditions, including:
  - GvHD
  - Heart attacks, heart failure
  - Stroke
  - Diabetes
  - Degenerative disc disease
  - Arthritis
  - And numerous others

MSCs: Immunoregulatory Properties[1]



1. Eggenhofer et al. Front Immunol. (2014) 19;5:148

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Modified MSCs: rationale

- In addition to their natural functions, MSCs can also be modified to target other diseases, including cancer
- MSCs are known to home to tumours, so MSCs modified to secrete cancer-killing toxins can be used to release anticancer agents where they are needed

→ This could facilitate selective killing of cancer cells, without affecting normal cells, which could improve efficacy with reduce side effects

→ Could be especially useful for inaccessible cancers, such as brain tumours

→ A similar approach can be taken with other drugs/bioactive molecules to target other diseases

The potential of **modified** MSCs

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Cancer-killing stem cells engineered in lab

25 October 2014 | Health

Scientists from Harvard Medical School have discovered a way of turning stem cells into killing machines to fight brain cancer.

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Stem cell technology can mass-produce cancer-killing cells to target tumours

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Home » September » Genetically Engineered Stem Cells Could Be Tomorrow's Cancer Treatment

FROM THE SEPTEMBER 2015 ISSUE

Genetically Engineered Stem Cells Could Be Tomorrow's Cancer Treatment

Stem cells can serve as delivery vehicles for tumor-eradicating drugs.

By Elie Dolgin | Thursday, July 23, 2015

FierceDrugDelivery

NEWS TOPICS ANALYSIS

Topics: R&D

Harvard team uses stem cells to deliver toxic doses to cancer cells

October 29, 2014 | By Michael Gibney

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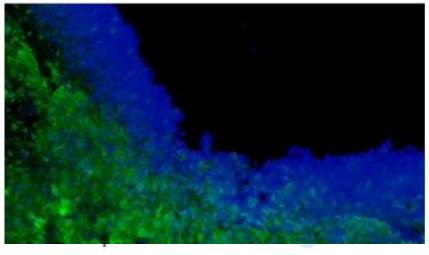
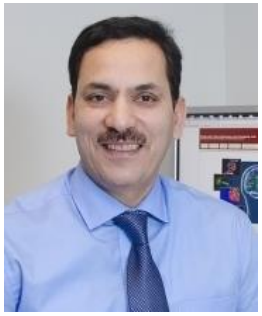
Researchers at Harvard have programmed stem cells embedded in a mouse tumor to deliver a toxic dose of cytotoxins, killing the cancer cells from the inside. The research was published in the journal *Stem Cells*.



Cynata's collaboration with Harvard

- Cynata has commenced a collaboration with Dr Khalid Shah, of Massachusetts General Hospital, Harvard Medical School and Harvard Stem Cell Institute
- Dr Shah's team are pioneers of technology to modify stem cells to secrete cancer-killing toxins
- Particular focus on glioblastoma (brain tumour) – one of the most difficult types of cancer to treat: 2 year survival is currently just 30%, with 5 year survival just 10%



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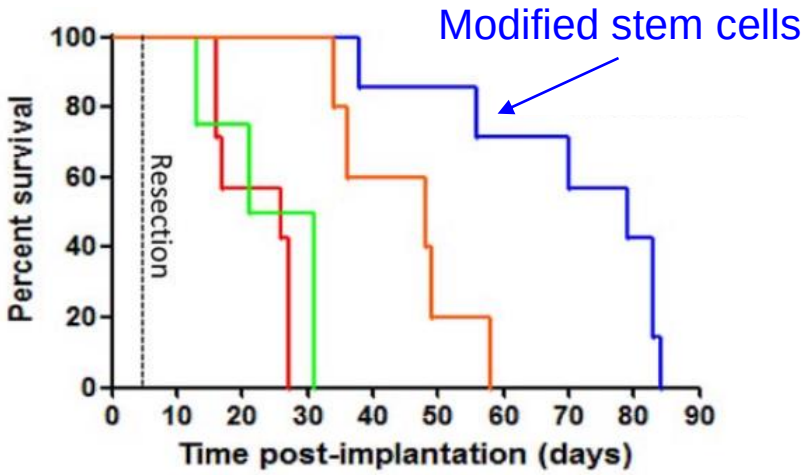
Modified Stem Cells to Treat Brain Tumours



- Dr Shah's group has previously found that modified stem cells killed cancer cells and prolonged survival in a clinically relevant animal model of glioblastoma (brain tumours)
- Dr Shah's group are now investigating similar modification of Cynata's Cymerus™ MSCs, as a first step in a potential additional clinical development program

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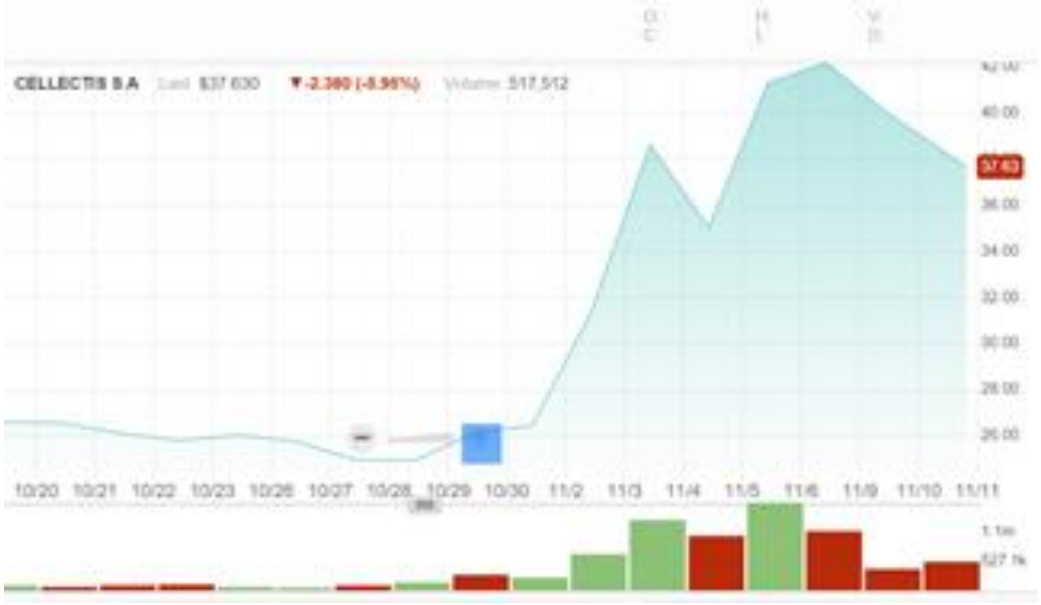
Investor interest

- Immense investor interest in cell-based therapies for cancer
- Last week, Cellectis announced data from a single patient treated with their cell-based therapy for leukaemia, which resulted in a ~60% increase in share-price
- Note: Cynata's new program targets solid tumours, unlike most other cell-based cancer therapies, which target blood cancers



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Thank you for your attention