The Actuarial Profession
making financial sense of the future

Highlights of 2012 Life Conference
Dr Catherine Prescott, John Woodford

The Potential Impact of Stem Cell Therapy on our Industry

20th March 2013

Preamble
What the papers say

THE TIMES

Stem-cell treatments help ease patients' blindness

First windpipe transplant on a child is declared a success

The Telegraph

Teenager injected with own stem cells in groundbreaking immune treatment

Scarred hearts can be restored to health with stem cell treatment, say researchers

Spinal cord injury treatment hope after new stem cell breakthrough

The INDEPENDENT

Stem cells safe for rare brain disorder

Vein grown using girl's stem cells

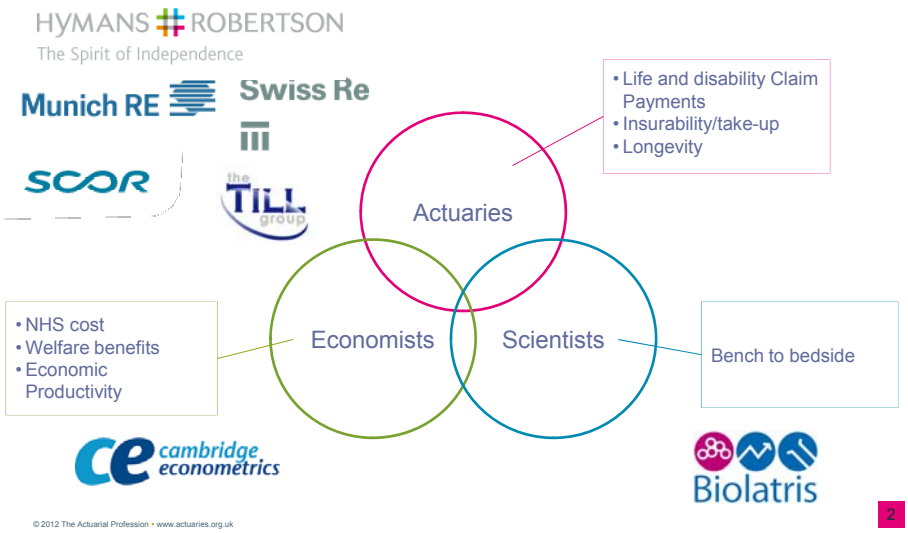
theguardian

Neural stem cells injected into the brain of a stroke patient in world first

Tests begin on stem cell cure for rare heart disease

The potential of stem cell research is almost biblical in its scale, *The Guardian, February 2009*

Preamble
Cross-Industry Working Group



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Preamble
The Working Group

Aim

Develop an evidence-based value proposition of the potential impact of regenerative medicines on the protection and pensions industries.

Premise

1. Anticipated benefits of regenerative medicines are aligned with re/insurance products;
2. Hurdles limiting regenerative medicine development and market uptake represent an opportunity cost

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Agenda for today

- The scientist's perspective — Dr Cathy Prescott
  - Science of stem cell therapy
  - Cell therapy products and pipeline
  - Challenges facing the stem cell Industry
  - Introduction to diabetes case study
- The economic and insurance perspective — John Woodford
  - The scale of the burden of ill health and the benefits of regenerative medicines
  - Costs and benefits within the health system and the wider economy
  - Case study: diabetes, the silent epidemic
  - Multi-state modelling and the challenges we face

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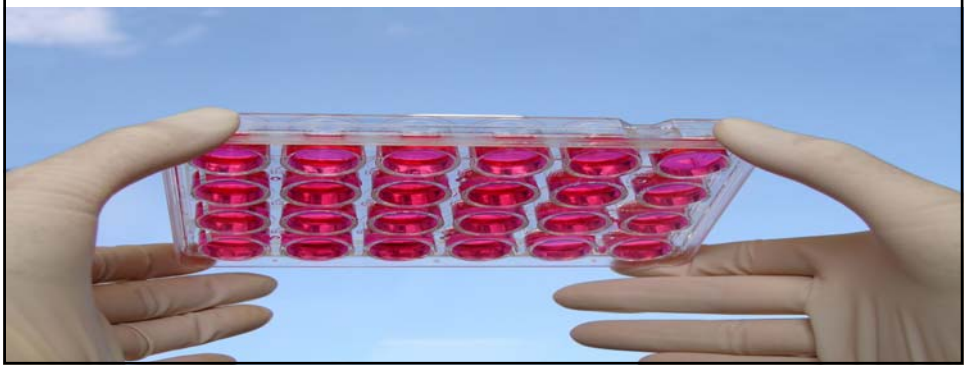
The scientist's perspective

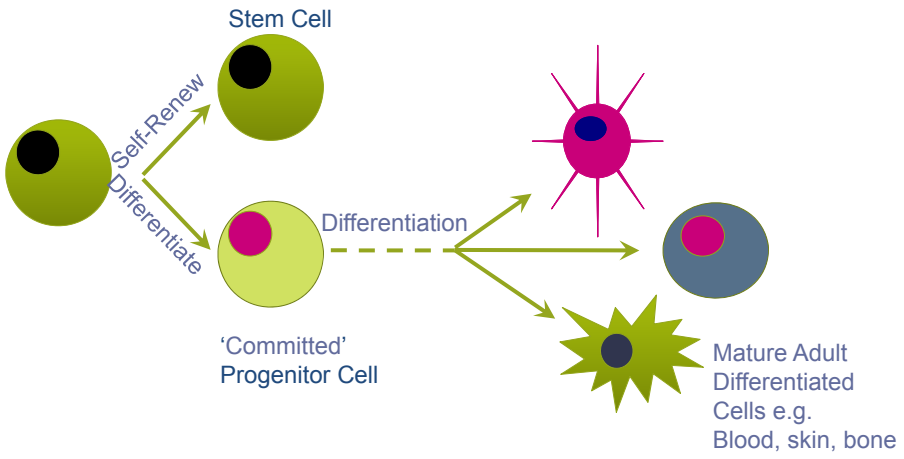
Dr Catherine Prescott

Biolatris

the TiLL group



What is a stem cell?



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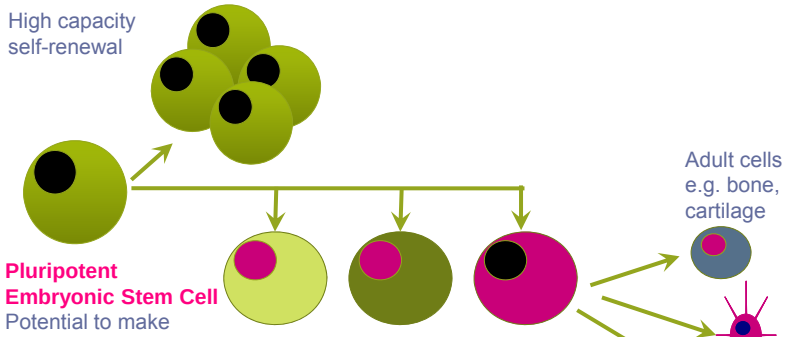
Types of stem cells



Pluripotent
Embryonic Stem Cell
Potential to make
'all' cell types

Committed Progenitor **Adult Stem Cells**
Limited capacity self-renewal
'**Multipotent**' – potential to make some cell types
e.g. Hematopoietic stem cells make blood cell types
Mesenchymal stem cells make bones, cartilage, connective tissue

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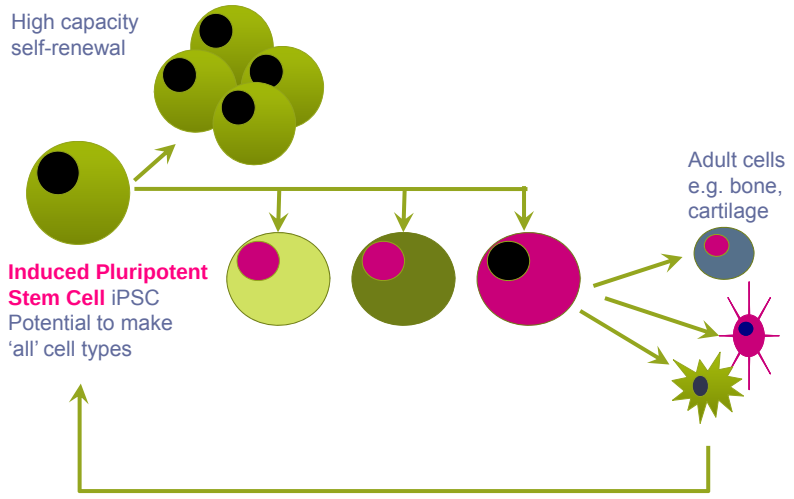
Types of stem cells



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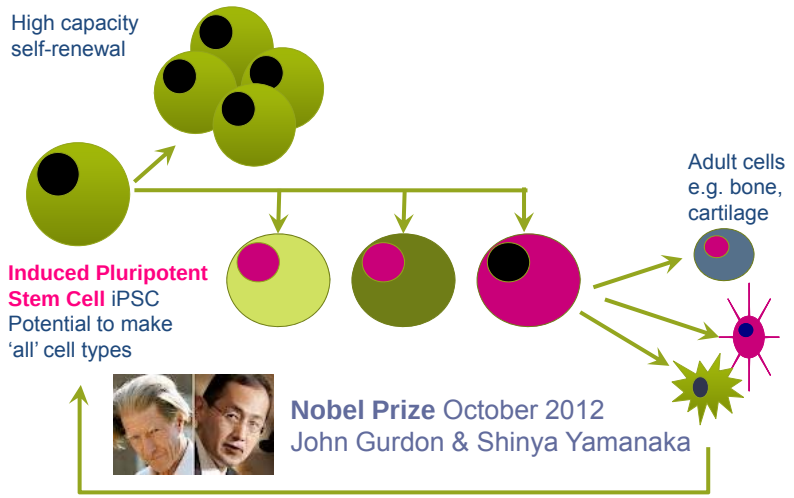
Types of stem cells



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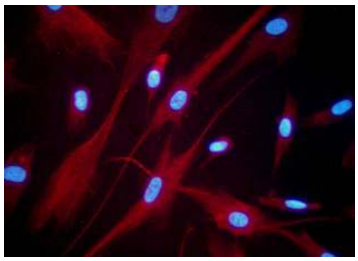
What is regenerative medicine?

Clinical applications focused on the repair, replacement or regeneration of cells, tissues or organs to **restore** impaired function.

Fibroblasts have been used to treat – venous stasis ulcers, diabetic ulcers, scar contractures, hypertrophic scars, stretch marks, acne scars, naso-labial folds & epidermolysis Bullosa erosions.



Fluorescent-labeled human fibroblasts
Source: Image courtesy of Intercytex

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What are regenerative medicines?

Cells, chemicals (drugs) or biologics

Cell therapies may function transiently to deliver signals that

- **stimulate** a patients own stem cell-based **repair** system and/or
- exert an anti-inflammatory immuno-modulatory effect thus creating a better environment for natural repair processes

Cell therapies may engraft/transplant > **replacing** the diseased or damaged cells.

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Where do cells for therapies come from?

Mature cells e.g. pancreatic islets, skin
- isolated from the living donor or cadaver
- derived from stem cells

Adult stem cells e.g. mesenchymal stem cells
- from bone marrow or cord blood

Pluripotent stem cells (embryonic/iPSC) - **derived** cells

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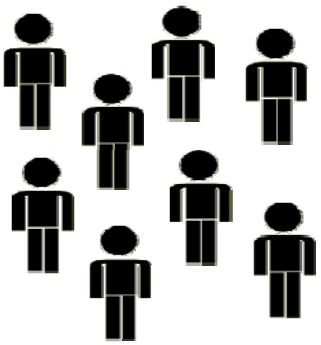
Where do cells for therapies come from?

Donor = Patient
Autologous
Personalized Medicine
e.g. Chronic applications

1 Donor ≠ Patient
Allogeneic
Could be one or multiple patients
'Off-the-shelf'
Acute & chronic



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Cell therapies on the market

COMPANY	PRODUCT	TARGET
Shire (Advanced BioHealing)	Dermagraft	Skin
Altrika	MySkin	Skin
Avita Medical	ReCell	Skin
BioTissue Technologies GmbH	BioSeed-C	Cartilage
Dendreon	Provenge	Cancer
Euroderm	Epidex, Epigraft	Skin
Japan Tissue Engineering Co.	J-TEC Epidermis Cartilage Corneal Epithelium	Skin Cartilage Eye
Nuvasive	Osteocel Plus	Bone
Sanofi (Genzyme)	Epicel, Carticel	Skin Cartilage
TiGenix	ChondroCelect	Cartilage

All Autologous except Dermagraft (allogeneic)

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Cell therapy pipeline

Year	Trials initiated	Completed	Phase 1	Phase 2	Phase 3
2005	13	0	10	2	0
2006	15	0	9	3	2
2007	19	2	10	7	2
2008	21	4	12	6	1
2009	32	5	20	11	2
2010	32	15	21	8	2
2011	25	2	18	7	0
Total	157	28	100	44	9

Clinical trial data for all major indications (excluding oncology)

Source: Alliance for Regenerative Medicine

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The potential and impact of regenerative medicines

Regenerative medicines have the potential to:

- restore function ('cure')
- improve the condition (partial restoration of function)
- decrease the probability and/or timing of onset of co-morbidities

Impact?

- alter morbidity and mortality risk profiles

Predicted benefits:

- cost savings (cure/improved disease management)
- decreased claims (cure/improved disease management)
- new market access ('higher-risk' population)
- recover loss of economic productivity

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Cell therapy industry challenges

CHALLENGE	FEATURE	POTENTIAL IMPACT
Cost of Goods	Cell-based regenerative medicines anticipated to be relatively expensive	Reimbursement status uncertain Limited uptake Shared-risk reimbursement models
Time to Benefit	Maximal benefit anticipated to accrue over time (years)	Misalignment with budget cycles Reimbursement status uncertain Limited uptake
Evaluation	Evidenced-based value proposition across multiple benefits	Cost of complex clinical trials (multiple endpoints and time) Data capture for co-morbidities and non-healthcare benefits
Business Model	Product/service: market penetration and profit margins	Limited engagement by large corps Sub-optimal VC model Alternative source of funding required

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Limited Pharma engagement

2007 Novocell (ViaCyte) $25M led by JJDC
2007 Cellerix (merged TiGenix) $38M incl. Roche & Novartis Ventures
2008 EyeCyte $3M form Pfizer
2008 Pfizer launch regen med unit Cambridge UK/US
2008 HSCI/GSK collaboration $25M/5 yrs
2009 Athersys/Pfizer collaboration
2010 UCL/AstraZeneca collaboration
2010 iPierian $28M SR1, Biogen Idec
2010 Cephalon 20% Mesoblast for $220M ($1.7Bn milestone payments)
2011 Shire acquires Advanced BioHealing $750M (5x revenue)
2011 Pfizer spins-out Neusentis
2012 Shire acquires Pervasis Therapeutics deal worth up to $200M

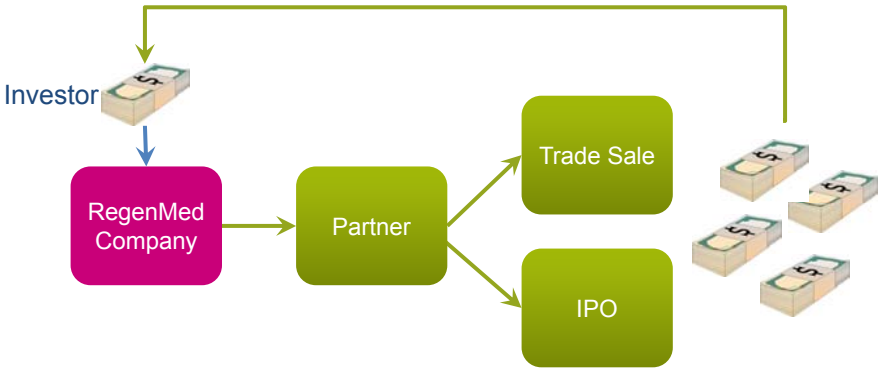
Limited Pharma engagement – why?

Business model – unclear & different

Route to market relatively untested (“unknown unknowns”)

Limited Pharma engagement – impact?

Venture Capital



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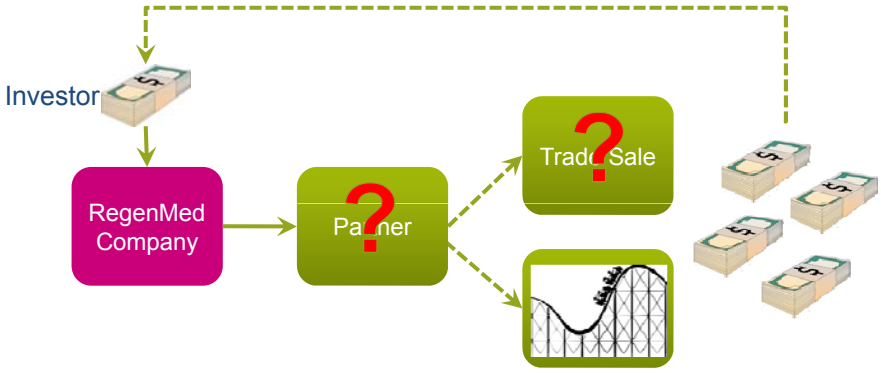
Limited Pharma engagement – impact?

Sub-optimal venture capital model
Limited development capital for regenerative medicines



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Interim summary

- Increasing & ageing population > Economic burden on healthcare and pensions provision.
- Chronic diseases are the leading causes of death and morbidity.
- Regenerative medicines:
  - potential to influence morbidity and longevity;
  - potential multiple benefits (health and productivity)
  - hurdles limit their market penetration
  - lack of adequate development capital

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Key questions

1. Which industries have long-term perspectives on morbidity & longevity?
   - Re/insurance
   - Pension
2. How can regenerative medicines influence the value of re/insurance-product revenue?
3. What is the potential value?
4. Is the potential value a sufficient incentive to
   - support the development of regenerative medicines?
   - support the market penetration of regenerative medicines?

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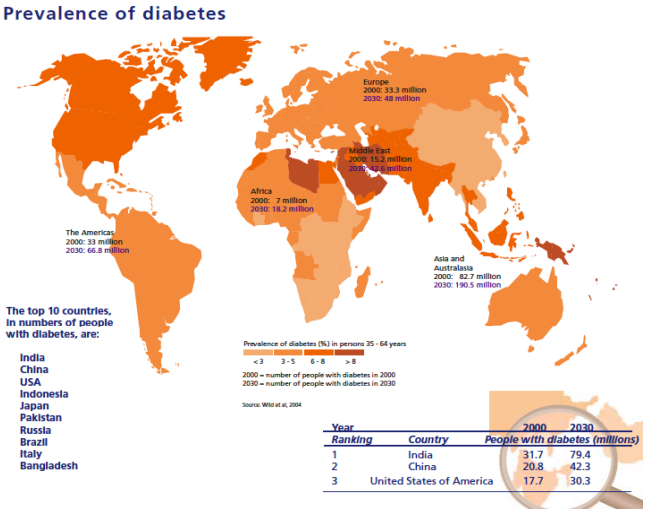
The potential impact of regenerative medicines
Case study: Targeting Types 1 and 2 diabetes

DIABETES THE SILENT EPIDEMIC



The top 10 countries, in numbers of people with diabetes, are:

India
China
USA
Indonesia
Japan
Pakistan
Russia
Brazil
Italy
Bangladesh

Year		2000	2030
Ranking	*Country*	*People with diabetes (millions)*	
1	India	31.7	79.4
2	China	20.8	42.3
3	United States of America	17.7	30.3

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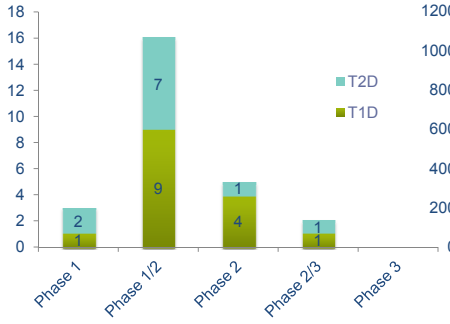
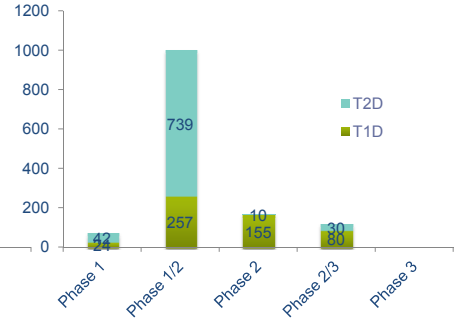
Cell therapy clinical trials for diabetes

Number of clinical trials*
~26 cell therapy trials for diabetes



Estimated enrollment target to exceed 1300



*Results exclude clinical trials that have been withdrawn or terminated and those for which details are unavailable

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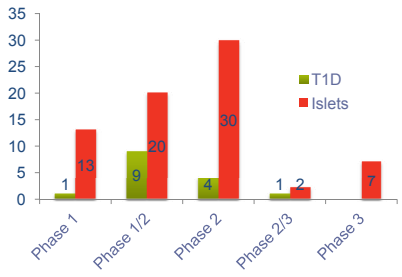
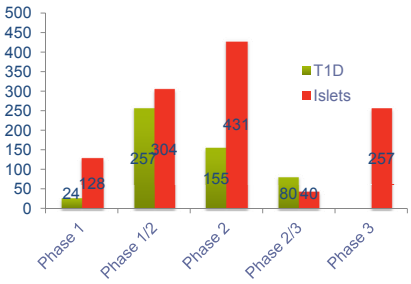
Rapid progress in the clinic

Number of clinical trials targeting Type 1 Diabetes using either stem cells (green) or islets (red)



Estimated enrollment target for Type 1 Diabetes using either stem cells (green) or islets (red)



*Results exclude clinical trials that have been withdrawn or terminated and those for which details are unavailable

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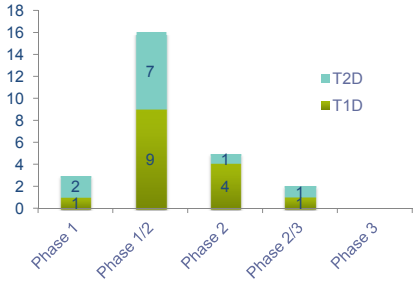
Probability of reaching the market?

Overall probabilities of success:

Biologics	26%*
NMEs	14%*
Cell Therapies ?	Too early to determine (but consistent safety record)



If comparable to biologics 26% current active product-pipeline would predict the number of stem cell-based products to reach the market to treat:

- **Type 1 Diabetes ~ 4**
- **Type 2 Diabetes ~ 3**

*BIO/BioMedTracker BIO CEO & Investor Conference Feb 2011

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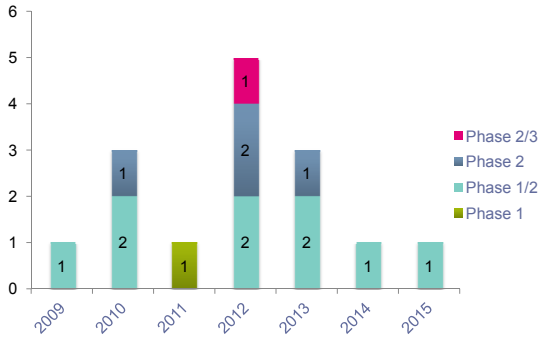
Time to market?

Estimated primary completion dates for stem cell-based clinical trials targeting Type 1 Diabetes



Data source: clinicaltrials.gov

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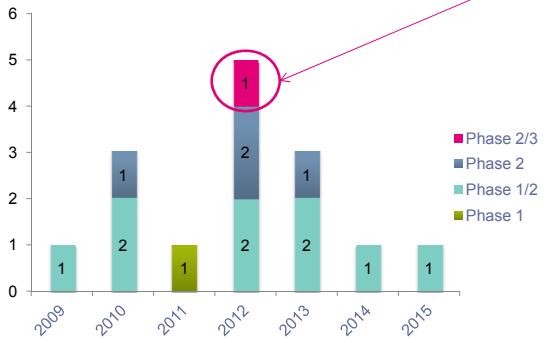
Time to market?



Data source: clinicaltrials.gov

Autologous Transplantation Of Mesenchymal Stem Cells For Treatment Of Patients With Onset Of Type 1 Diabetes

Phase 2/3 Study
Primary completion date
July 2012 (25 month study)

Primary Outcome Measures:
C peptide release test
[Time Frame: 24 Months after intervention]
The concentration of C-peptide at 90 mins after the start of the C-peptide release test at 24 Months following the infusion or not with bone marrow mesenchymal stem cells

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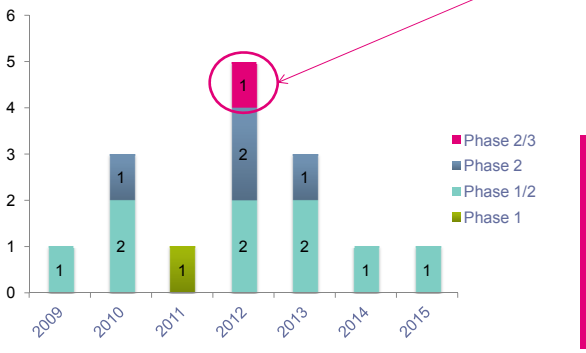
Time to market?



Autologous Transplantation Of Mesenchymal Stem Cells For Treatment Of Patients With Onset Of Type 1 Diabetes

Phase 2/3 Study
Primary completion date
July 2012 (25 month study)

Regulatory preference for two Phase 3 trials? Assume parallel studies > 5-6 years to market authorization?

- **2017-2018**

Data source: clinicaltrials.gov

Examples of cell therapies for diabetes
1. Stem Cell Educator

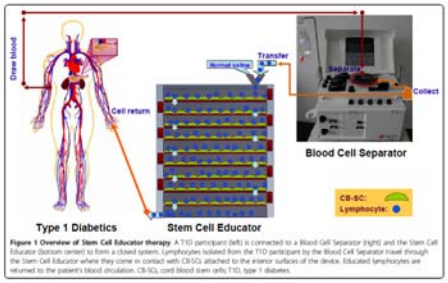
Zhao et al. BMC Medicine 2012, 10:3
http://www.biomedcentral.com/1741-7015/10/3

BMC Medicine

RESEARCH ARTICLE Open Access

Reversal of type 1 diabetes via islet β cell regeneration following immune modulation by cord blood-derived multipotent stem cells

"….. a single treatment produces lasting improvement in metabolic control. Initial results indicate Stem Cell Educator therapy reverses autoimmunity and promotes regeneration of islet β-cells…."



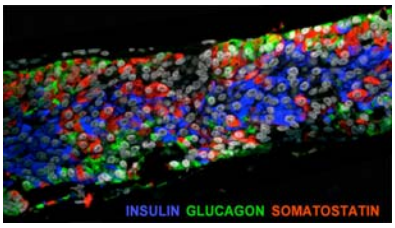
Phase 2 – recruiting
- Estimated enrollment target 100
- Estimated study completion date Sept 2014

Examples of cell therapies for diabetes
2. Embryonic stem cell – Derived Precursor Islets

VIACYTE

Cells + Encaptra® - retrievable, non-biodegradable, vascularizing encapsulation technology that enables implanted cells to survive and differentiate into functioning islet cells.

Optimized for release of insulin in response to the recipient's blood glucose

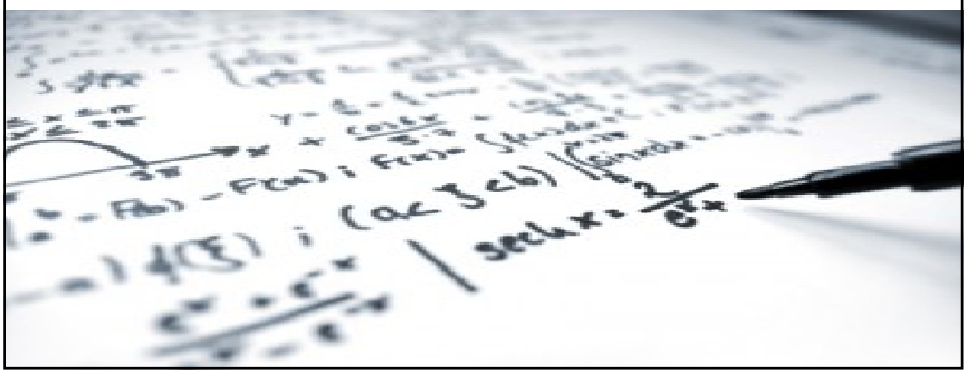


ViaCyte intends to test Pro-Islet in diabetic patients in a Phase 1 clinical trial in the foreseeable future.

Economic and insurance perspectives

John Woodford

Munich RE



Insurance perspective
Our first reactions …*show me the return*

Life industry

- If regenerative medicine reduces mortality:
  - Improved profitability life insurance
  - Increased cost of annuities?
- Increased pool of insurable lives
- Opportunities for innovative rider products

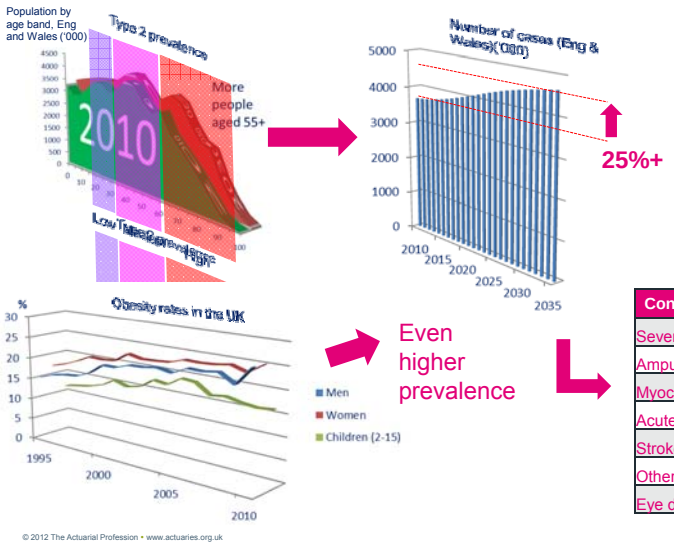
Pensions industry

Are we net winners or net losers?
Or, is it simply a matter of timing?

Targeting conditions we care about

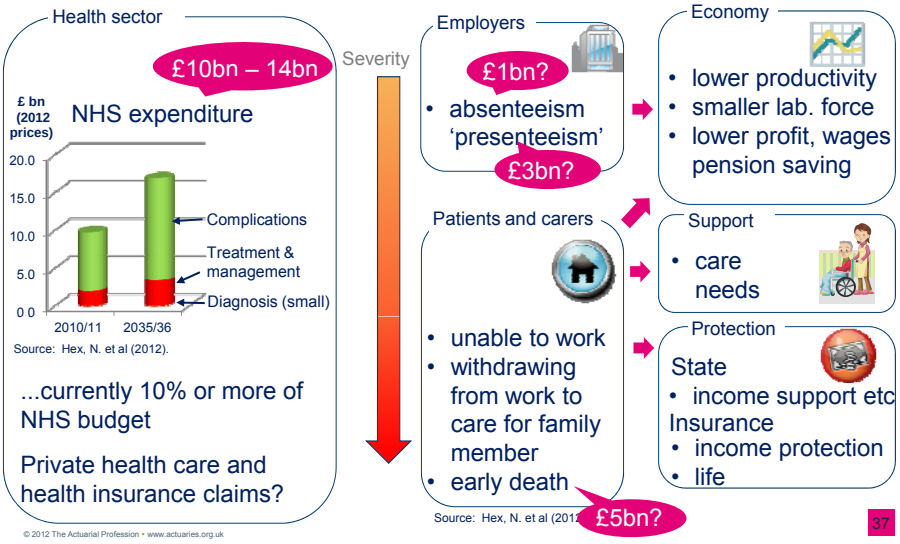
Source: univercellmarket, National Horizon Scanning Centre, Alliance for Regenerative Medicine

The Diabetes Epidemic - trends and consequences



Conditions
Severe hypertension
Amputation
Myocardial infarction
Acute/chronic kidney failure
Stroke
Other vascular
Eye disease

The Diabetes Epidemic - economic impacts



The Diabetes Epidemic - key sources

- Diabetes UK (2011) 'Diabetes in the UK 2011/2012:Key statistics on diabetes',
- Hex N, Bartlett C, Wright D , Taylor M, and Varley D (2012) 'Estimating the current and future costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs', York Health Economics Consortium Ltd, University of York, York, UK(accepted for publication in *Diabetic Medicine*)
- Kanavos, P. van den Aardweg, S. and Schurer W. (2012) 'Diabetes expenditure, burden of disease and management in 5 EU countries', LSE Health, London School of Economics

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Why diabetes?.... *...impacts lots of insurance products*

Term Assurance

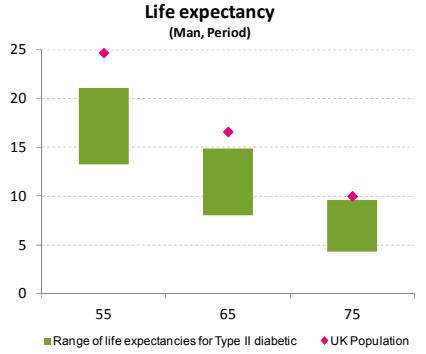
A typical insurer might find:

- ~1% applicants diabetic (Type I or II)
- **~1:3 declined**
- Average premium **double** that of a healthy life

Critical Illness

- Diabetics (Type I or II) generally declined

Annuities



- Eligibility for enhanced annuities?

Source: Development of life-expectancy tables for people with type 2 diabetes, Leal et al, European Heart Journal (2009) **30** 834-839

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The approach we are taking...
...multi-state modelling

Healthy

Dead

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The approach we are taking...
...multi-state modelling

Healthy → Diagnosed diabetic → Dead

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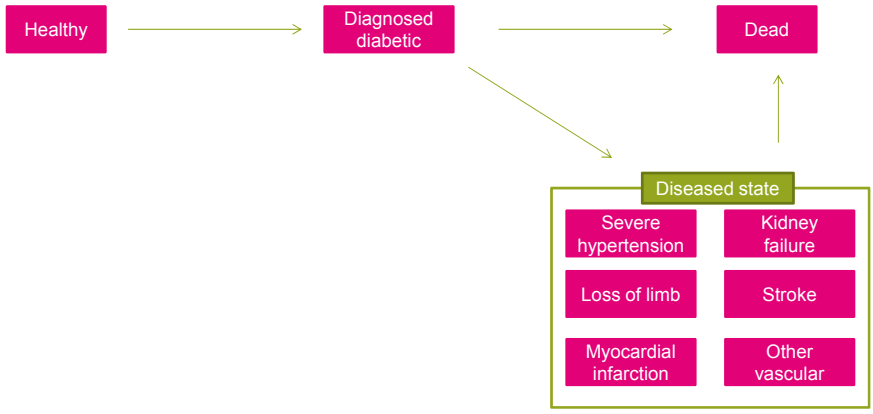
The approach we are taking...
...multi-state modelling



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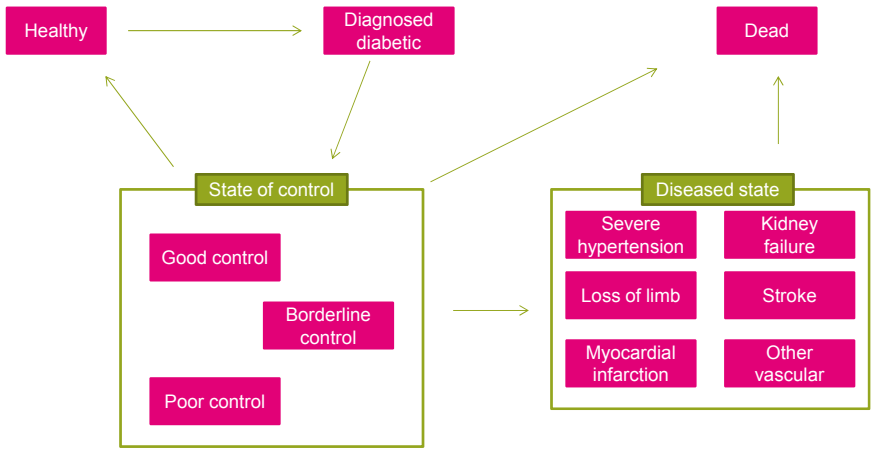
The approach we are taking...
...multi-state modelling



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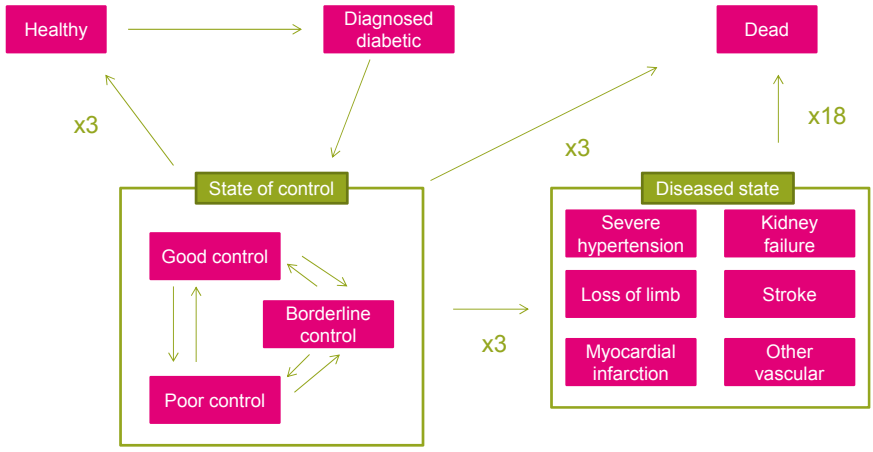
The approach we are taking...
...multi-state modelling



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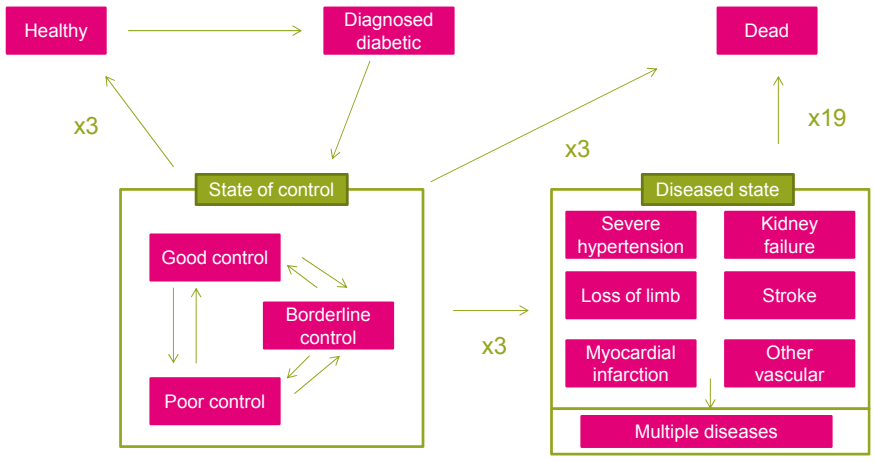
The approach we are taking...
...multi-state modelling



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The challenges we are facing

Impact on products

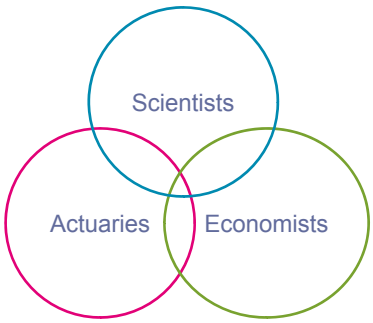
- Product take-up varies by SEC
- =>Need probabilities split by SEC

Estimating transition probabilities

- Need records of patient outcomes
- Possible sources:
  - GPRD
  - THIN
  - Q-Research
  - UKPDS Outcomes Model
  - Scottish Diabetes Study
- Access to most useful sources restricted and expensive

How you can help

Working Group



- Share your thoughts and ideas with us today
- Do you have access to data which can help calibrate the models?
  - Co-morbidities
  - Benefit claims on health protection products
  - Costs of absenteeism
- Model-building and calibration

In summary

Cell therapies will change our market place:

- First generation of cell therapies are already on the market
- Significant pipeline of products in clinical development
- Cell therapy product pipeline aligned with drivers of protection claims and longevity
- Should expect more products come to the market within 10 years
- Development supported by UK Government initiatives e.g.:
  - Cell Therapy Catapult Centre (£50m over 5yrs)
  - Technology Strategy Board (£21.5m)
  - UK Regenerative Medicine platform (£25m)
  - Catalyst Fund (£180m including provision for Regenerative Medicine)

Possible support role for the life sector

- Development capital would accelerate products to market
  - Is the insurance and pensions sector a potential long term investor?
- Innovative insurance products and reimbursement models could support the adoption of cell therapies

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Questions or comments?

Expressions of individual views by members of The Actuarial Profession and its staff are encouraged.

The views expressed in this presentation are those of the presenter.