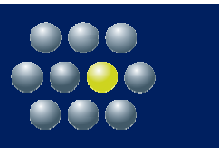
EMA Regulatory Workshop

Advanced Therapy in Retinal and Macular Degeneration

Stem Cell Organization Industry View

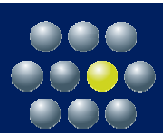
28 October 2011

janssen PHARMACEUTICAL COMPANIES OF Johnson & Johnson

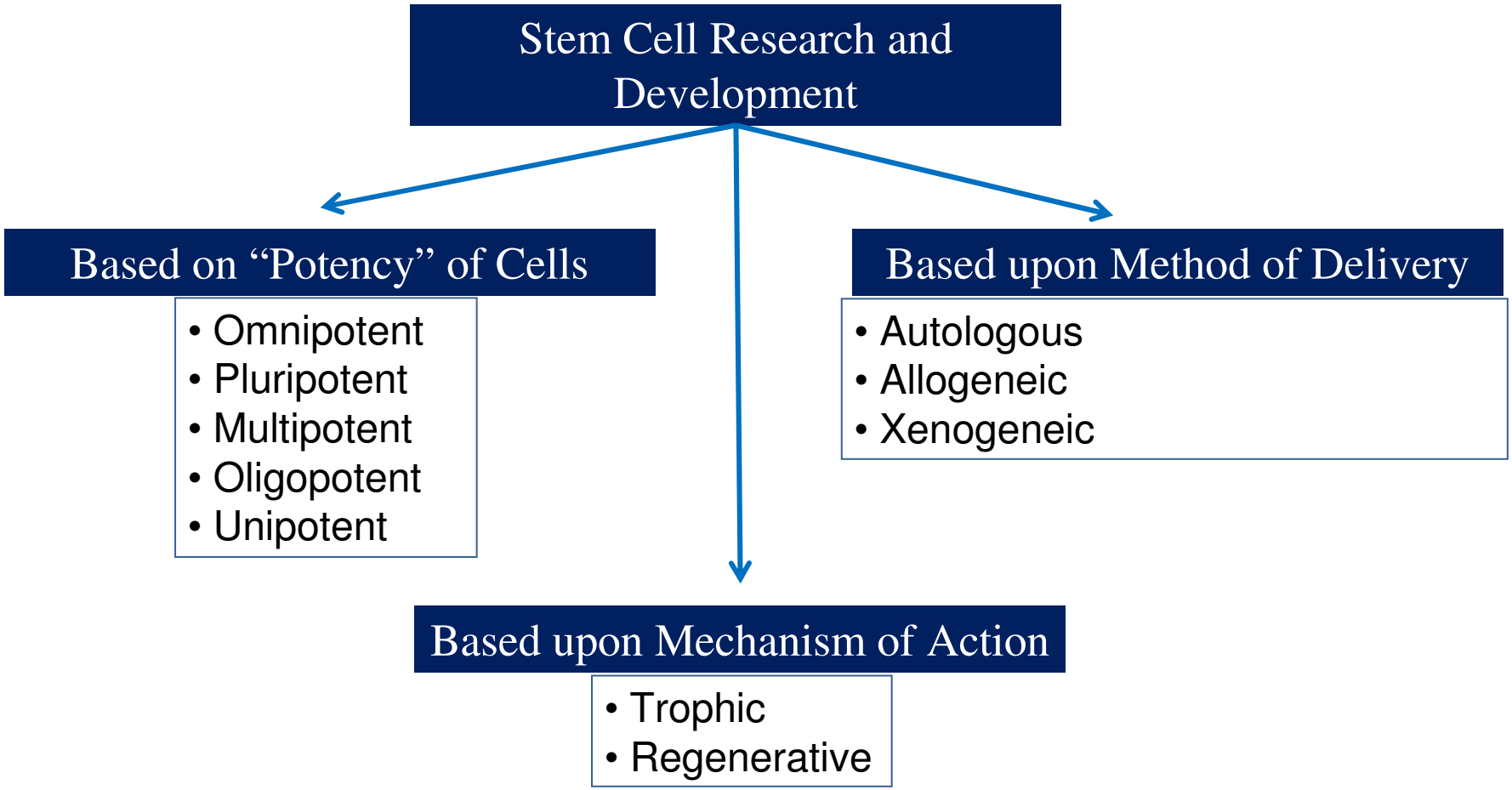


Objective

- To review retinal stem cell therapies:
  - Strategy
  - Potential approaches in clinical development
  - Population
  - Potential endpoints in different phases
  - Duration of trials
  - Challenges



Stem Cell Research & Development Segmentation

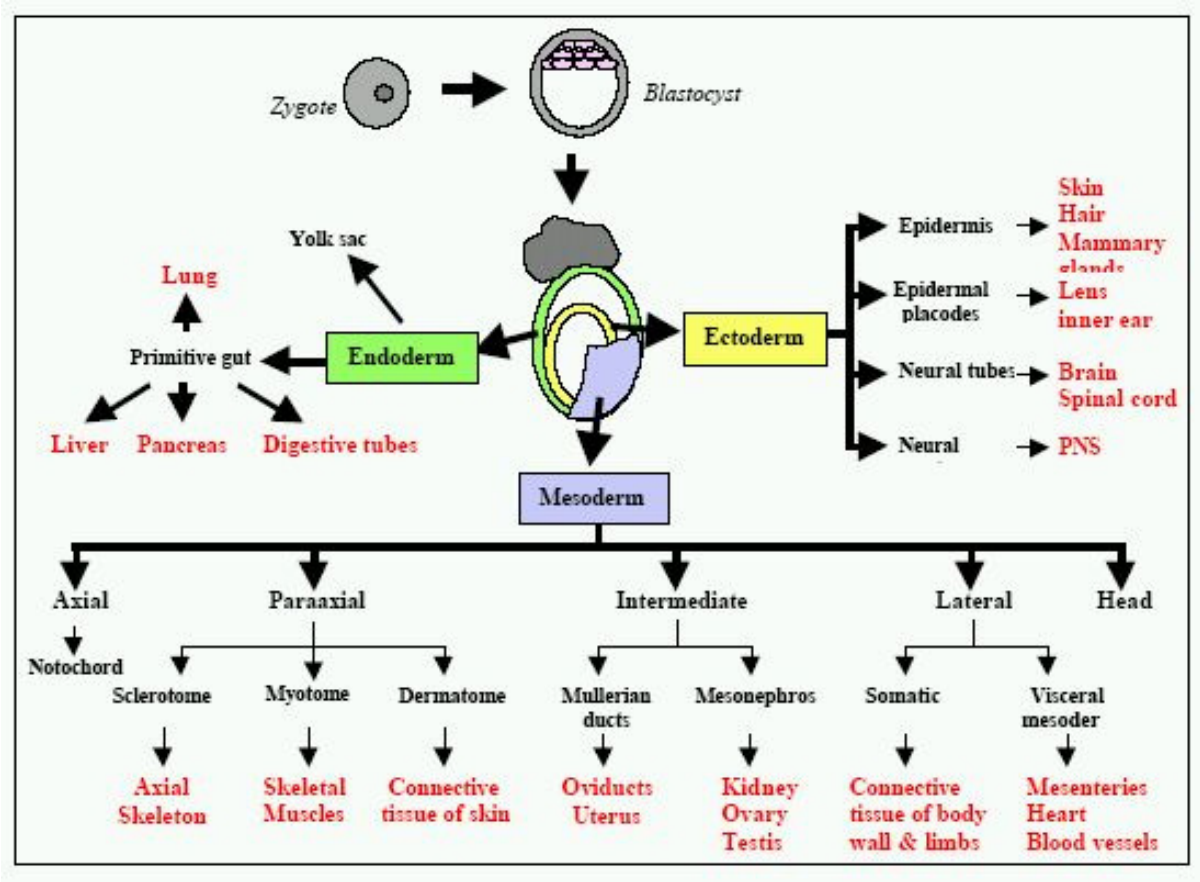


Stem Cell Research - Market Trends, Investment Trends and Pipeline Analysis. *GBI Research*, February 2010.

Types of ATMP

- Somatic cell
- Differentiated cell
- Tissue-engineered product
- Combined ATMP

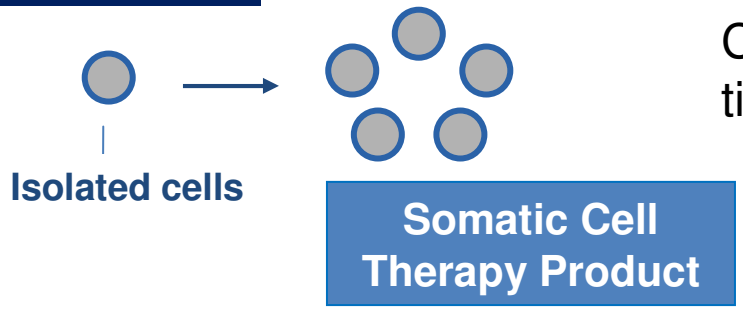
Embryology



Mechanisms of Action for Allogeneic Products

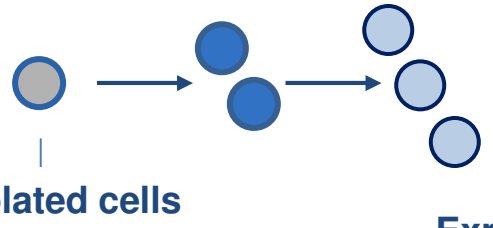
Two pathways for Cell Therapies in treating disease:

Trophic



Cells *support or repair* injured native tissue and *preserve function*

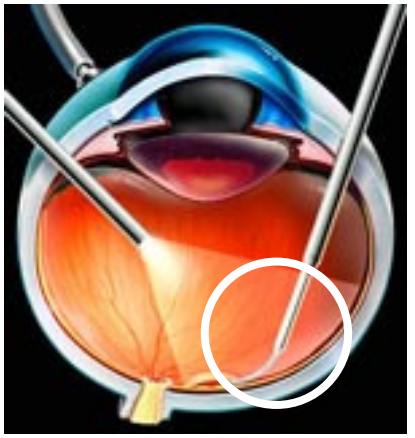
Regenerative



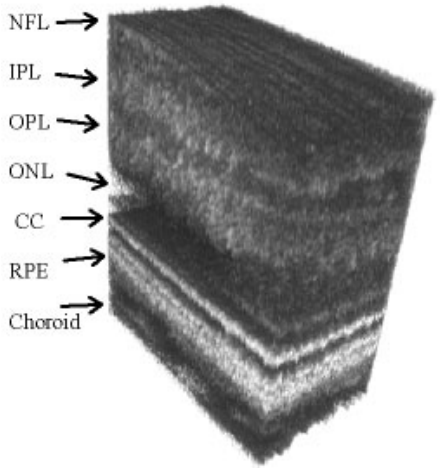
Cells *replace injured native tissue* and *restore function*

Strategy

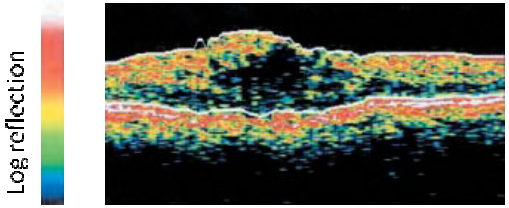
- Unmet medical needs
- Targeted delivery
- Commercial manufacturing scale
- Potential immune privilege
- Clinical biomarker (imaging) strategy
- Approach: pursue proof-of-concept

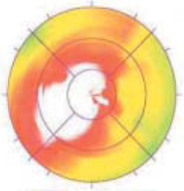


Adaptive Optics OCT

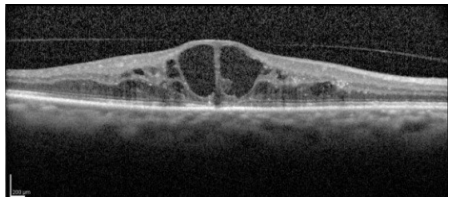


OCT Image—Diabetes





SD-OCT Image—Diabetes



NEJM 2004;350:48-58 and http://vsri.ucdavis.edu/research/retinal/ao-oct

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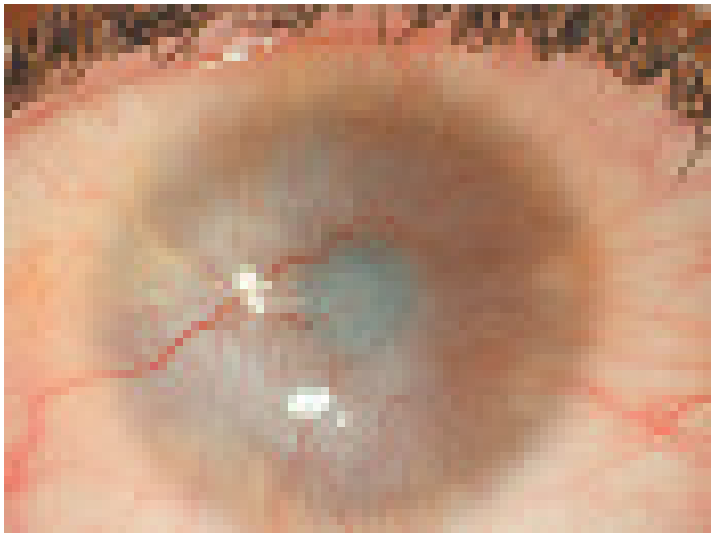
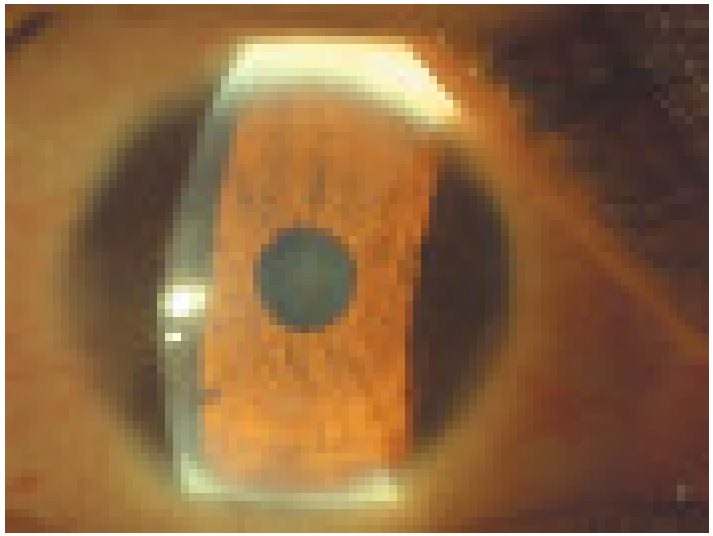
Autologous Limbal Stem Cell Treatment

Before



After

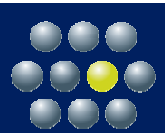


NEJM 2010;363:147-155

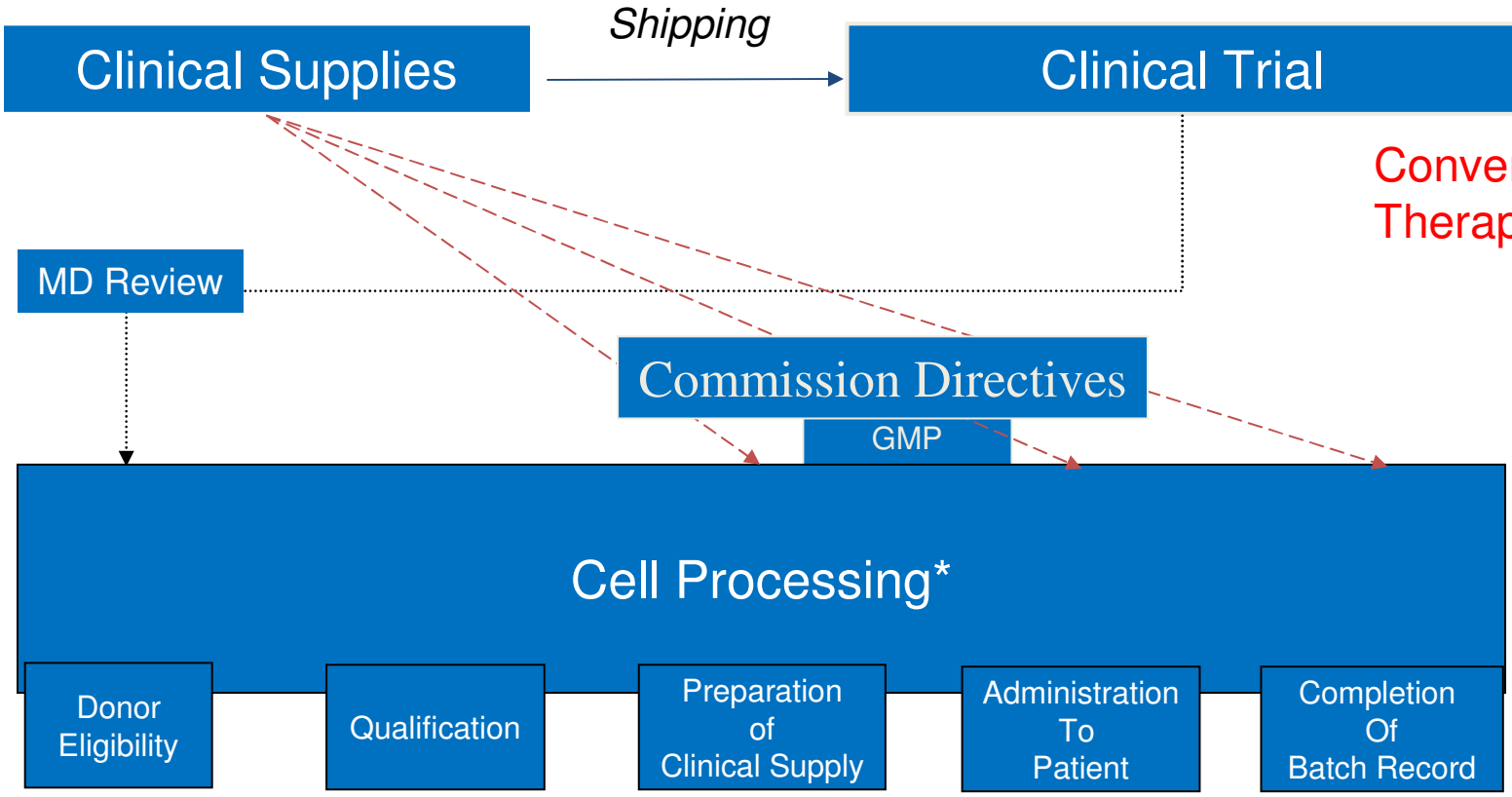
Clinical Trials of ATMP in Retinal Disease*

Cell	MoD	Indication	Sponsor
hESC-derived RPE cells	Allogeneic	GA, Stargardt's Macular Dystrophy	Advanced Cell Technology
Encapsulated CNTF-producing cells (NT-501 implant)	Allogeneic	RP, Dry AMD	Neurotech
Hematopoietic stem cell transplantation	Autologous (post ablation)	Autoimmune-related Retinopathy	Northwestern University
Bone marrow stem cells	Autologous	RP	University of São Paulo
hUTC	Allogeneic	RP, Dry AMD	Centocor

* Source: www.clinicaltrials.gov



New Workstreams: Cell Therapy in Clinical Trials



** 2004/23/EC as amended; also Regulations and Guidelines*

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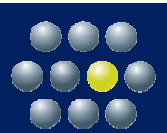
Challenges

- Understanding the science
  - Predictive animal models
    - Presence of a macula
    - Allo/Xeno conundrum
  - Tumorgenicity
- Quality
  - Donor testing and eligibility
  - Methodology
    - Time and product-consuming test methods (e.g., sterility testing)
    - Necessity to release product under restrictions (tests may not have been completed prior to administration to patient)
    - Aseptic, rather than sterile, product
  - Comparability
    - Characterisation
  - Ability to scale

Challenges

- Clinical
  - Dose development: Cyto-kinetics
  - Targeted delivery
    - Surgical procedures and devices
    - Placebo controls
  - Immunogenicity
  - Endpoints for new indications
    - Sequenced through phases to achieve desired label
      - Safety
      - PoC
      - Dose
      - Confirmation of clinically meaningful benefit
    - Need biomarkers and response instruments (e.g., ACR criteria)
  - Retreatment
  - Long-term safety follow-up



Challenges

- Regulatory
  - Global Harmonization – ICH
    - Definition of Combination Product
  - Uncertainty
    - Limited regulatory experience
    - Risk/benefit of ATMP
  - Address Pediatric Rule
- Commercial Development
  - Reimbursement for therapy and delivery procedure
  - Data must be generated by end of Phase 3