

Aging and Regeneration: Commercial Implications of the New Science

May 18, 2018

## Forward Looking Statements

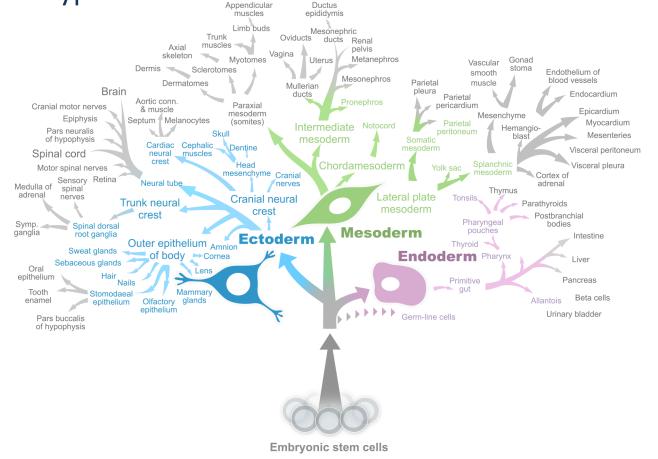
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#### Pluripotency

- Scalable source of all human cell types
- Immortal cells allow sophisticated genetic modifications

Regenerative phenotype

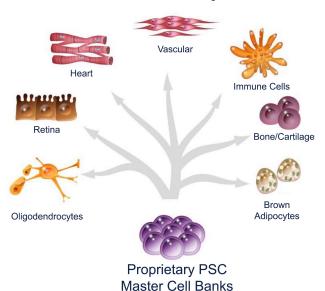




#### Pluripotency

#### Twin technologies: Cells & Matrix

#### Pluripotent Cell-Based Therapeutics



- Pluripotent Stem Cells (PSCs) allow the manufacture of all human cell types on an industrial scale
- Our cGMP-compatible PSCs scale indefinitely as a source of product
- Our cells are government (NIH) approved

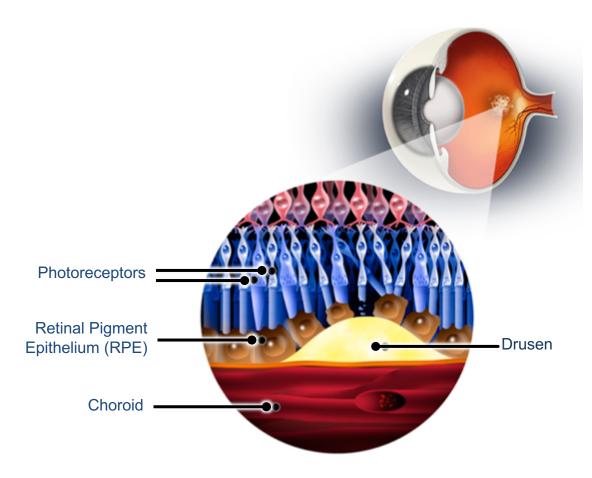
# *HyStem*® Matrix Delivery





#### BioTime's OpRegen

#### DRY AGE-RELATED MACULAR DEGENERATION (DRY-AMD)



Loss of RPE cells in the eye may cause both dry or wet AMD

The leading cause of blindness in people over age 60

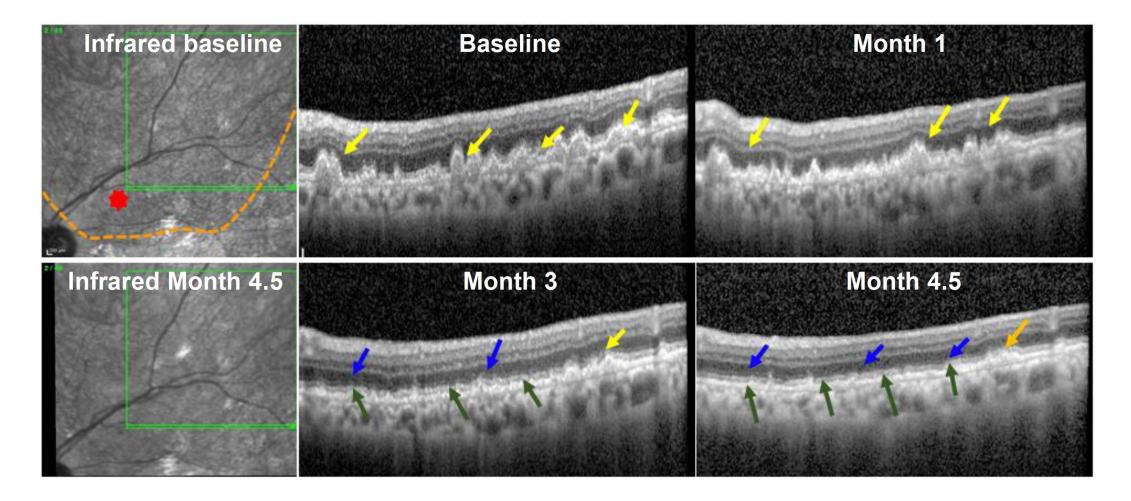
Off-the-shelf injection as a one-time therapy

OpRegen® cells integrate into subretinal space to replace missing RPE cells

FDA Fast-Track designation



# BioTime's OpRegen





#### Asterias's OPC-1

- ➤ AST-OPC1 is a cellular therapy utilizing oligodendrocyte progenitor cells (OPCs)
- ➤ OPCs are found in the human body and are precursors to oligodendrocyte cells which, among other things, provide electrical insulation for nerve axons in the form of a myelin sheath
- ➤ AST-OPC1 administers OPCs into the body to supplement the body's own internal supply of OPCs with a non-patient specific supply of cells
- ➤ AST-OPC1 is made from a well-established, pluripotent embryonic stem cell line originally isolated in the 1990s

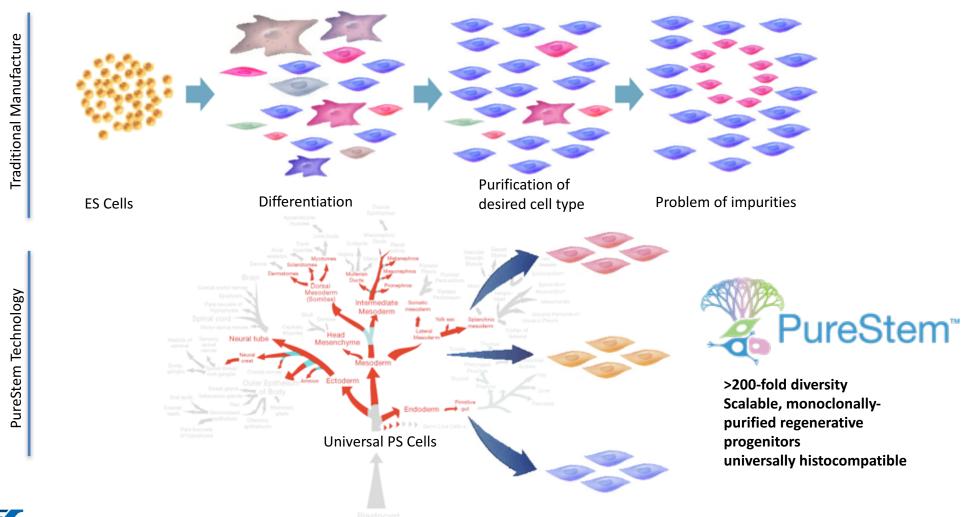


**AST-OPC1** Injection Procedure





#### 2<sup>nd</sup> Generation - Universal *PureStem<sup>TM</sup>* Technology



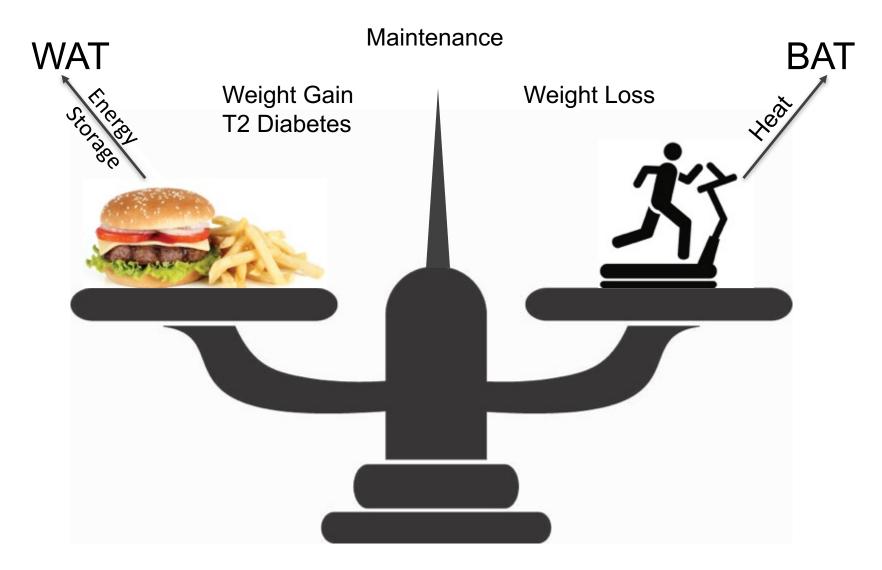


# **Product Pipeline**

	Pre-Clinical		Phase I	Phase II	Phase III/Pivotal
THERAPEUTICS					
AGEX-BAT1 (Brown Adipocytes)	T2D				
AGEX-VASC1 (Vascular Progenitors)	MI				
AGEX-iTR1547 (NCE in HyStem)	CHF				
Renelon™ (Repurposed Drug) 510(k)	Scarless Healing		510(k) Clearance		
RESEARCH PRODUCTS					
Universal cGMP ES Cells, Cytiva			Marketed Research Products		
DATABASE PRODUCTS					
GeneCards/LM Discovery			Marketed NGS Interpretation		
CANCER DIAGNOSTICS & THERAPY					
Cancer Stem Cell EFT Dx & Tx			To be Partnered for Cancer Dx		

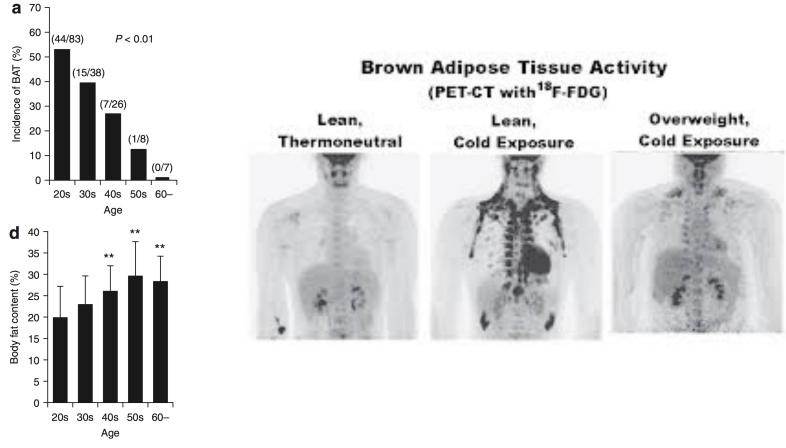


## Brown Adipose Cells Regulate Metabolism





#### Brown Adipose Cells Regulate Metabolism

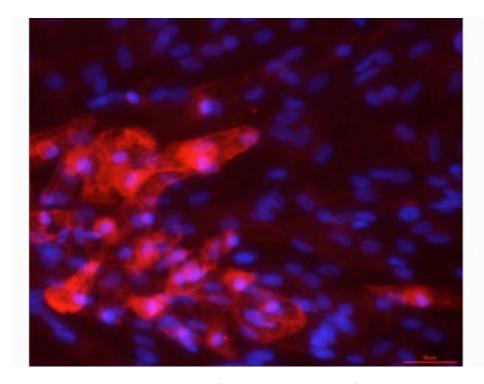




Obesity (2011) 19, 1755–1760. doi:10.1038/oby.2011.125

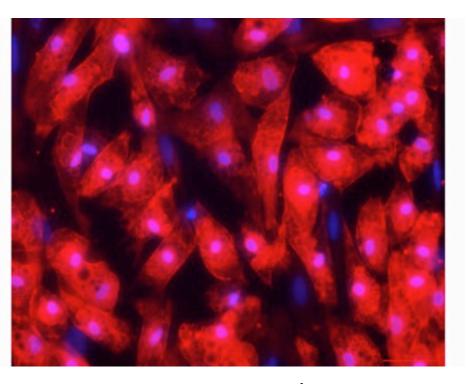
## Industrially-Scalable AgeX-BAT1

#### Stained for Brown Adipocyte Marker UCP1



Tissue-Sourced Brown Adipocytes

Data from AgeX publication in preparation



PureStem Brown Adipocytes

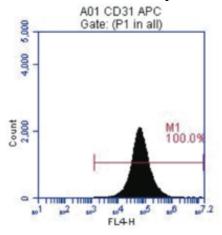


# Cardiac Program: AGEX-VASC1

#### Regenerative Vascular Progenitors



#### 100% Purity



- Highly scalable with high purity & potency
- Extensive IP estate
- Formulated in a proprietary matrix with good safety profile for human lipotransfer



Repair > Breakdown

Repair = Breakdown

Breakdown > Repair

**Embryonic** 



Fetal - Adult



Aging Adult



Highly Regenerative



**Limited Regeneration** 



Non-Regenerative

Construction

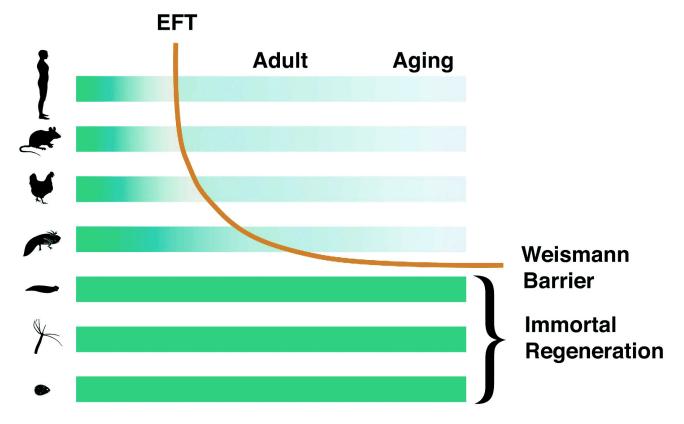
Maintenance

Destruction

iTR: induced Tissue Regeneration

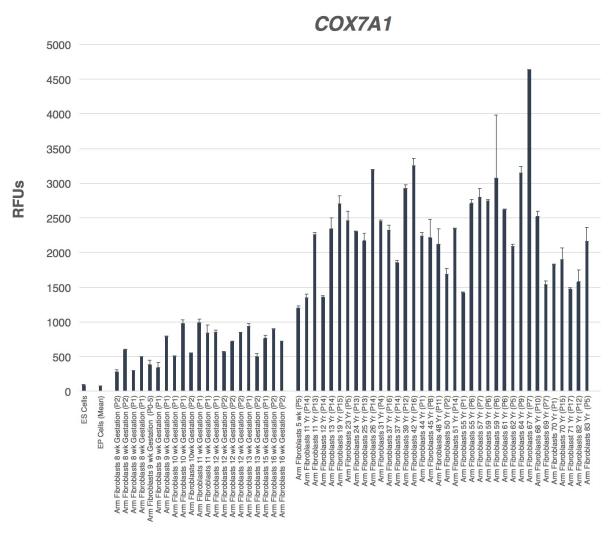


Animals that have telomerase expression and full regenerative potential do not age





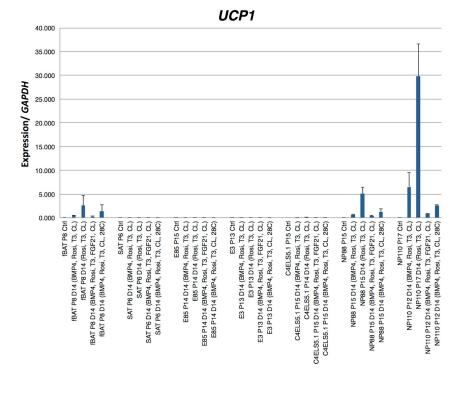
Mod from Int. J. Mol. Sci. 2015, 16, 25392-25432

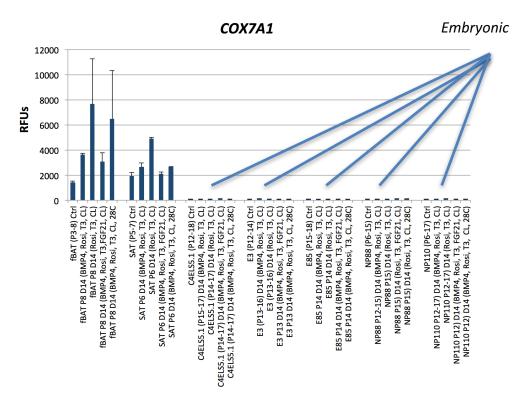




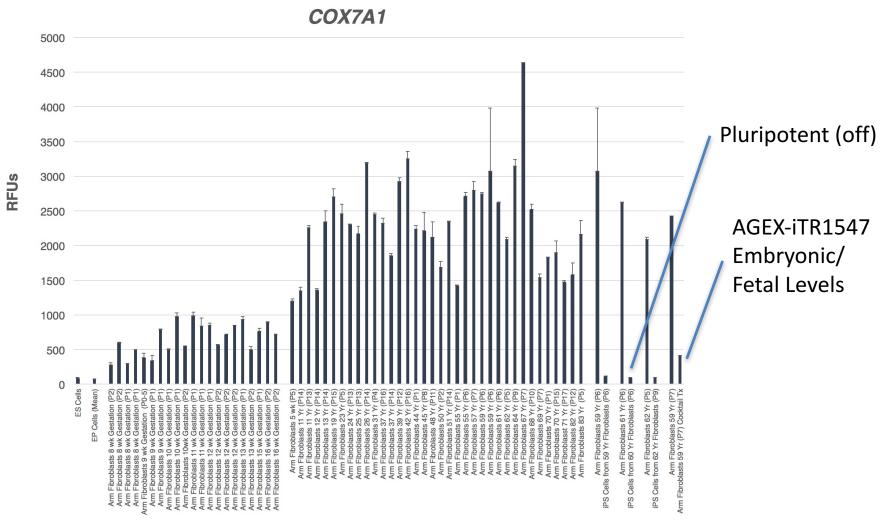
#### PureStem Lines are Regenerative

SAT – Adult Subcutaneous Wht Preadipo fBAT – Adult (Fetal) Brown Preadipo C4ELS5.1 Embryonic Beige Preadipo E3 Embryonic Wht Preadipo E85 Embryonic Ctrl NP88 – Embryonic Brown Preadipo NP110 - Embryonic Brown Preadipo





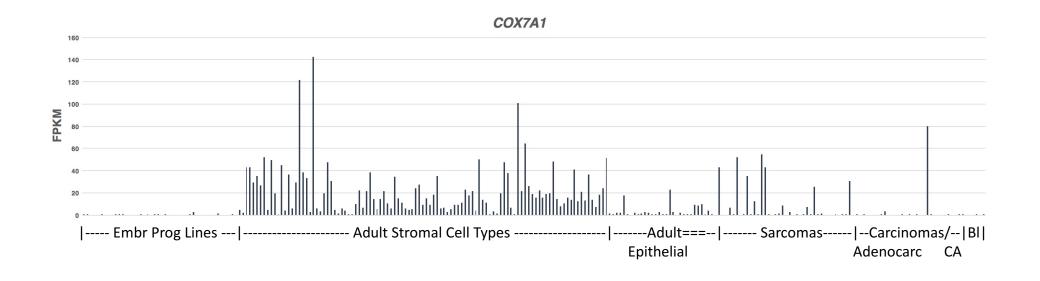






#### COX7A1 Off in Majority of Cancers

Embryonic Pattern of off in majority (73%) of Cancer lines by RNA-Seq:



Using cutoff of 0.5 FPKM:

- •104/110 (95%) Normal Adult Stromal Cells COX7A1+ (5% -) (Neg mostly CNS)
- •16/40 (40%) Sarcoma Lines COX7A1+ (60% -)
- •17/23 (74%) Normal Adult Epithelial Cells *COX7A1*+ (26%-)
- •3/30 (10%) Carcinoma/Adenocarcinoma COX7A1+ (90% -)
- •19/70 (27%) Total Cancer Lines *COX7A1*+ (73% -)



#### Summary

- Pluripotency offers a means of manufacturing diverse regenerative progenitors to address degenerative diseases of aging
- PSC-derived clonal embryonic progenitors simplify manufacture
- AgeX focused on three therapeutic programs:
  - BAT cells for T2D/Obesity
  - Vascular endothelial cells for ischemic disease
  - iTR: Therapy designed to induce scarless tissue regeneration implications for cancer Dx and Tx as well

