



# RepliCel™

Using Cells for Healing

Today's Innovation. Tomorrow's Products.

**Rejuvenation | Regeneration | Regrowth**

Hair regrowth.  
Skin rejuvenation.  
Tendon regeneration.



Innovative cell therapies.



A revolution in sports medicine and aesthetics

  
RepliCel



Unparalleled dermal  
injection technology.





Today's  
Innovation.

Tomorrow's  
Products

# RepliCel Financial

Current market cap:	~\$14M
Total capital raised by private placement:	~\$34M (+ 3.5M pending to MainPointe)
Total transactional revenue to-date:	~\$4M (upfront licensing payments from Shiseido) ~\$5M (upfront licensing payment & investment from YOFOTO) ~\$2.7M (upfront fee & investment from MainPointe)
Target for initial product sales:	2021
Money spent to-date (accumulated deficit):	~\$39M
Average monthly burn for next 12 months:	~\$300,000
Equity outstanding:	~34M common shares issued ~ 1.5M options outstanding (@ \$0.43 & \$0.60) ~ 1.1M pref shares (convertible @ \$0.33) 3.5M share issuance pending to MainPointe ~ 1.8M warrants outstanding (@ \$0.36) ~ 42M fully diluted



# RepliCel Ownership \*

Management Ownership:	~6.4M (~17%)
Strategic Partnership Ownership	~\$9.4M (25%) YOFOTO: 5.3M @ \$0.95 / share (2018) MainPointe: 4.0M @ \$0.675 / share (2021)
Retail investor base (Canadian, US, European)	~21.2M (~58%)
No institutional investor ownership	

\* of issued equity (including full MainPointe allotment but excluding warrants & options)



# RepliCel Strategic Partnerships



1 . 2 . 3 . 4

SPORTS MEDICINE

AESTHETICS

1 company.

2 clinical segments.

3 technologies.

4 products.



Two cell therapies

NBDSCs



One medical device



DSCCs





RepliCel™

Using Cells for Healing

1 . 2 . 3 . 4 .

**Two Clinical Segments**



Total Available Market:

One in three people



It is estimated

**one in three people** in industrialized nations

are affected by conditions RepliCel is targeting:

Aging and sun-damaged skin

Hair loss

Chronic tendon degeneration..



# 656,211

Annual incidence rate of mid-portion Achilles tendinopathy in **North America alone**<sup>1</sup>

# 232,000

Estimated annual number of Achilles tendon sports injuries in the US (2002)<sup>2</sup>

# 5-9%

 of recreational runners develop Achilles tendinopathy<sup>3</sup>

# 4%

 of all patients seen in sports clinics have Achilles tendinopathy

<sup>1</sup> British Journal of Sports Medicine – Incidence of mid-portion Achilles tendinopathy in the General population = 1.85 per 1,000 registered persons

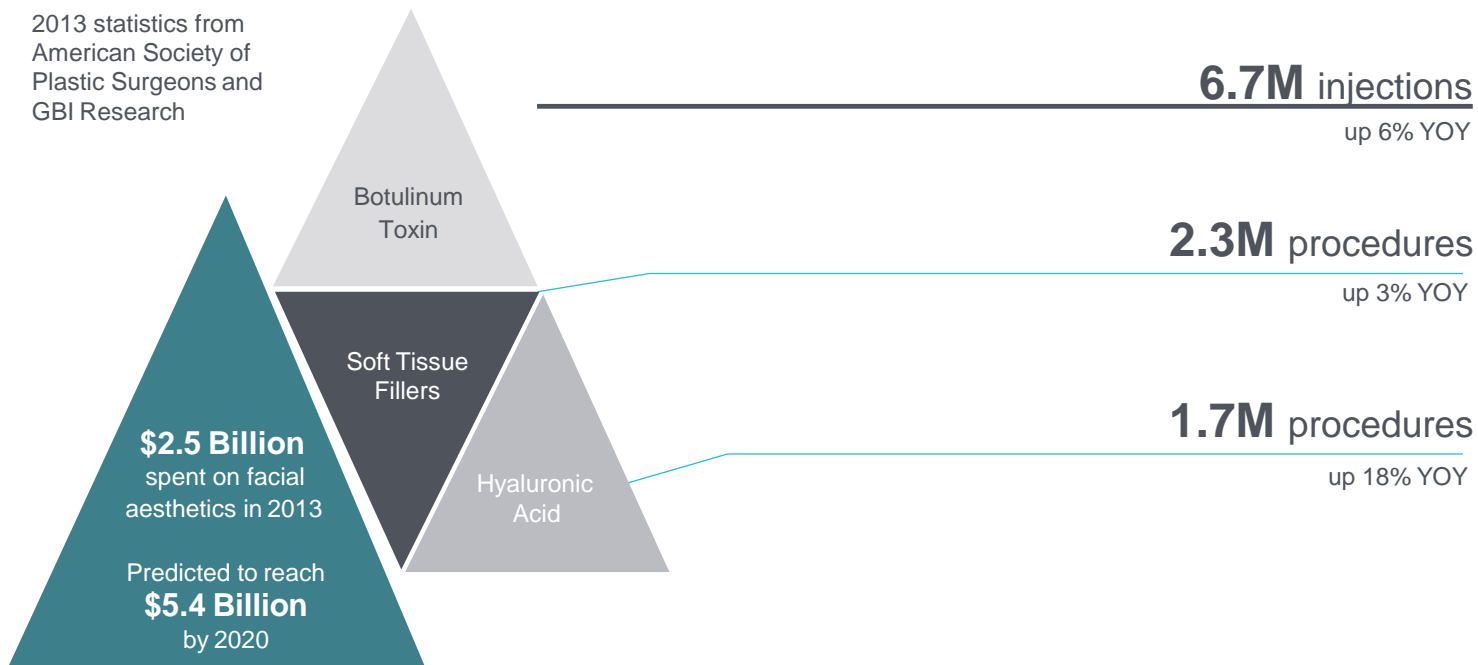
<sup>2</sup> Achillestendon.com

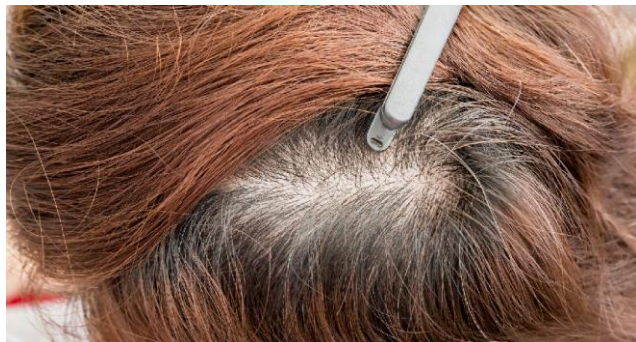
<sup>3</sup> Journal of Science and Medicine in Sport, vol. 23, Issue 5, May 2020, Pages 448-452; Mulvad B, Nielsen RO, Lind M, Ramskov D, Diagnoses and time to recovery among injured recreational runners in the RUN CLEVER trial. PloS one. 2018; [PubMed PMID: 30312310]

# Market Metrics - Global Aesthetics Market (RCS-01 & RCI-02)



2013 statistics from  
American Society of  
Plastic Surgeons and  
GBI Research





Androgenetic Alopecia affects an estimated

**50M** men  
**30M** women  
in the United States alone.



**1** There is currently only one FDA-approved treatment for female androgenetic alopecia. This has an average success rate of **1 in 5** and all efficacy reverses upon cessation of use.

2015 Practice Census  
Results – International  
Society of Hair  
Restoration Surgery  
All figures in USD



# RepliCel™

Using Cells for Healing

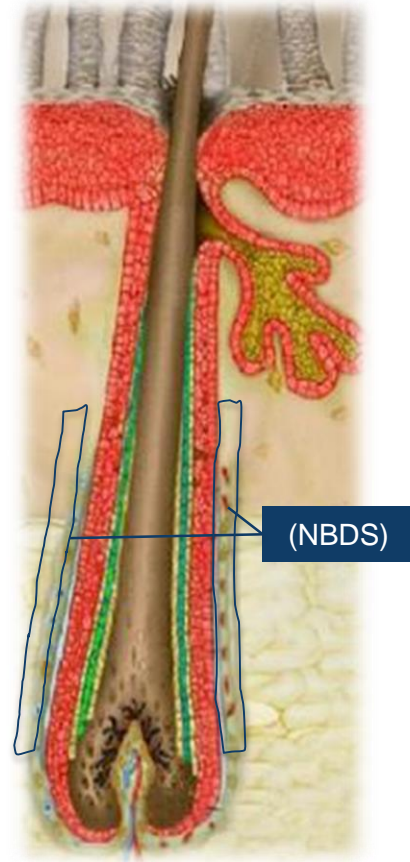
1 . 2 . 3 . 4 .

## Three Technologies



## RepliCel NBDS cells

The NBDS technology treats two indications both caused by collagen deficiencies – skin aging and tendinopathy.



## NBDS Technology

### RCT-01 Tendon Regeneration

### RCS-01 Skin Rejuvenation

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Non-bulbar dermal sheath (NBDS) cells are prolific producers of tissue building proteins especially type I collagen (5x that of dermal fibroblasts)

NBDS cells have been shown to promote *in vivo* tissue collagen regeneration

Developed as a treatment for tissue degeneration caused by a deficit of collagen-producing cells. The RCT and RCS cell therapy products are designed to regenerate tissue by injecting a new population of these collagen-generating, protein-expressing cells.



## RepliCel DSC cells

The DSC  
technology treats  
hair loss caused  
by a deficit of  
dermal sheath cup  
cells.



## DSC Technology

### RCH-01 Hair Regrowth

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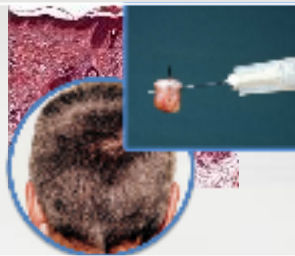
The dermal sheath cup (DSC) cells manufactured by RepliCel are resistant to the effects of androgenetic alopecia.

DSC cells have been shown to engraft and regrow hair fibers in follicles which have become dormant for lack of a viable dermal sheath cup cell population

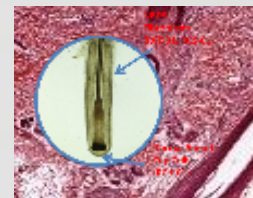
Developed as a treatment for androgenetic alopecia (the primary cause for hair loss in men & women) caused by a deficiency of dermal sheath cup cells critical to hair growth. RCH-01 is a cell therapy product designed to inject a new population of these cells which are immune to the condition and act as a functional cure for the treated area.



**1** Condition Diagnosed



**2** Biopsy taken from scalp



**3** Cells isolated from tissue



**4** Cells grown (4-6 weeks)



**5** Cells frozen in vials



**6** Cells injected



# Ensuring controlled delivery



- More consistent dermal injections; more consistent outcomes
- Less local anesthetic; better patient experience
- Shorter procedure time
- Increased control over injection depth, dose, and dispersion



# RepliCel™

Using Cells for Healing

1 . 2 . 3 . 4 .

## Four Products

# Today's Innovation. Tomorrow's Products.



RepliCel

## Chronic Tendinopathy

(Achilles Tendon, Golfer's Elbow, Tennis Elbow, Jumper's Knee, Rotator Cuff)

## Aging and Sun-Damaged Skin

## Androgenetic Alopecia

(male and female pattern hair loss)

Improved delivery of cells, toxins, fillers, fat transfers, steroids, drugs, genes, biologics, enzymes, compounds



✓ open-label data  
(Achilles, Tennis Elbow, Jumper's Knee)

✓ phase 1 data  
(randomized, placebo-controlled, double-blind)

NBDS cell therapy product



✓ phase 1 data  
(randomized, placebo-controlled, double-blind)

DSC cell therapy product



✓ phase 1 data

✓ phase 2 data  
(randomized, placebo-controlled, double-blind, dose-finding)



✓ 1<sup>st</sup> commercial-grade units in pre-approval testing

Dermal Injector



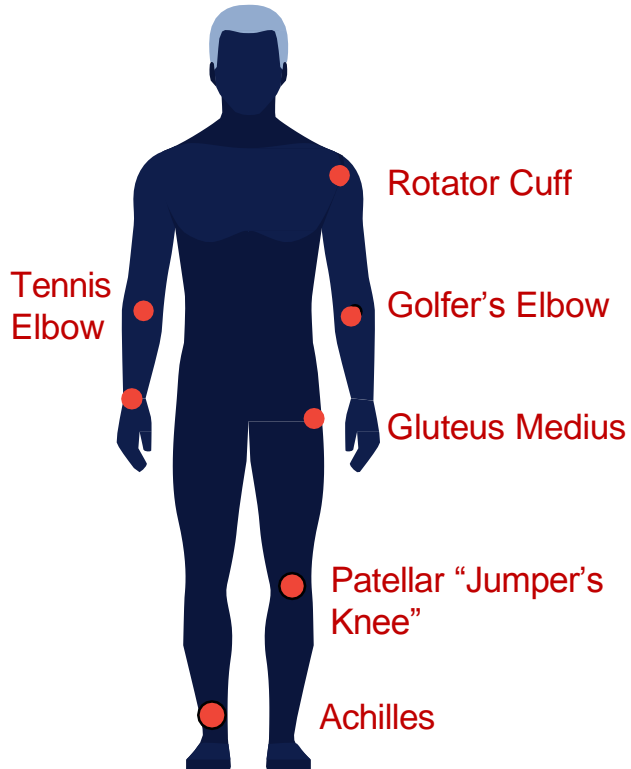
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Your health.**  
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# RCT-01 Tendon Regeneration



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# Tendinopathy - Numerous Applications



Strong safety profile and indicative efficacy data suggests a potential for RepliCel's RCT-01 therapy to treat multiple types of tendon degeneration, clinically diagnosed as "tendinopathy" or "tendinosis".

## PHASE 1/2a CLINICAL TRIAL

Randomized (3:1) double-blind,  
placebo-controlled trial at  
UBC Sports Medicine Clinic  
(8 participants)

**Primary Endpoint:** Safety

**Secondary Endpoint:** Efficacy at 6 months

**Final Results:** Trial met its goal to prove safety. No serious adverse events. Most clinically material improvements seen 6 months after receipt of injections include:

### VISA-A Scale of Tendon Function

- Overall 15.3% improvement in total function score compared to baseline.
- Two patients showed select measures of near-complete recovery in function (by VISA-A scoring).

### VAS Scale of Tendon Pain Severity

- 80% of treated patients had an average 62.9% improvement over baseline in pain on loading (running/jumping) score
- 60% of treated patients had an average **55.2% improvement over baseline score in pain on palpation** score
- 40% of treated patients showed select measures of **near-complete elimination of pain**

# Sample Tendon Regeneration

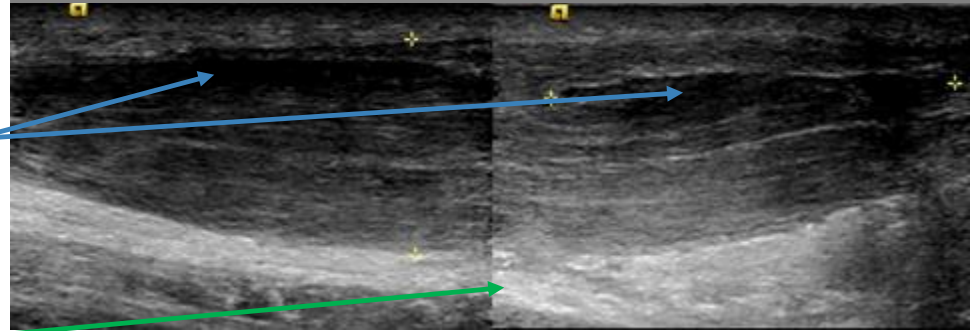
Sample Patient Image  
Demonstrating  
Potential for Tendon  
Regeneration

Darkened  
areas show  
damaged  
tendon

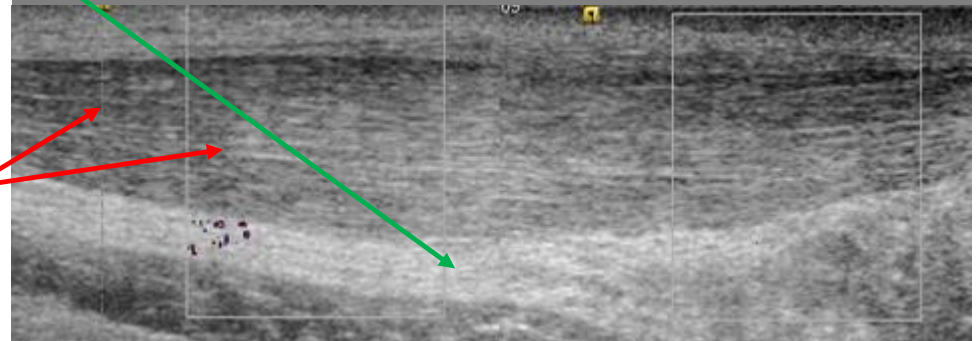
White areas  
show Ankle  
bone

Long white  
striations  
show new  
tendon growth  
after single  
injection of  
cells

Ultrasound Image of 65 Yr. Old Before Treatment – Day 1



Ultrasound Image of 65 Yr. Old After Treatment – 6 Months





## RCT-01 Program Status and Plan

Completed: Successful randomized, double-blind, placebo-controlled phase 1 clinical trial completed (Canada)

(chronic Achilles tendinopathy)

2021: Phase 2 clinical trial expected to commence in 2021 in Republic of China

with RepliCel's Chinese partner



2021: Clinical research study under ASRM expected to commence late 2021 in Japan

Final clinical consult with PMDA for clinical trial expected to be held in 2021.

2023: First product launch expected in Japan

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**RCS-01 Skin Rejuvenation**



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# Aging and Sun-Damaged Skin (fine wrinkles)

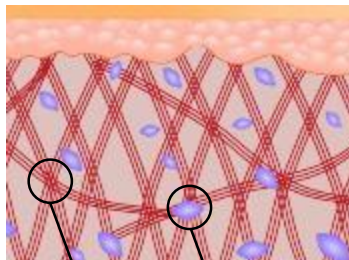


**YOUNGER SKIN**

**OLDER SKIN**

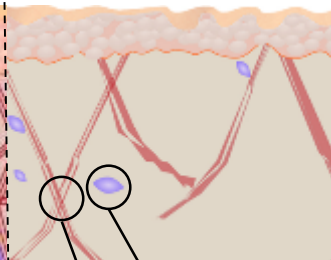


Histology



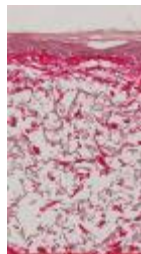
Collagen

Fibroblasts



Collagen

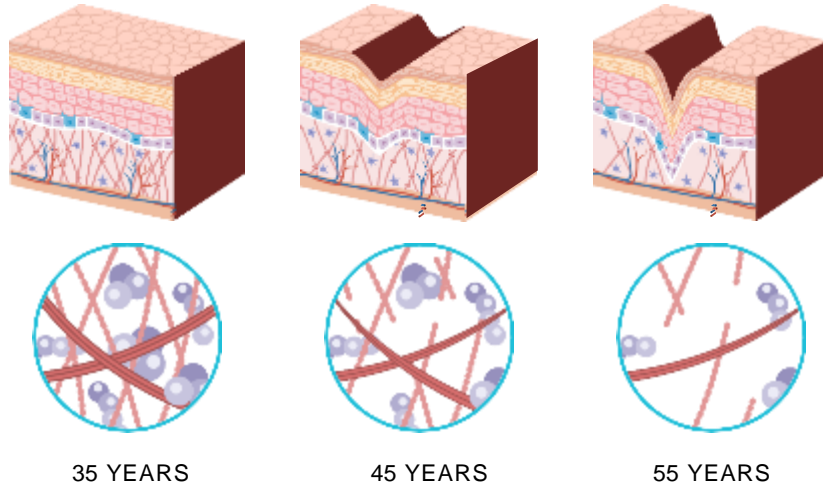
Fibroblasts






Histology

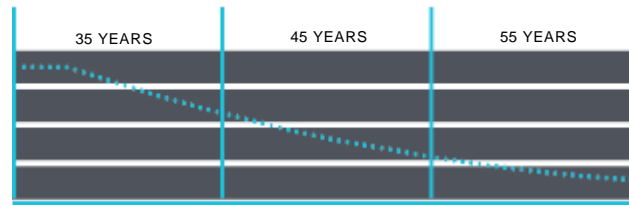


Strong safety profile and statistically significant post-injection *in vivo* biological data showing impact on established biomarkers highly correlated with collagen production, suggest potential for RepliCel's RCS-01 to regenerate the extra-cellular matrix under aging skin and impact the skin's topical aesthetic.



UV exposure appears to be responsible for **80%** of visible facial aging signs\*

-  Hyaluronic Acid
-  Collagen
-  Elastin



SKIN AGING AND COLLAGEN LEVELS

## PHASE 1 CLINICAL TRIAL

Phase 1 randomized, double-blinded, placebo-controlled trial at IUF Leibniz-Institut für umweltmedizinische Forschung (completed)

(Germany) (17 Participants)

**Primary Endpoint:** Safety (**successfully met**)

**Secondary Endpoint:** Efficacy at 6 months

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**Publication:** S. Grether-Beck, A. Marina, T. Jaenicke, P. Goessens-Rück, K. John McElwee, R. Hoffmann, J. Krutmann. *Autologous Cell Therapy for Aged Human Skin: A Randomized, Placebo-Controlled, Phase-I Study*. *Skin Pharmacology and Physiology (Skin Pharmacol Physiol)*

<http://dx.doi.org/10.1159/000502240>


## Results:

- No serious adverse events at the interim point of the trial were reported.
- A nearly two-fold increase in gene expression of collagen-related biomarkers was measured in participants' skin after a single injection of RCS-01. These results are statistically significant despite the small trial size.
- This increase in collagen-related biomarkers is a signal that the injected cells have increased collagen production and reduced collagen degradation resulting in healthier, younger-looking skin.

## RCS-01 Program Status and Plan

Completed: Successful randomized, double-blind, placebo-controlled phase 1 clinical trial completed (Germany).

2021: Phase 2 clinical trial expected to commence in 1H 2021 in Republic of China

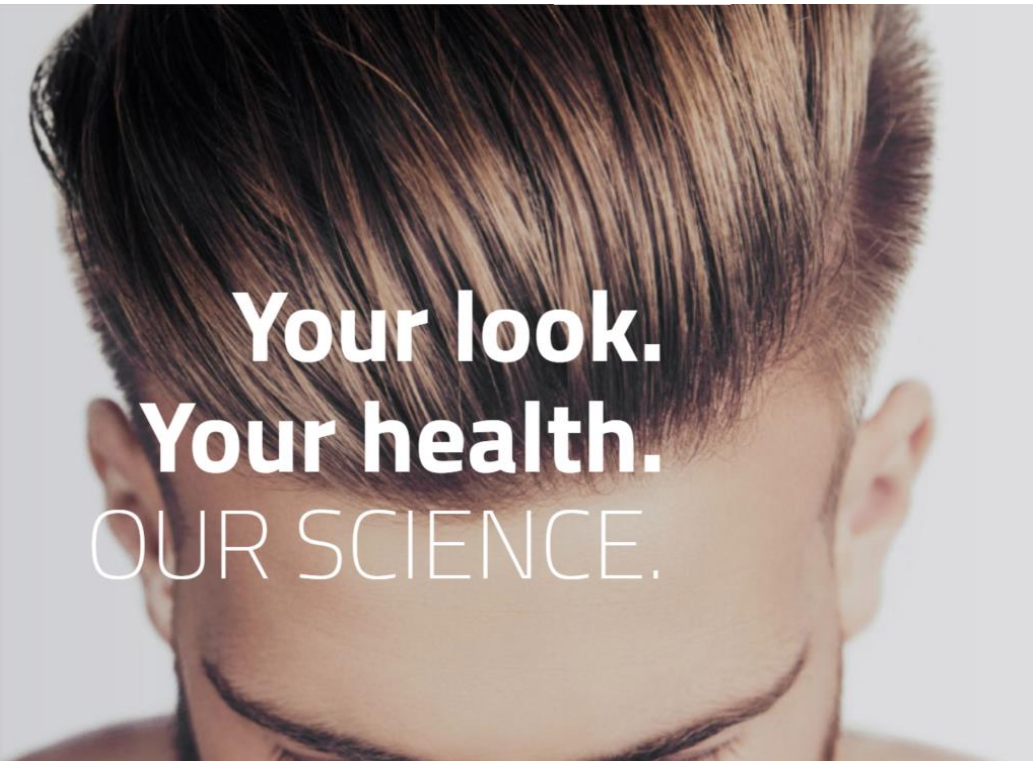
with RepliCel's partner 

2021: Clinical research study under ASRM expected to commence late 2021 in Japan

2023: First product launch expected in Japan

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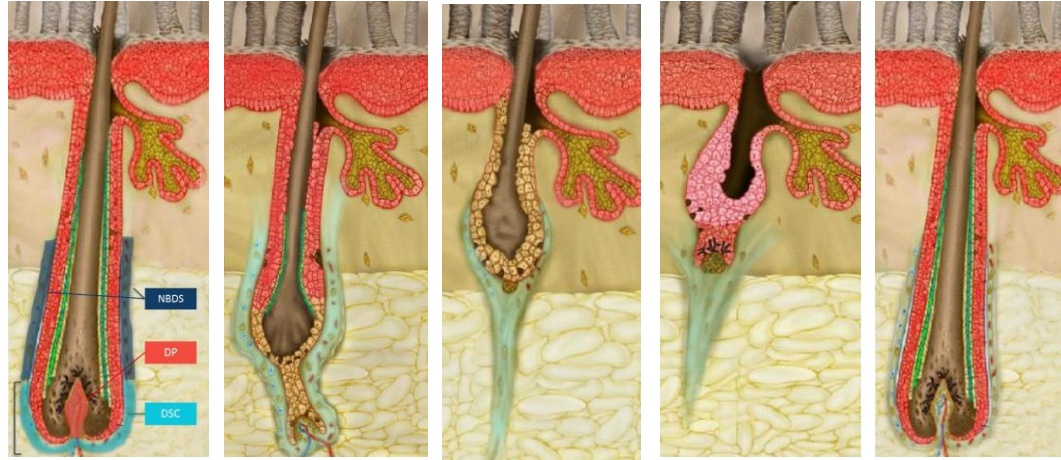
**RCH-01 Hair Regrowth**





## The Hair Cycle: From growth phase to resting phase

Cellular structure of a hair follicle bulb disaggregates during the regression to resting phase.



**GROWTH PHASE**

**DISASSEMBLY PHASE**

**FOLLICLE QUIESCENCE**

**FOLLICLE REASSEMBLY**

**GROWTH PHASE**

Anagen = up to 3 years

Catagen = 3 weeks

Telogen = 2-3 months

Early Anagen = 2-3 wks

Anagen = up to 3 yrs



Strong safety profile and efficacy data in two clinical studies suggest the potential for RepliCel's RCH-01 cell therapy to restore hair fiber growth in areas of pattern hair loss in men and women with androgenetic alopecia (the primary cause for human hair loss).

### PHASE 1 CLINICAL TRIAL

Randomized, double-blind, placebo-controlled, phase 1 clinical trial of a single injection of RCH-01 in men and women with androgenetic alopecia hair loss (completed)

(Georgia) (19 participants)

**Primary Endpoint:** Safety (successfully met)

**Secondary Endpoint:** Efficacy at 12 months

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**Publication:** McElwee K, Panich D., Hall D., Hoffmann R. *Toward a cell-based treatment for androgenetic alopecia in men and women: 12-month interim safety results of a phase 1/2a clinical trial using autologous dermal sheath cup cell injections.* J Invest Dermatol. 2013; 133: 1401

[https://www.jidonline.org/article/S0022-202X\(15\)36211-4/fulltext](https://www.jidonline.org/article/S0022-202X(15)36211-4/fulltext)

### Results:

- First-in-human, five-year follow-up firmly establishes product safety
- Efficacy data collected from all 19 patients over 24 months produced provocative insights from treated area after only a single injection of RCH-01 :
  - The most significant patient response was an increase in hair density over baseline of 21% at 24 months
  - The top seven responders had an >10% increase in hair density over baseline at six months and an 8.3% increase after 24 months with three of these participants maintaining an >10% increase in density over baseline at 24 months.
  - While there was a high degree of variability in hair density changes between individual participants at 24 months post-injection compared to baseline, an overall stabilization of hair loss was observed among all the patients treated per protocol.

## PHASE 2 CLINICAL STUDY

Randomized, placebo-controlled, double-blinded, clinical study on the efficacy and safety of cultured (human) autologous hair follicle dermal sheath cup cells (DSCC) on androgenetic alopecia.

(Japan) (65 male and female participants)

**Primary Endpoints:** Tolerance and Hair Density Changes (successfully met)

**Secondary Endpoint:** Dose-finding

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**Publication:** Tsuboi, Niiyama, Irisawa, Harada, Nakazawa, Kishimoto. *Autologous Cell-based Therapy for Male and Female Pattern Hair Loss using Dermal Sheath Cup Cells: A Randomized Placebo-Controlled Double-Blinded Dose Finding Clinical Study*. Journal of the American Academy of Dermatology (JAAD).

<https://doi.org/10.1016/j.jaad.2020.02.033>

## Design:

- Participants received single injections of  $7.5 \times 10^6$ ,  $1.5 \times 10^6$ , or  $3.0 \times 10^5$  DSC cells or a placebo in four randomized separate regions on the scalp, and hair densities and diameters were measured for 3, 6, 9, and 12 months. Fifty men and 15 women aged 33 to 64 years were injected with DSC cells.

## Results:

- Best response was at the  $3.0 \times 10^5$  DSC cells injection site at which total hair density and cumulative hair diameter was significantly increased compared with the placebo after 6 and 9 months.
- Best responders were those at stage Norwood III/IV (versus those at V/VI) who had a range of 5-13 more hairs per square centimeter at nine-months after treatment which is a statistically significant result produced from a one-time injection

## PHASE 3 CLINICAL STUDY

Multicenter clinical study on the efficacy and safety with extensive and repeated injections of cultured (human) autologous hair follicle dermal sheath cup cells on male and female pattern hair loss

(actively recruiting)

(Japan) (36 participants)

**Primary Endpoint:** Hair Density

**Clinical trial registry:** <https://jrct.niph.go.jp/en-latest-detail/jRCTb032200148>

## Design:

- Interventional, open label, uncontrolled, single-arm study studying effect of repeated injection treatments of DSC cells in male subjects with pattern hair loss characterized as type III vertex to type VI on the Norwood Scale, or equivalent type and female subjects with pattern hair loss characterized as type 3 to type 6 on the Shiseido Scale.

## Results:

- TBD

## RCH-01 Program Status and Plan

Completed: Randomized, double-blind, placebo-controlled phase 1 clinical trial

Completed: Randomized, placebo-controlled, double-blinded, dose-finding clinical study

Ongoing: research being conducted at the University of British Columbia and the University of Victoria. Directional data offering insights into pathways for improving efficacy and manufacturing.

2023: Pivotal multicenter clinical study testing the efficacy of “extensive and repeated” injections of RCH-01 on male and female pattern hair loss.

funded by RepliCel’s licensee 

2023: First product launch expected in Japan



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# Ensuring controlled delivery



- More consistent dermal injections; more consistent outcomes
- Less local anesthetic; better patient experience
- Shorter procedure time
- Increased control over injection depth, dose, and dispersion

## To control the outcome, control the delivery.

Delivery of cells has been a highly under-valued aspect of the cell therapy product development continuum.

- injection (standard vs proprietary; system vs local)
- spray
- pill / capsule (encapsulated)
- cell-loaded matrix/scaffold
- engineered tissues (bioprinting, biospinning, biospraying, using artificial or decellularized constructs)



The RCI-02 dermal injector is designed to deliver cells, dermal fillers, drugs and biologics



Electronic activator  
(improves over manual plunger)

Disposable Cartridges



- Digital controls program for depth, volume, rate of dispersion
- Provides exact repeatable dispersion across 3 dimensions
- Removes human variability
- Built-in Peltier element reduces need for anesthetics
- Proprietary multi-needle heads
- Exclusive cartridge & components
- Near-term commercial launch

## RCI-02 -Dermal Injector and Consumables. Program Status and Plan



Completed: First functional prototypes built and initially tested 2017 and optimized through 2020.

2021 Q1: Commercial-grade prototypes manufactured in first production run.

2021 2H: FDA 510(k) expected

2021 Q4: First product launch in USA and Hong Kong expected in late 2021.

2021 2H: Launch of initial series of clinical testing by multiple clinical KOLs and company-sponsored clinical evaluation

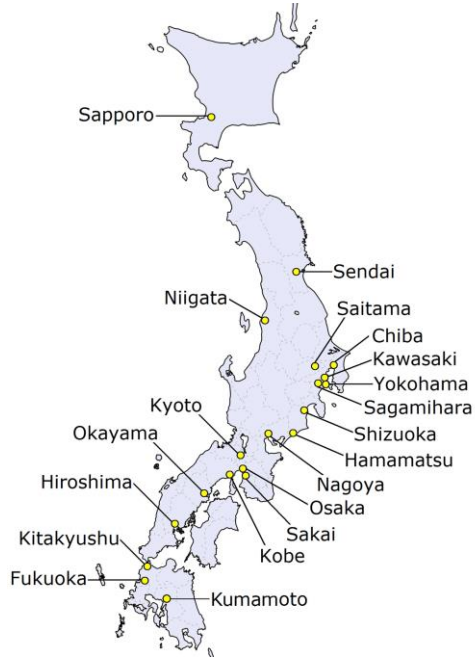
Commercialization partner\* already in place in Hong Kong which accepts US or EU approvals for medical devices.

Commercialization partner \*\* already in place in USA.

\* RepliCel's licensee YOFOTO

\*\* Replidel distributor MainPointe Pharmaceuticals

# Next Steps in Japan



# RepliCel™

Using Cells for Healing

## Cell Therapies Positioned for Success in Japan



- ✓ RepliCel's products have already been the subject of 4 well-controlled, clinical studies involving 100+ patients
- ✓ Successful completion of first 2 PMDA consults
- ✓ Both cell therapies being prepared for ASRM clinical research & commercialization
- ✓ Japanese-owned contract manufacturer preparing for PMDA-certification under MHLW guidelines
- ✓ Preparing for the 3rd (clinical) consult with PMDA for RCT-01 to position the product for a PMDA clinical trial and PMDA approval and MHLW reimbursement
- ✓ Experienced cell therapy CRO onboarding
- ✓ Key Japanese clinical advisors engaged; commencing study design and preparations
  - Well respected Japanese orthopedic sports medicine clinical advisor for RCT-01
  - Highly regarded Japanese clinical dermatology researcher advisor for RCS-01

Seeking co-development and commercialization partners in Japan



One Platform. Two innovative cell therapies.

- ❑ RCT-01 Tendon regeneration
  - Preparing to launch ASRM clinical study
  - Preparing for 3<sup>rd</sup> / final consult with PMDA for PMDA trial with potential to lead to conditional approval / reimbursement
  
- ❑ RCS-01 Skin rejuvenation



One unparalleled dermal injection technology

- ❑ RepliCel Dermal Injector Portfolio (RCI-02)



A REVOLUTION IN SPORTS MEDICINE and AESTHETICS



# RepliCel™

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[www.replicel.com](http://www.replicel.com)

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