FOLLICA CLINICAL SUMMARY

CONFERENCE CALL | 8:00 AM PDT (11:00 AM EDT)

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CONTENTS

Overview of completed and planned clinical studies.

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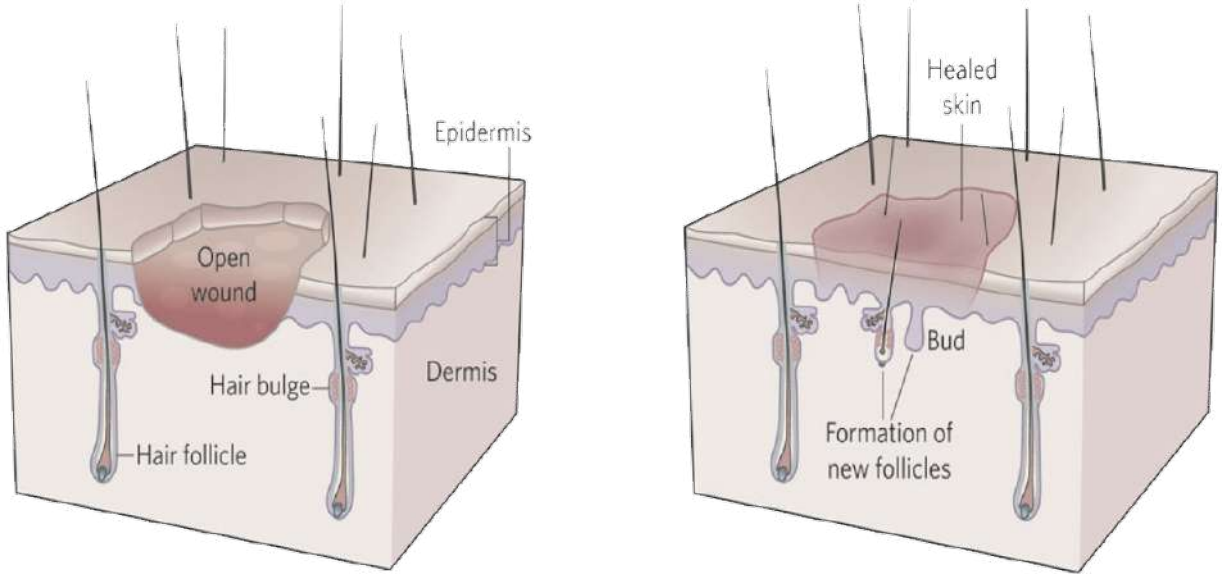
SCIENTIFIC FOUNDATION

Creating an embryonic window: our scientific founders were the first to observe and characterize the connection between wound healing and new follicle formation.

When cells move in to heal epidermal disruption, they are trying to make a decision:

Should I make epidermis, or should I make a hair?

There is a window of opportunity in which we can push them to make hair, and multiple biological pathways to target to enhance the effect.



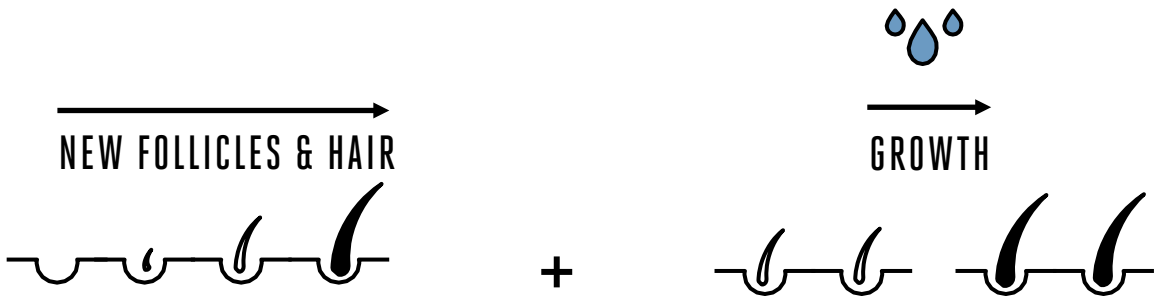
Source: Ito M., Yang Z., Andl T. Cui C, Kim N, Millar SE, Cotsarelis G. Wnt-dependent de novo hair follicle regeneration in adult mouse skin after wounding. Nature. 2007;447(7142):316–320.

TREATING HAIR LOSS IN A NEW WAY

Our technology creates new follicles, and improves the application of a range of treatments to grow new hair.

1. SKIN DISRUPTION

2. NEW HAIR GROWTH



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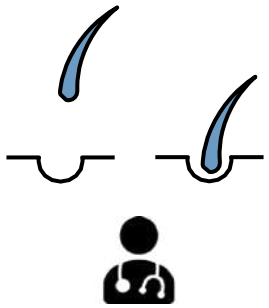
EXISTING TREATMENTS

Currently approved treatments only move around or preserve **existing** hair.

MOVE HAIR AROUND

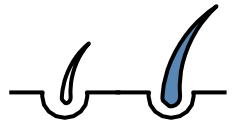


SURGERY
(TRANSPLANTS)

Very high-cost
Invasive
Multiple visits

Existing hair only

PRESERVE HAIR



FINASTERIDE
(PROPECIA)

Rx-only
Men-only
Side-effects

Existing hair only

MINOXIDIL
(ROGAINE)

Unguided
Messy application

Existing hair only

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WE ARE THE FIRST COMPANY TO CREATE DE NOVO HAIR FOLLICLES WHICH GROW HAIR.

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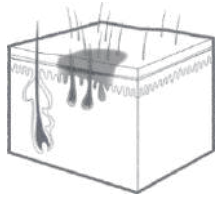
DEMONSTRATING FOLLICULAR NEOGENESIS IN HUMANS

2 objectives to provide evidence that the Cotsarelis technology can form the basis for a hair loss treatment in humans.



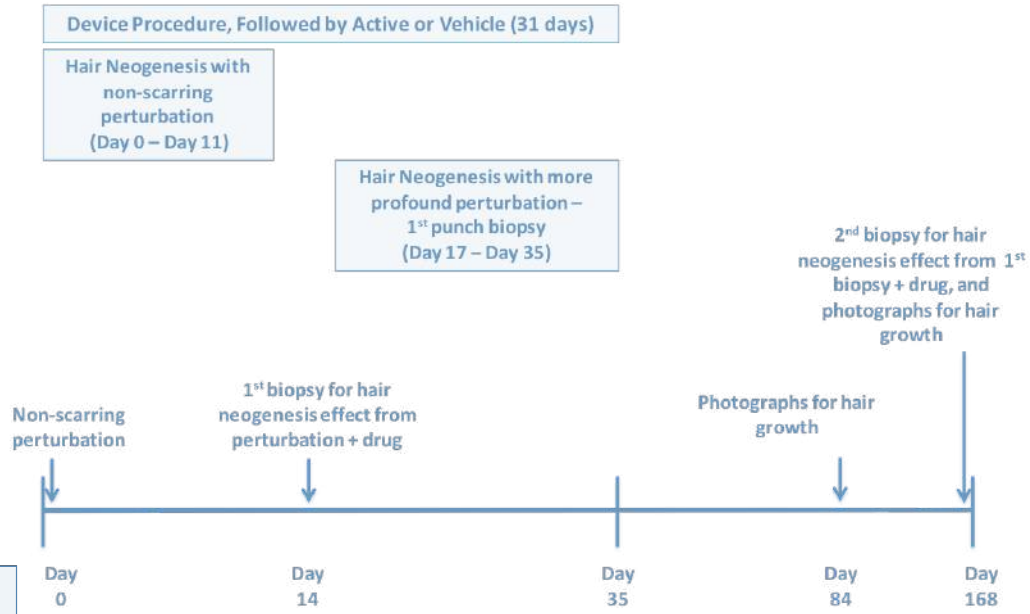
1. Induce neogenesis with a method practical for human use, i.e., a **non-scarring disruption** vs. full thickness excision

2. **Pharmacologically enhance** hair repopulation with a small molecule drug.

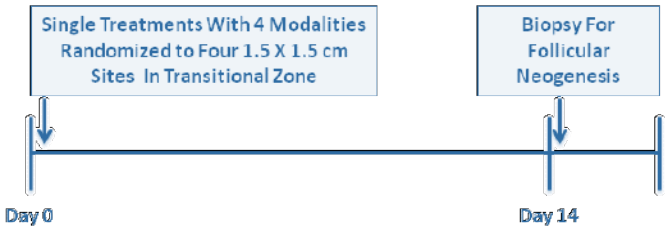
3 COMPLETED CLINICAL STUDIES

Follica's 3 completed clinical studies:

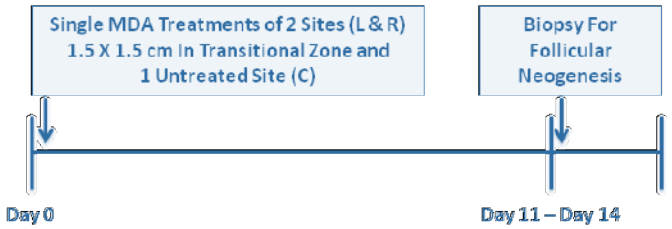
PHASE IIA (FOL-003, N=65)



EXPLORATORY (FOL-002, N=15)



PILOT (FOL-001, N=15)



3 COMPLETED CLINICAL STUDIES

Follica's 3 completed clinical studies:

FOL-001 – PHASE 1 PILOT STUDY

- Non-scarring MDA device, no drug
- Healthy male subjects with AGA (N=15)

FOL-002 – PHASE 1 EXPLORATORY STUDY

- 4 non-scarring device modalities, no drug
- Healthy male subjects with AGA (N=15)

FOL-003 – PHASE 2A STUDY

- Non-scarring DA device combined with topical drug or vehicle control
- Healthy male subjects with AGA (N=65)

FOLLICA FOL-001 (PILOT STUDY)

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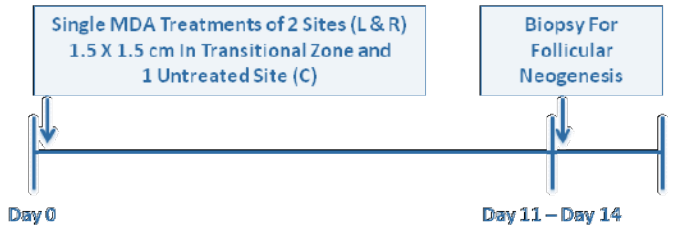
FOL-001 PILOT STUDY

FOL-001, N=15 (MGH)

Study Exploring Induction Hair Follicle Neogenesis Using MDA Device.

Non-scarring device, no drug.



A PILOT STUDY TO DETERMINE THE EFFECTS OF SKIN ABRASION ON FORMATION OF NEW HAIR FOLLICLES

Design	Exploratory, single-center, single- group, open-label, within-patient comparative trial
Main Endpoint	Number of neogenic follicles by histology in a 4-mm punch biopsy
Subject Population	15 adult males with androgenetic alopecia
Treatments	Microdermabrasion [MDA] device (aluminum oxide - disruption depth ~100- 150 microns) vs untreated skin. No topical drug treatment.
Study Site	MGH; Principal Investigator Dr. Alexa Kimball

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OBSERVATIONS VIA BIOPSY

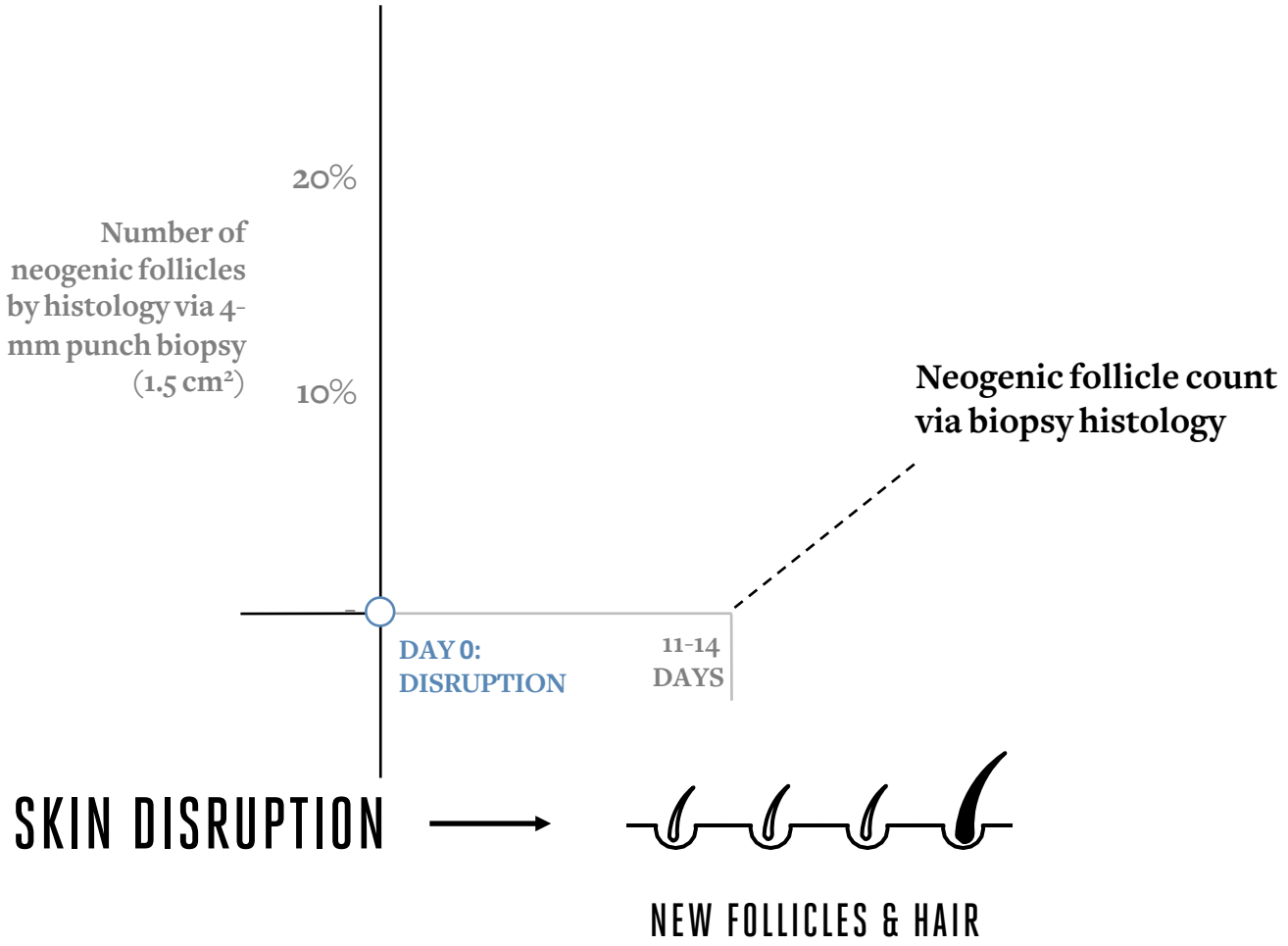
FOL-001, N=15 (MGH)

Study Exploring Induction Hair Follicle Neogenesis Using MDA Device.

Non-scarring device, no drug.

PILOT STUDY (FOL-001, N=15):

NEOGENIC FOLLICLES BY HISTOLOGY VIA 4-MM PUNCH BIOPSY FOLLOWING SKIN DISRUPTION VIA MICRODERMABRASION (MDA)

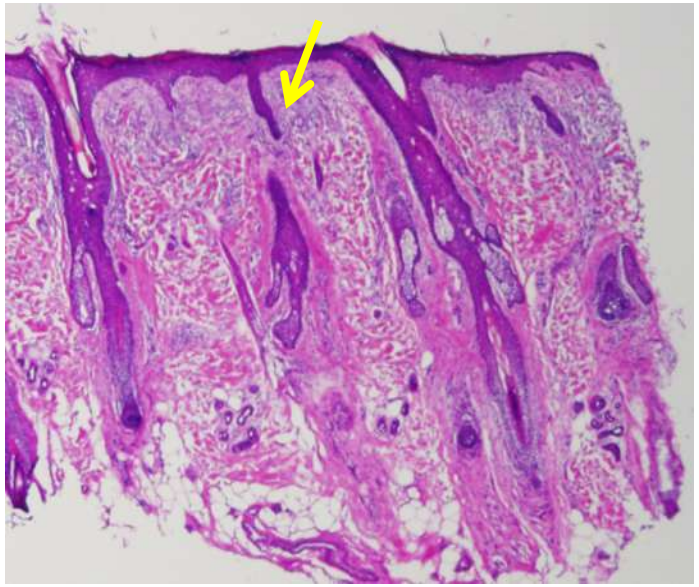


NEOGENIC-LIKE STRUCTURES CHARACTERIZED

FOL-001, N=15 (MGH)

Study Exploring Induction Hair Follicle Neogenesis Using MDA Device.

Non-scarring device, no drug.



- Morphology comparable to primitive structures in embryonic hair follicle development
  - Peg-like down growth from epidermis
  - Sebaceous gland negative
  - Hair shaft negative
  - Skin surface pore negative
- BerEP4 positive (embryonic hair follicle marker)
- Alkaline phosphatase positive (dermal papilla positioned)
- Ki67 positive (matrix positioned)
- Dermal channel negative (absence of streamer)

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ADULT STRUCTURES REPRISING EMBRYONIC FOLLICLES

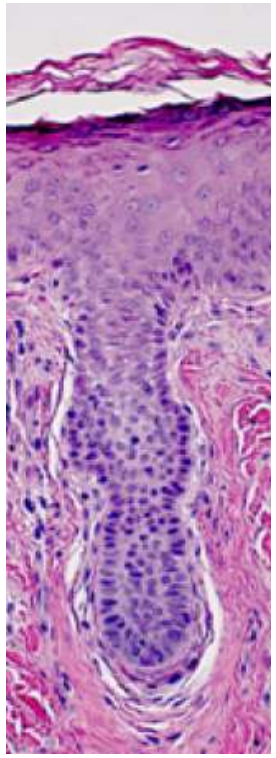
FOL-001, N=15 (MGH)

Study Exploring Induction Hair Follicle Neogenesis Using MDA Device.

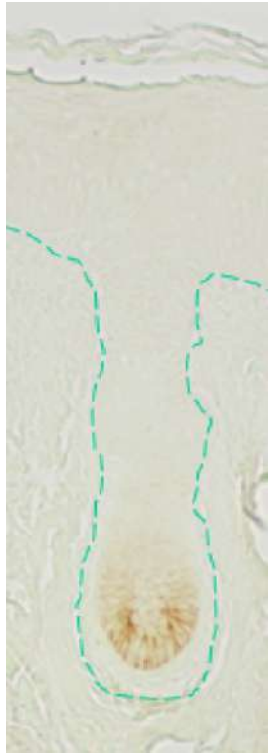
Non-scarring device, no drug.

NEOFOLLICLE FOLLOWING DISRUPTION

H&E



Ber-EP4



H&E: Hematoxylin & Eosin

HUMAN DEVELOPING FOLLICLE

Ber-EP4

Ber-EP4: EpCAM antibody

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PILOT STUDY CONCLUSIONS

FOL-001, N=15 (MGH)

Study Exploring Induction Hair Follicle Neogenesis Using MDA Device.

Non-scarring device, no drug.

Neogenic Follicles In 4-mm Punch Biopsies

	MDA N=22	Control N=10	Fold Increase
% (number) of 4-mm biopsies with at least 1 Neogenic-Like HF (NL)	18% (4)	10% (1)	1.8
Mean NLs / 4 mm punch	0.5	0.2	2.5
Mean NLs / 1 cm2 (scaled)	3.8	1.5	2.5
Mean NLs / 2 cm2 (scaled)	7.7	3.1	2.5

- Follicles with neogenic attributes are present rarely in the transitional area of scalp in adult men with AGA (< 1% of follicles)†
- MDA disruption increases neogenic follicles by approximately 2.5-fold

† Total hair count of 236.6 +/- 10.99 (SEM)/cm2 in 11 men aged 35 to 45 years without male pattern baldness used as proxy for hair follicle count - Olsen JAAD 2003

- De novo, neogenic hair follicles can be identified in balding scalp skin of men with AGA
- In the natural state, these structures are rare
- Non-scarring disruption can increase the number of neogenic hair follicles
- Responder rate & treatment magnitude to disruption from FOL-001 require substantial improvement

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FOLLICA FOL-002 (EXPLORATORY STUDY)

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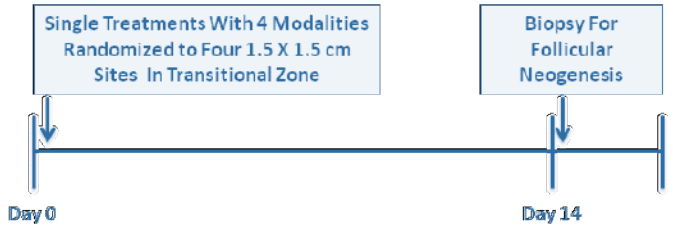
FOL-002 EXPLORATORY STUDY

FOL-002, N=15

Study Exploring Induction Hair Follicle Neogenesis Using Other Devices (DA and 3 Laser).

4 non-scarring device modalities, no drug



EPIDERMAL DISRUPTION: EVALUATION OF NEW HAIR FOLLICLE GROWTH AFTER VARIOUS METHODS OF SKIN DISTURBANCE

Design	Exploratory, single-center, single- group, open-label, within-patient controlled trial
Main Endpoint	Number of neogenic follicles by histology in a 4-mm punch biopsy
Subject Population	16 adult males with androgenetic alopecia
Treatments	Dermabrasion [DA] device (diamond fraise - disruption depth ~100- 150 microns) and 3 laser type of ablative lasers; No topical drug treatment
Study Site	Stephens and Associates; Principal Investigator Dr. R. Todd Plott

PILOT STUDY (FOL-002, N=15):

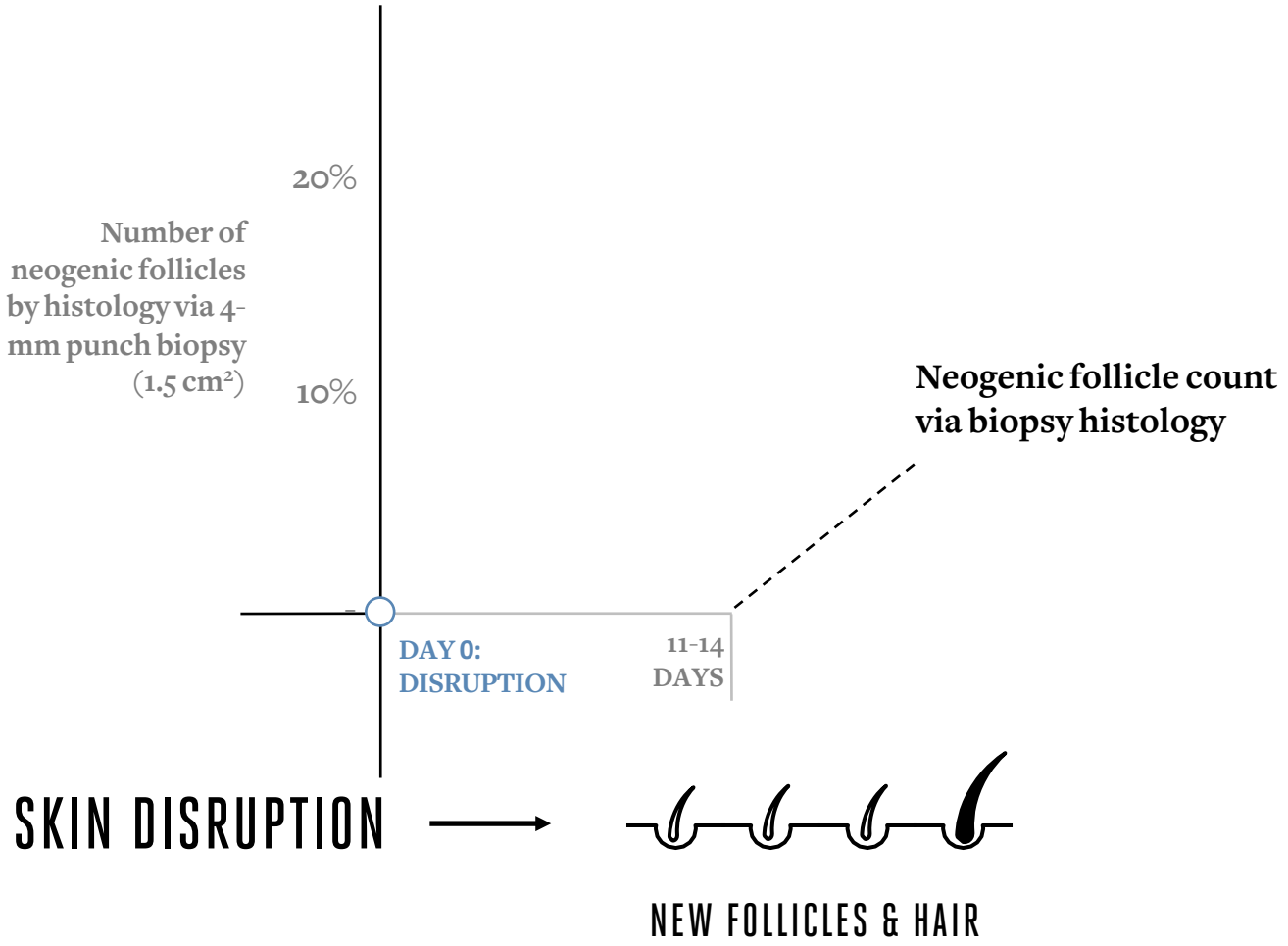
NEOGENIC FOLLICLES BY HISTOLOGY VIA 4-MM PUNCH BIOPSY FOLLOWING SKIN DISRUPTION VIA 4 DEVICE MODALITIES: 3 LASER DEVICES AND DERMABRASION (DA)

OBSERVATIONS VIA BIOPSY

FOL-002, N=15

Study Exploring Induction Hair Follicle Neogenesis Using Other Devices (DA and 3 Laser).

4 non-scarring device modalities, no drug



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ANOTHER STRUCTURE OF INTEREST

FOL-002, N=15

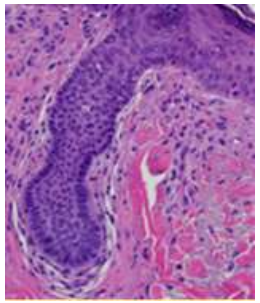
Study Exploring Induction Hair Follicle Neogenesis Using Other Devices (DA and 3 Laser).

4 non-scarring device modalities, no drug

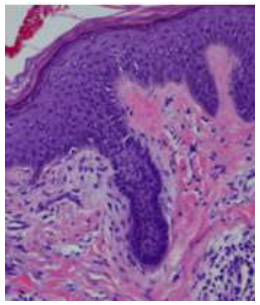
1. NEOGENIC-LIKE (NL)

As in FOL-001, quantified neogenic follicles as targets for pharmacologic modulation and hair repopulation in AGA.

FOL-001

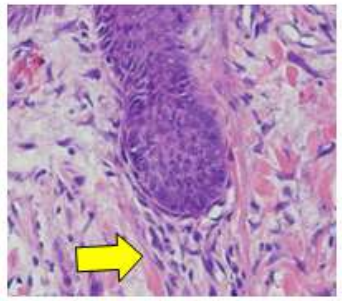


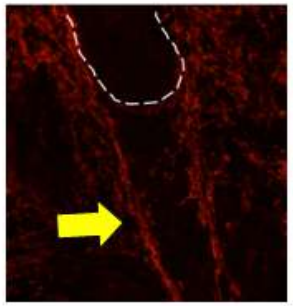
FOL-002



2. PRE-EXISTING-LIKE (PEL)

With G Cotsarelis and the SAB, identified an additional target – a primitive follicular structure with dermal channels (arrow), representing pre-existing senesced structures that have reorganized with disruption





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EXPLORATORY STUDY CONCLUSIONS

FOL-002, N=15

DA Creates a Substantial Number of Hair Follicle Structures of Interest (strongest signal of 4 modalities).

Hair Follicle Structures of Interest (SOI) In 4-mm Punch Biopsies

	NL N=16	PEL N=16	Both SOIs N=16
Number (%) of 4-mm biopsies with at least 1 SOI	9 (56%)	12 (75%)	15 (94%)
Mean # of SOIs/ 4 mm punch	1.0	6.6	7.6
Mean SOIs / 1 cm2 (scaled)	7.7	51.0	58.7
Mean SOIs / 2 cm2 (scaled)	15.4	101.9	117.3

- As in FOL-001, quantified neogenic follicles as targets for pharmacologic modulation & hair repopulation in AGA
- With G Cotsarelis and the SAB, identified an additional target – a primitive follicular structure with dermal channels, representing pre-existing senesced structures that have reorganized with disruption

- Non-scarring disruption from all 4 modalities tested increased the number of new hair follicles, with DA creating strongest signal
- De novo, neogenic hair follicles (NLs)
- Reorganized, pre-existing structures (PELs)
- Quantity of additional new hair follicular substrate induced is in the range for contributing to a clinically meaningful increase in hair count, if new structures produce terminal-sized hair shafts
- Disruption modality creating most robust neofollicular response, i.e. dermabrasion, was brought forward into next clinical trial that combined TCP with candidate drug and measured production of new hair shafts associated with inducing SOIs (FOL-003)

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FOLLICA FOL-003 (PHASE IIA STUDY)

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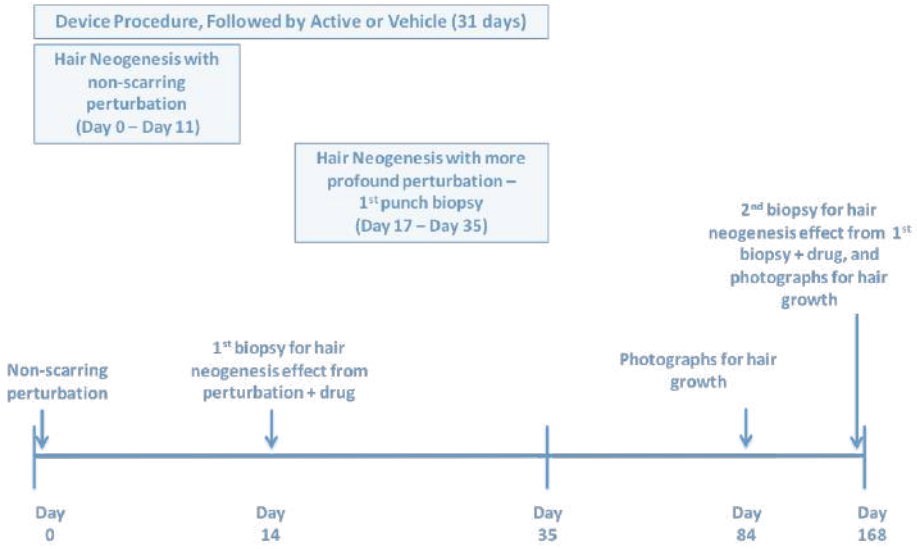
FOL-003 PHASE IIA STUDY

FOL-003, N=65 (Germany)

DA Device + Drug Combination Study To Evaluate Hair Follicle And Hair Shaft Generation.



A STUDY TO EVALUATE THE EFFECT OF CONTROLLED CUTANEOUS DISRUPTION AND PHARMACOLOGIC MODULATION FOR INDUCING FOLLICULAR NEOGENESIS

Design	2-parallel-group, randomized, double-blind placebo controlled trial
Main Endpoint	**Primary:** Hair counts (TAHC) **Secondary:** Number of neogenic follicular structures of interest by histology; hair width
Subject Population	65 males with androgenetic alopecia
Treatments	Europe (Lead Principal Investigator Professor Dr. Ulrike Blume-Peytavi)
Study Site	Device Disruption followed by FC-007 (lithium gluconate 8% gel as a wnt pathway activator) vs. Device Disruption followed by vehicle (gel without the API)

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A VALIDATED ENDPOINT: TARGET AREA HAIR COUNT (TAHC)

A Validated Phase 3 Primary Endpoint Used In Previous Drug Approvals.

- **Target Area Hair Count** (**TAHC**) is validated a Phase 3 Primary endpoint in PROPECIA and ROGAINE FOAM and ROGAINE SOLUTION approvals
- Continuous variable
- Technique used:
  - Canfield Scientifics' standardized equipment for image capture and analysis (the gold standard)
  - Rigorous training, QC, stereotactic positioning, and tattoo reference for accuracy and reproducibility over time
  - A system that is 21 CFR Part 11 compliant
- As done in the PROPECIA and ROGAINE studies, Canfield technicians mapping hairs for automated computer image analysis and compilation are blinded to treatment

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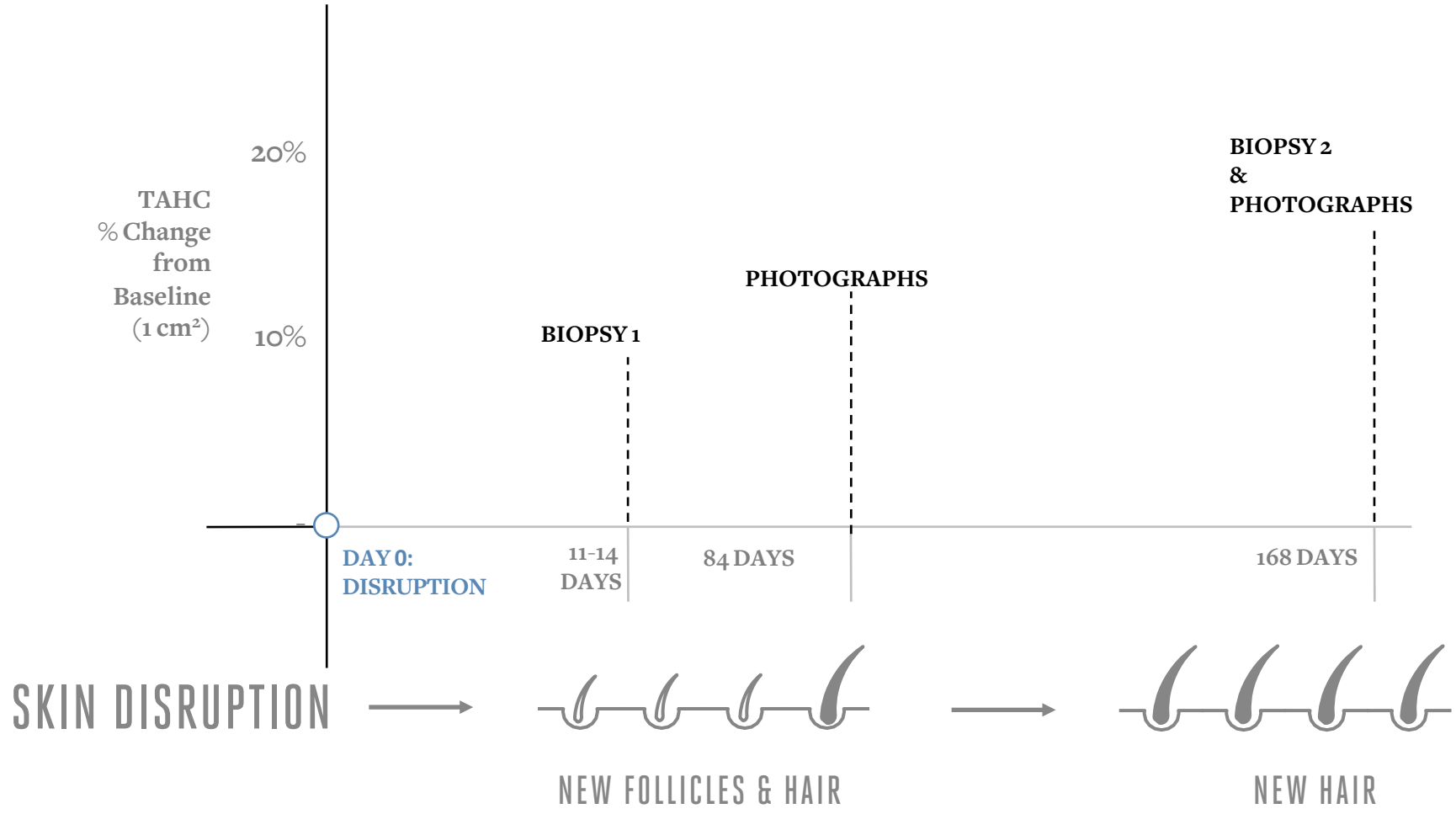
OBSERVATIONS VIA BIOPSIES & PHOTOGRAPHS

FOL-003, N=65 (Germany)

DA Device + Drug Combination Study To Evaluate Hair Follicle And Hair Shaft Generation.

PHASE IIA STUDY (FOL-003, N=65):

% CHANGE FROM BASELINE IN TARGET AREA HAIR COUNT (TAHC) FOLLOWING SKIN DISRUPTION ALONE



DISRUPTION WAS WELL-TOLERATED

Scalp Sites Healed Well After Disruption.

Day 0 Before Disruption

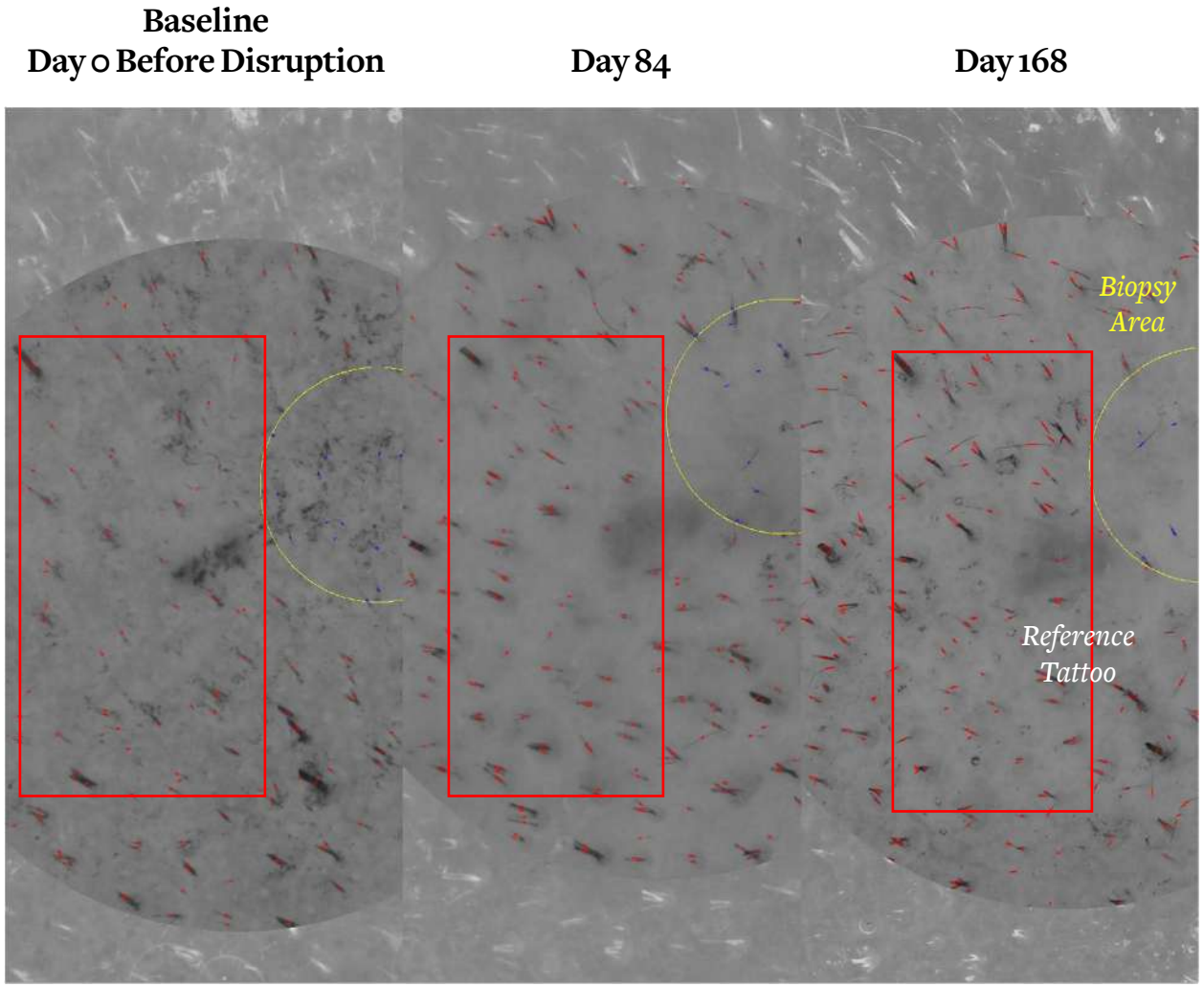
Day 168 After TCP

**Red marking at image center is an ink tattoo which serves as a reference for hair counting via photography.*

Photographs taken from Study FOL-003 showing good healing after treatment.

OBSERVED HAIR FOLLICLE NEOGENESIS

Creation of Neofollicles By Disruption Is Associated With Formation of New Hair Shafts In Humans.



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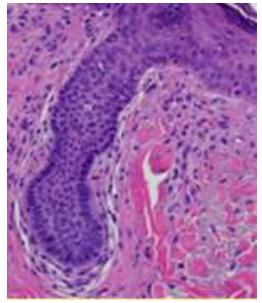
A THIRD STRUCTURE OF INTEREST

Additional Primitive Attached Structures Added to Targets (Structures) of Interest.

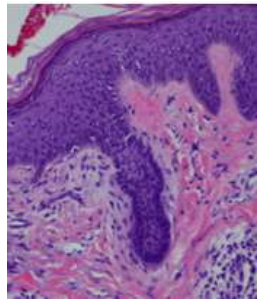
1. NEOGENIC-LIKE (NL)

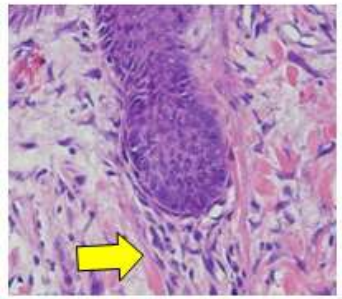
FOL-001



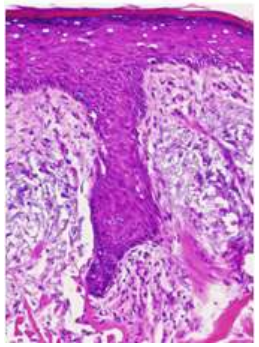
2. PRE-EXISTING-LIKE (PEL)

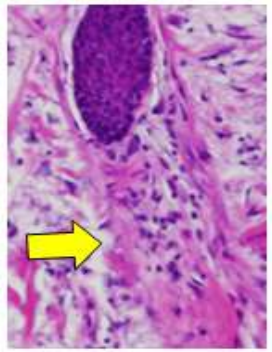
FOL-002





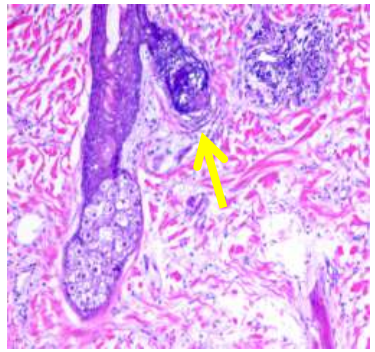
FOL-003





3. PRE-EXISTING-LIKE ATTACHED (PELA)

With G Cotsarelis & the SAB, identified a 3rd primitive follicular structure of interest, attached to pre-existing hair follicles, as an additional target for pharmacologic modulation (PELA).



Activated structure (yellow arrow) is attached to a pre-existing hair follicle.

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FOL-003 DATA

Increases in **total** HC (All Hairs) with disruption are statistically significant and durable at both 3 & 6-months.

Summary of photographic hair counts in target analysis area (MITT)

	Group						Comparison of Device + Drug vs Device + Vehicle
	Device + Drug			Device + Vehicle			
Day 84 Results	**Baseline**	**Day 84**	**Change**	**Baseline**	**Day 84**	**Change**	
N	29	29	29	33	33	33	
Mean (SE)	492.8 (26.72)	528.8 (22.62)	36.0 (13.23)	522.1 (28.82)	575.4 (31.93)	53.4 (11.60)	-16.5 (9.75)
Min : Max	171 : 746	239 : 757	-124 : 227	185 : 885	280 : 1063	-47 : 178	
90% CI[a,b]			(13.50, 58.50)[a]			(33.71, 73.02)[a]	(-32.80, -0.21)[b]
P-value[a,b]			0.0055[a]			<0.0001[a]	0.9521[b]

	Group						Comparison Device + Drug vs Device + Vehicle
	Device + Drug			Device + Vehicle			
Day 168 Results	**Baseline**	**Day 168**	**Change**	**Baseline**	**Day 168**	**Change**	
N	29	29	29	33	33	33	
Mean (SE)	492.8 (26.72)	532.6 (26.87)	39.9 (15.34)	522.1 (28.82)	569.1 (32.38)	47.0 (14.75)	-10.0 (12.04)
Min : Max	171 : 746	199 : 863	-116 : 257	185 : 885	302 : 1026	-99 : 218	
90% CI[a,b]			(13.77, 65.95)[a]			(22.01, 71.99)[a]	(-30.10, 10.15)[b]
P-value[a,b]			0.0074[a]			0.0016[a]	0.7946[b]

CI [a] and P-value [a] are results for within-group mean changes.
CI [b] and P-value [b] are results for between-group differences in means.
PGM=DEVOPS/S_CLI/FOL00003/CSR/REPORT/PGM/S_photo_hc_mitt.sas OUT=REPORT/OUTPUT/S_photo_hc_mitt_i.rtf (11OCT2011 - 19:13)

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FOL-003 DATA

Increases in **terminal** HC (>30 uM Diameter) with disruption are statistically significant at 3-months, but did not persist to 6-months.

Summary of photographic hair counts in target analysis area (MITT non-vellus)

	Group						Comparison of Device + Drug vs. Device + Vehicle
	Device + Drug			Device + Vehicle			
Day 84 Results	**Baseline**	**Day 84**	**Change**	**Baseline**	**Day 84**	**Change**	
N	29	29	29	33	33	33	
Mean (SE)	325.2 (23.21)	357.4 (22.46)	32.1 (10.13)	358.7 (25.84)	406.3 (27.31)	47.6 (9.71)	-14.3 (7.33)
Min : Max	98 : 570	107 : 569	-109 : 171	106 : 611	87 : 752	-39 : 190	
90% CI[a,b]			(14.90, 49.38)[a]			(31.15, 64.06)[a]	(-26.54, -2.05)[b]
P-value[a,b]			0.0018[a]			<0.0001[a]	0.9721[b]

	Treatment Group						Comparison of Device + Drug vs. Device + Vehicle
	Device + Drug			Device + Vehicle			
Day 168 Results	**Baseline**	**Day 168**	**Change**	**Baseline**	**Day 168**	**Change**	
N	29	29	29	33	33	33	
Mean (SE)	325.2 (23.21)	328.2 (22.19)	3.0 (10.42)	358.7 (25.84)	365.2 (24.79)	6.5 (8.85)	-7.5 (7.12)
Min : Max	98 : 570	98 : 524	-137 : 165	106 : 611	90 : 635	-99 : 173	
90% CI[a,b]			(-14.77, 20.70)[a]			(-8.51, 21.48)[a]	(-19.41, 4.39)[b]
P-value[a,b]			0.3891[a]			0.2346[a]	0.8519[b]

CI [a] and P-value [a] are results for within-group mean changes.
CI [b] and P-value [b] are results for between-group differences in means.
PGM=DEVOPS/S_CLI/FOL00003/CSR/REPORT/PGM/S_photo_hc_mitt_vellus.sas OUT=REPORT/OUTPUT/S_photo_hc_mitt_vellus_i.rtf (11OCT2011 - 19:14)

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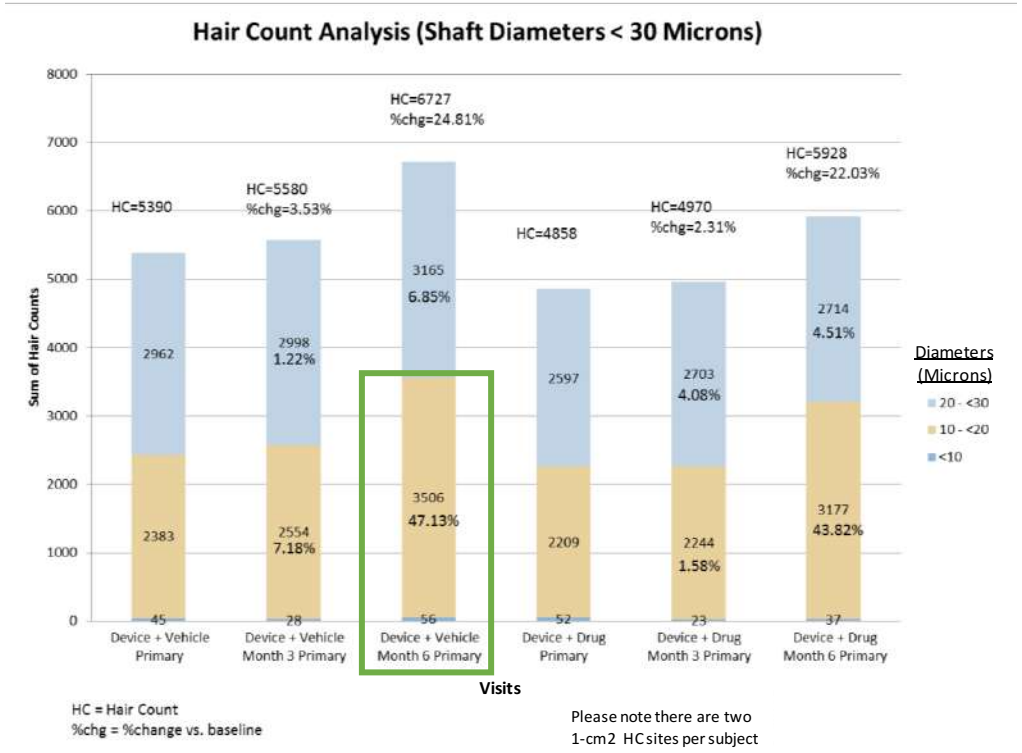
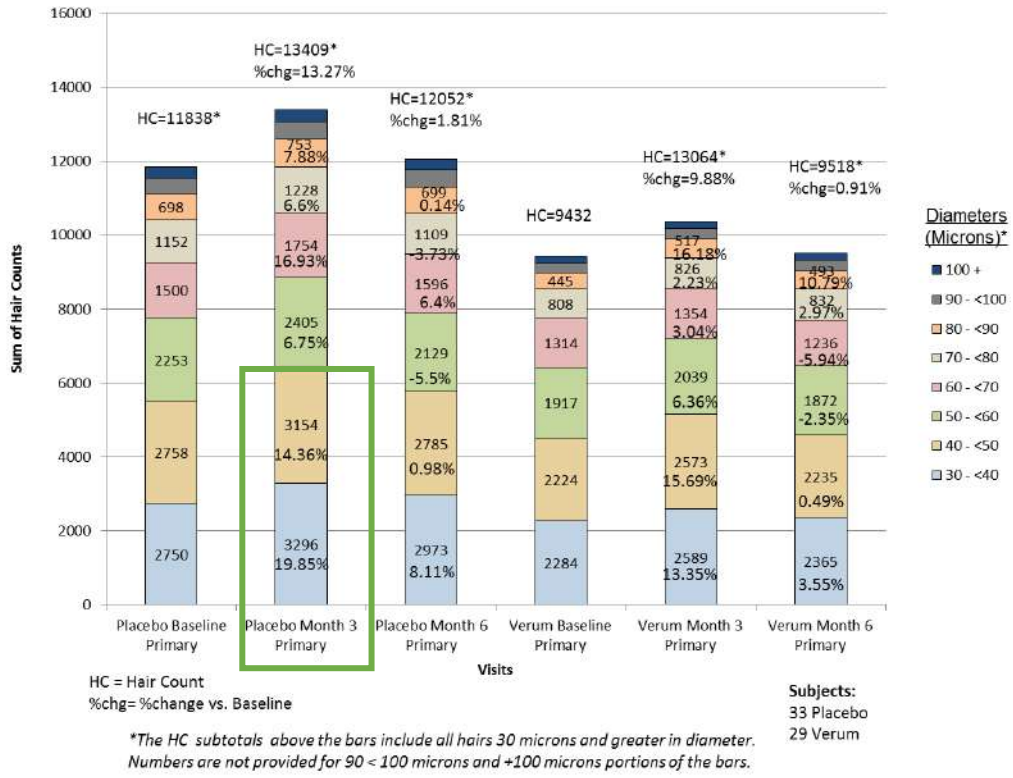
FOL-003 DATA

Hair count analysis.



Dramatic Increase And Pattern in Vellus Population (<30 uM Diameter) Suggest An Unprecedented Production of Neogenic Follicles



Terminal-Sized Hairs (Hair Shaft Diameters = and > 30 Microns), Increase At 3 Months Were Mostly In The 30–60 Micron Sized Groups

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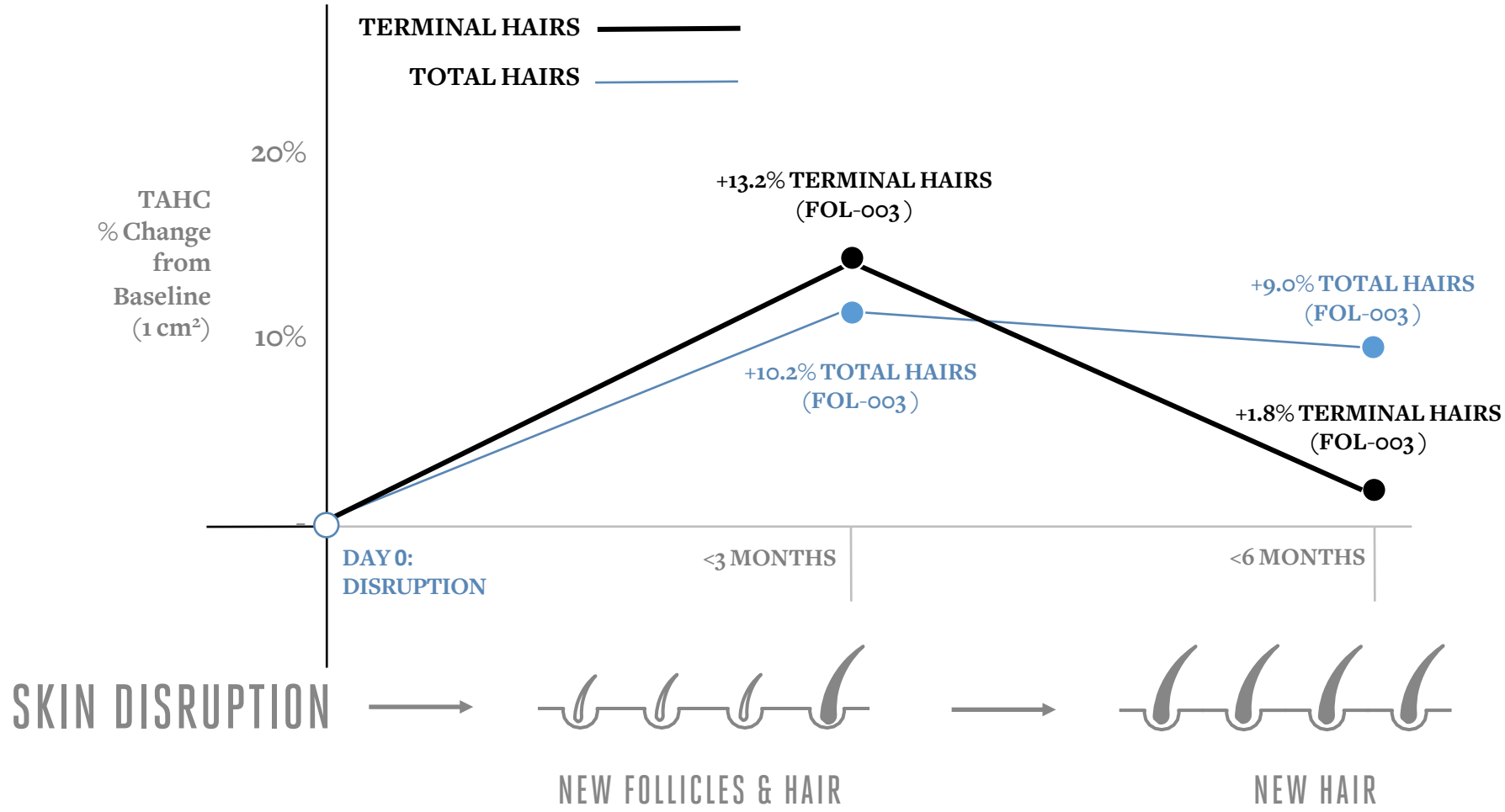
DISRUPTION ALONE CREATES NEW HAIR

Disruption alone creates new follicles and hair, increasing total hair count.

Source: Follica Phase 2A Study, FOL -003, unpublished (n=65).

PHASE IIA STUDY (FOL-003, N=65):

% CHANGE FROM BASELINE IN TARGET AREA HAIR COUNT (TAHC) FOLLOWING SKIN DISRUPTION ALONE



PHASE IIA STUDY CONCLUSIONS

FOL-003, N=65 (Germany)

DA Device + Drug Combination Study To Evaluate Hair Follicle And Hair Shaft Generation.

Hair Follicle Structures of Interest (SOI) In 4-mm Punch Biopsies

	NL	PEL	PELA	All SOIs
Number of 4-mm biopsies with at least 1 structure of interest (N=31)	25 (81%)	31 (100%)	25 (81%)	31 (100%)
Mean # of SOIs/ 4 mm punch (N=62)	0.9	7.5	1.9	10.3
Mean SOIs / (1 cm2 scaled)	6.9	57.6	14.5	79.0
Mean SOIs / (2 cm2 scaled)	13.8	115.2	29.0	158.0

- In contrast to current treatments, Follica's disruption of scalp histologically:
  - Creates true new hair follicles
  - Reorganizes and rejuvenates miniaturized pre-existing follicles
- This true hair follicle neogenesis from disruption observed in biopsies is associated with an increase in the total number of hair shafts, also unprecedented in AGA therapy
  - New hair shafts associated with disruption are durable to end of clinical trial
  - Currently, over time additional disruption-induced terminal hair shafts becomes vellus-sized
- Treatments were generally well-tolerated and there were no safety signals of concern
- The increased neofollicular vellus- and terminal-hair substrate, if convertible and sustainable to terminal hairs by the right hair-growth promoting drug, could provide for and result in breakthrough efficacy for AGA

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FOLLICA FOL-004 (REGISTRATION STUDY)

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SUPPORT FOR FOL-004

2 methods to support and inform the registration study design & device development.

1. To support skin disruption via proprietary **automated, mechanical needling** as a practical method to induce follicular neogenesis.

- Follica's 3 clinical studies
- Follica device development
- 2013 Dhurat pilot study [1]
- 2015 Chuong quorum sensing study [2]

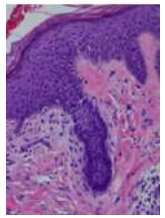
2. To **address unmet needs** of current devices & procedures, regulatory concerns, and hone design specifically for the scalp.

- Current device landscape
- Regulatory warnings
- In-depth user studies
- Leading industrial design

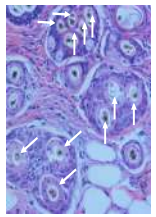
Select references:
1. Dhurat R, Sukesh MS, Avhad G, Dandale A, Pal A, Pund P. A randomized evaluator blinded study of effect of microneedling in androgenetic alopecia: A pilot study. Int J Trichology. 2013;5:6–11.
2. Chen CC, Wang L, Plikus MV, Jiang TX, Murray PJ, Ramos R, Guerrero-Juarez CF, Hughes MW, Lee OK, Shi S, Widelitz RB, Lander AD, Chuong CM. Organ-level quorum sensing directs regeneration in hair stem cell populations. Cell 161:277-290, 2015.

WHAT WE KNOW

We 've become experts in skin disruption to create new follicles and hair, and a strong collection of aggregated preclinical and clinical data supports our lead program.

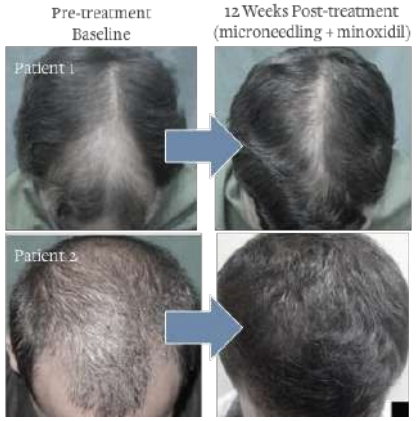


3 clinical studies demonstrate growth of de novo hair follicles in humans.[3]



Observed follicular neogenesis in preclinical studies.[2]

The connection between wound healing and new follicle formation.[1]



Independent study points to 4x hair growth via disruption + minoxidil vs. minoxidil alone in humans.[4]

SKIN DISRUPTION → NEW FOLLICLES & HAIR

MINOXIDIL → >4X NEW HAIR VS. MINOXIDIL ALONE

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Select references:

1. Ito M., Yang Z., Andl T. Cui C, Kim N, Millar SE, Cotsarelis G. Wnt-dependent de novo hair follicle regeneration in adult mouse skin after wounding. Nature. 2007;447(7142):316–320.
2. Demonstrating follicle neogenesis following wounding and application of an investigational compound. Source: Follica internal preclinical R&D (2008, unpublished)
3. Quantified neogenic follicle as targets for pharmacologic modulation &hair repopulation in AGA . Source: Follica internal Clinical R&D Findings – Fol-002(2008, unpublished)
4. Dhurat R, Sukesh MS, Avhad G, Dandale A, Pal A, Pund P. A randomized evaluator blinded study of effect of microneedling in androgenetic alopecia: A pilot study. Int J Trichology. 2013;5:6–11.

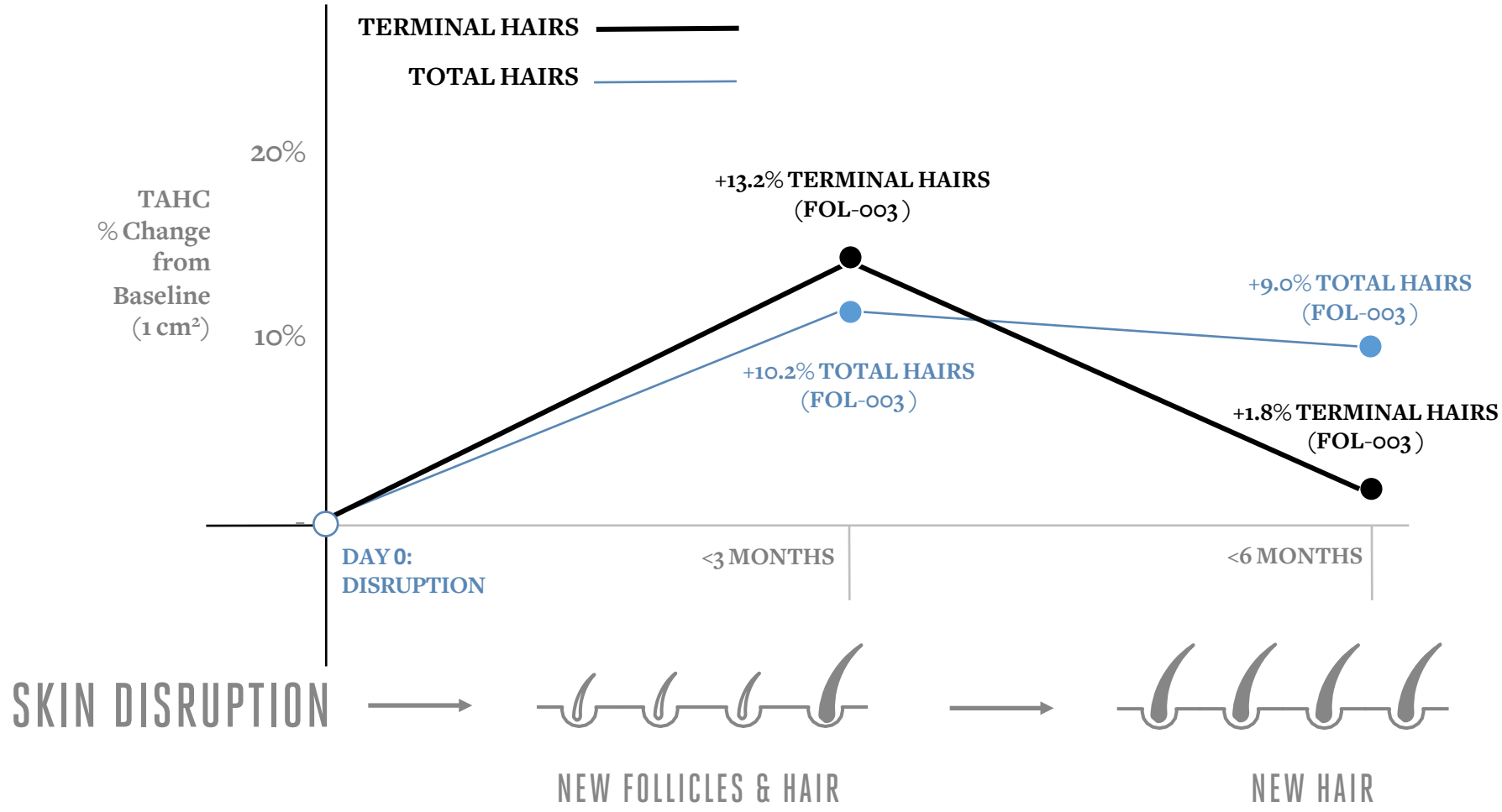
DISRUPTION ALONE CREATES NEW HAIR

Disruption alone creates new follicles and hair, increasing total hair count.

Source: Follica Phase 2A Study, FOL -003, unpublished (n=65).

PHASE IIA STUDY (FOL-003, N=65):

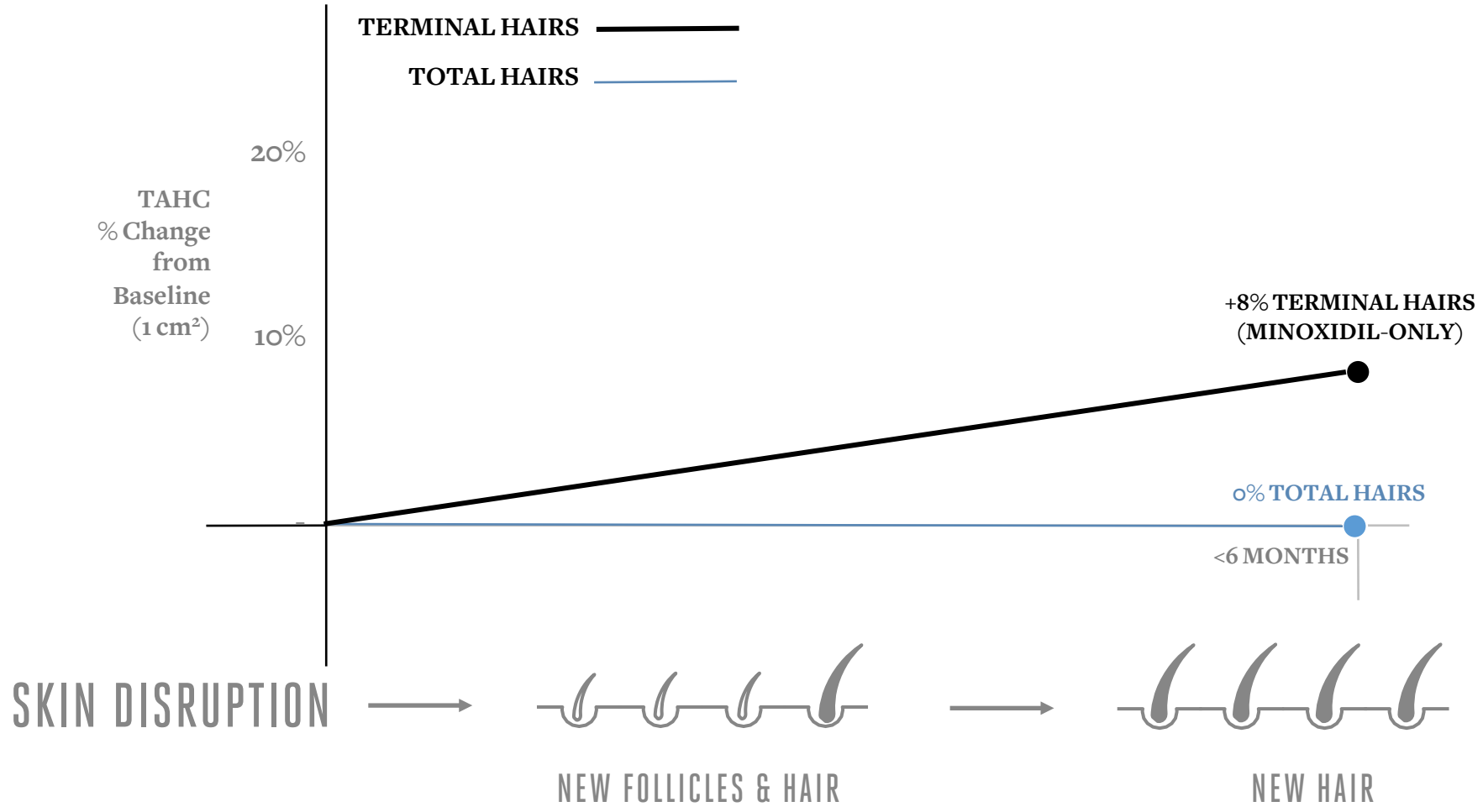
% CHANGE FROM BASELINE IN TARGET AREA HAIR COUNT (TAHC) FOLLOWING SKIN DISRUPTION ALONE



MINOXIDIL ONLY

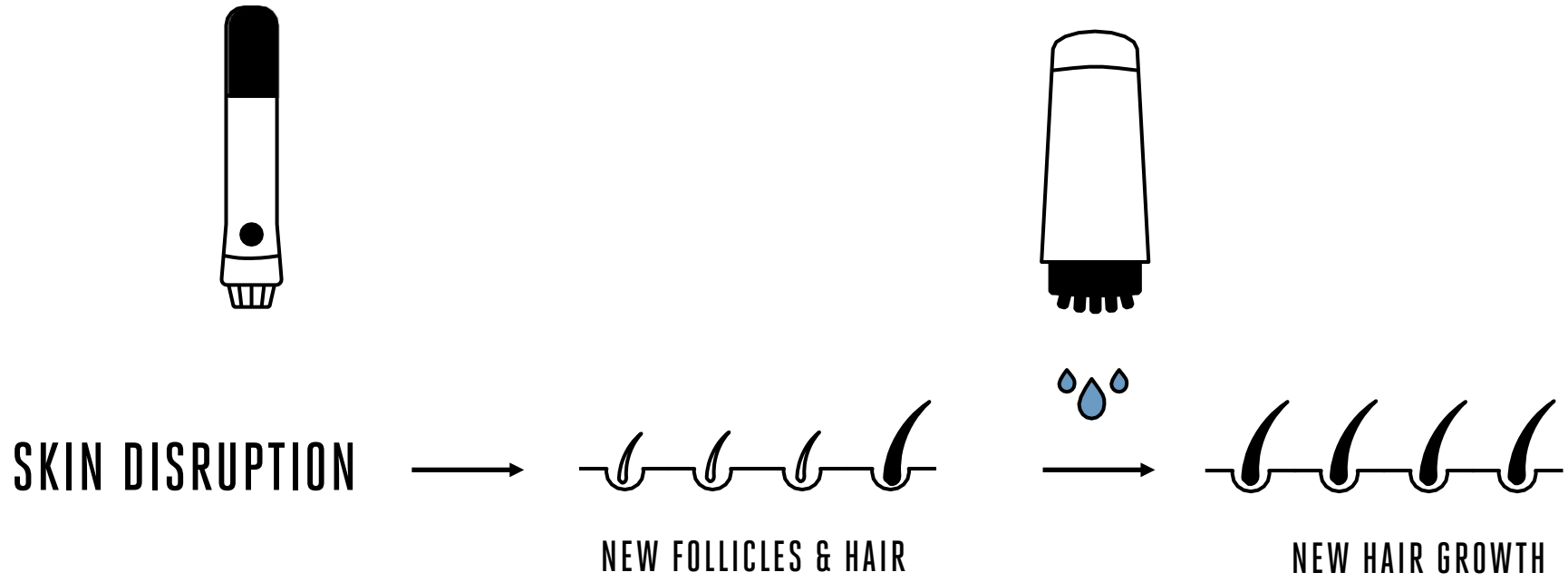
Increase in terminal hairs,
but no change in total number
(shift from vellus to terminal hair).

MINOXIDIL:
% CHANGE FROM BASELINE IN TARGET AREA HAIR COUNT (TAHC)



TREATING HAIR LOSS IN A NEW WAY

Our technology creates new follicles, and improves the application of a range of treatments to grow new hair.



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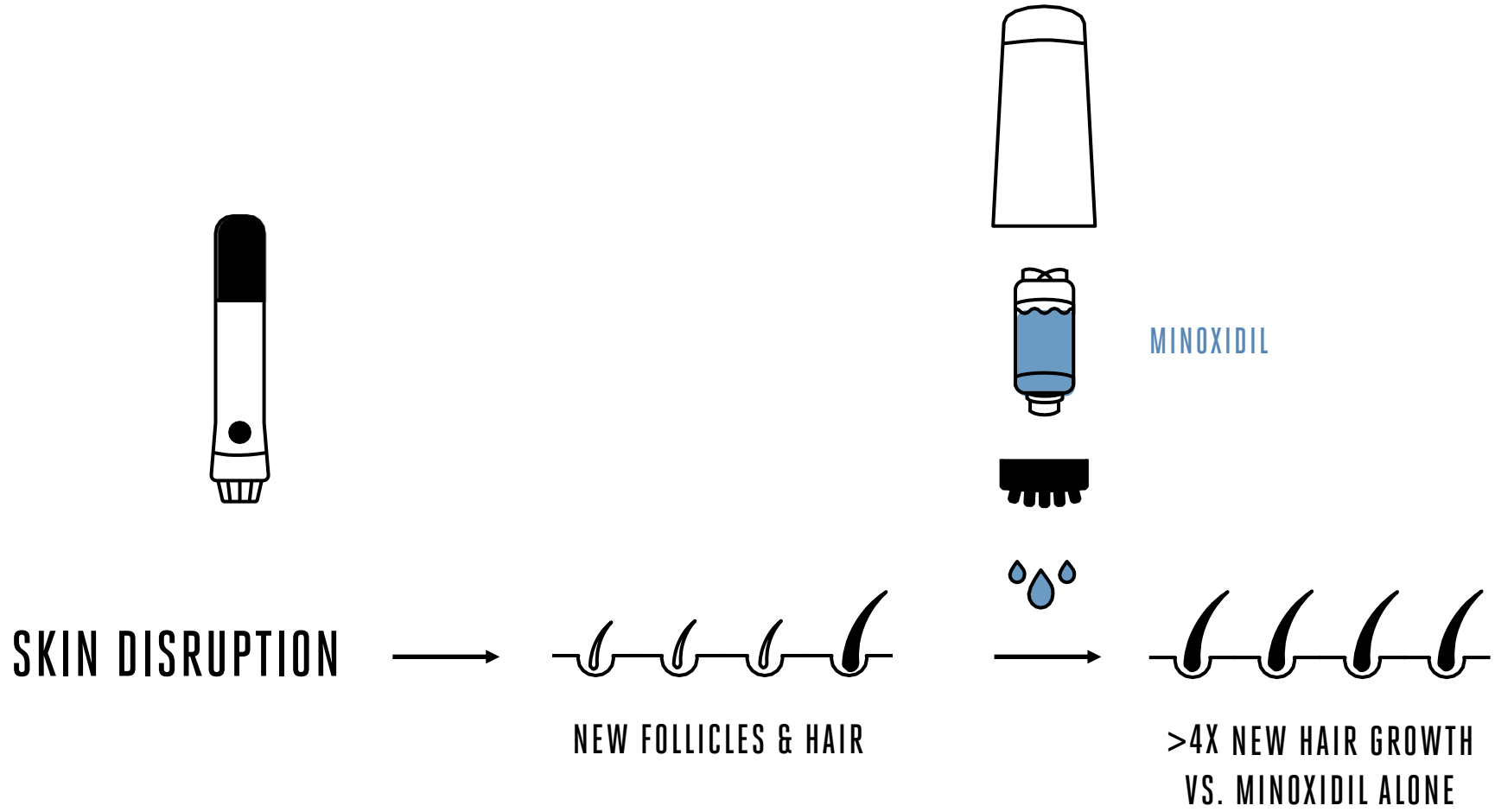
OUR LEAD PROGRAM

Skin disruption + minoxidil.



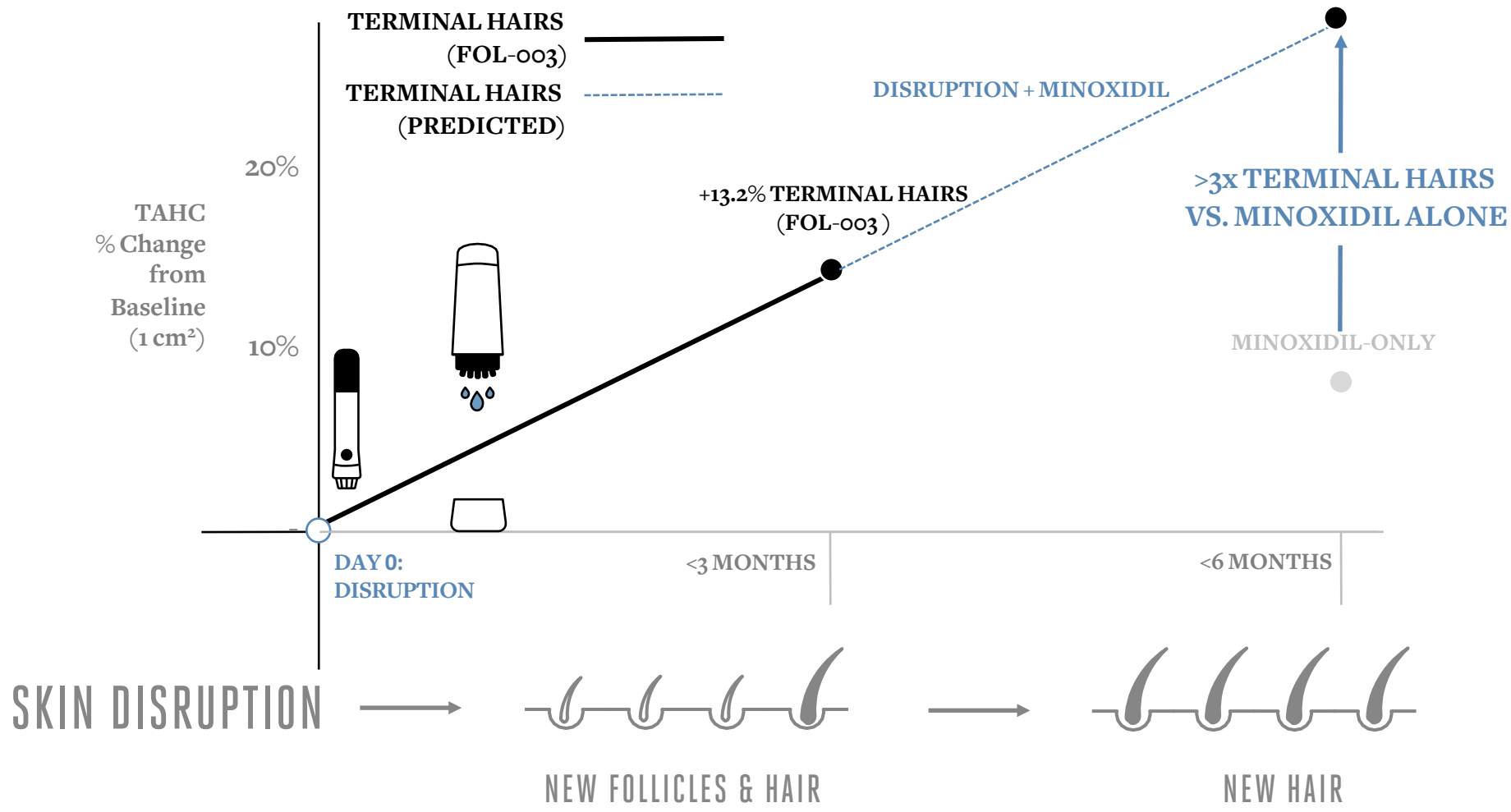
CONNECTING THE DOTS

RAIN system + minoxidil **2017 FOL-004 registration study.**

Target measurements (tbc):
- Terminal hair growth
- Total hair growth
- New follicle formation

2017 SYSTEM REGISTRATION STUDY (FOL-004):

PREDICTED % CHANGE FROM BASELINE IN TARGET AREA HAIR COUNT (TAHC) FOLLOWING SKIN DISRUPTION



FOLLICA REGULATORY STRATEGY

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REGULATORY STRATEGY AT A GLANCE

Developed with Precision for Medicine.

1. FDA FILINGS:

- **1 Pre-Submission** + **1 Pre-IND** to confirm pathway
- **1 IND** to cover investigational use of new minoxidil cartridge
- **2 ANDAs** for topical minoxidil (men 5% - vertex only; women 2%)
- **1 "System" De Novo** covering combined use of Microneedler, Smart Dropper, Mobile App
- **1 505(b)(2)** for topical minoxidil (men 5% - whole scalp; women 5%)

2. CLINICAL DATA:

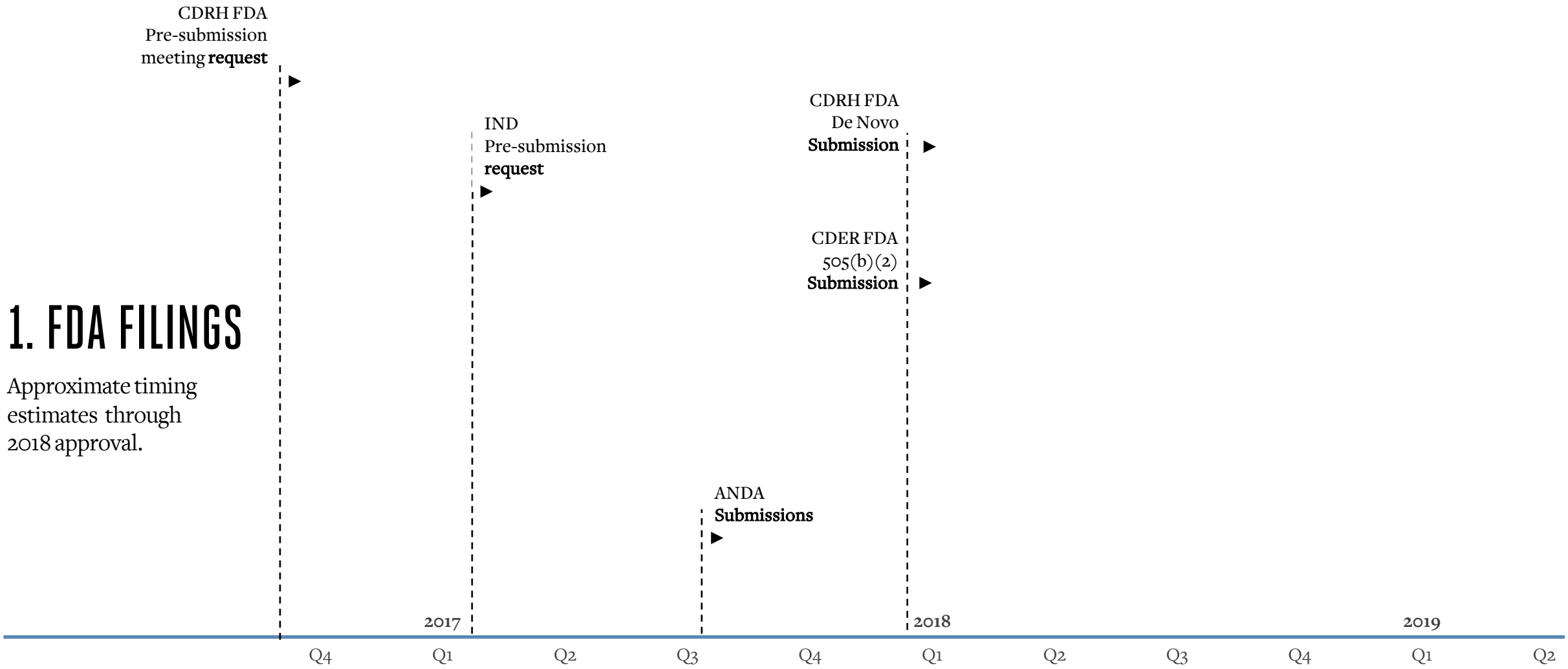
- IND & ANDA: **Stability data** only (bioequivalence waiver)
- De Novo: **"System" clinical studies**; 200 pts. 6 month endpoint
- 505(b)(2): **"System" clinical study** (same as above)

3. TIMELINE TO APPROVAL:

- 2Q2018: ANDA approvals
- 3Q/4Q2018: De Novo granted
- 4Q2018: 505(b)(2) approval

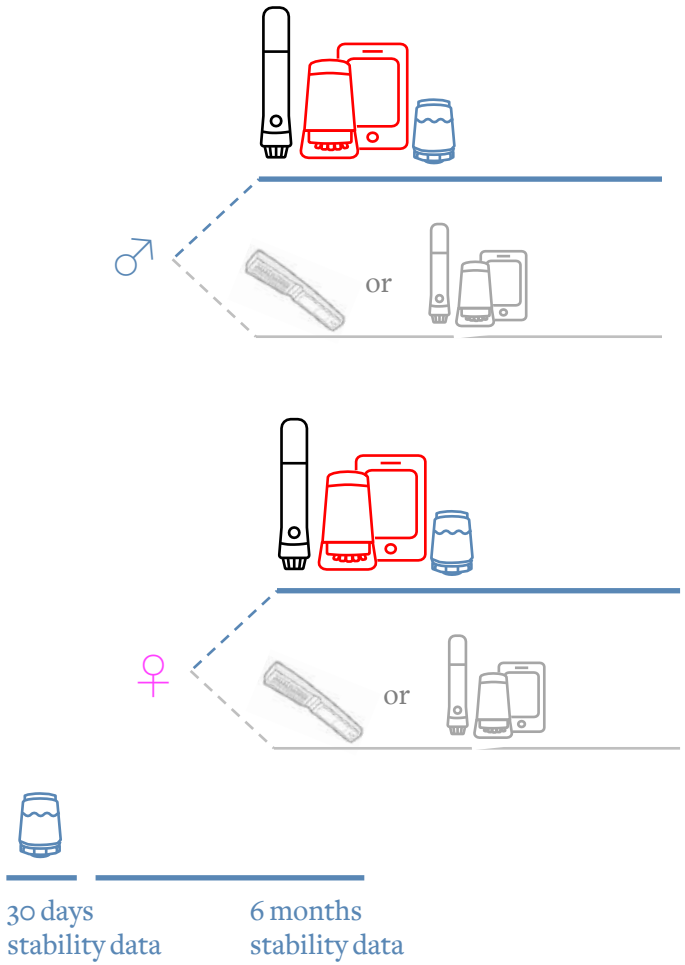
1. FDA FILINGS

Approximate timing estimates through 2018 approval.



2. CLINICAL DATA

Approximate timing estimates through 2018 launch.



♂ **"System" clinical studies;** 200 pts. 6 month endpoint

♀ **"System" clinical studies;** 200 pts. 6 month endpoint

(can be staggered / delayed which will impact 505 (b)(2) timing)

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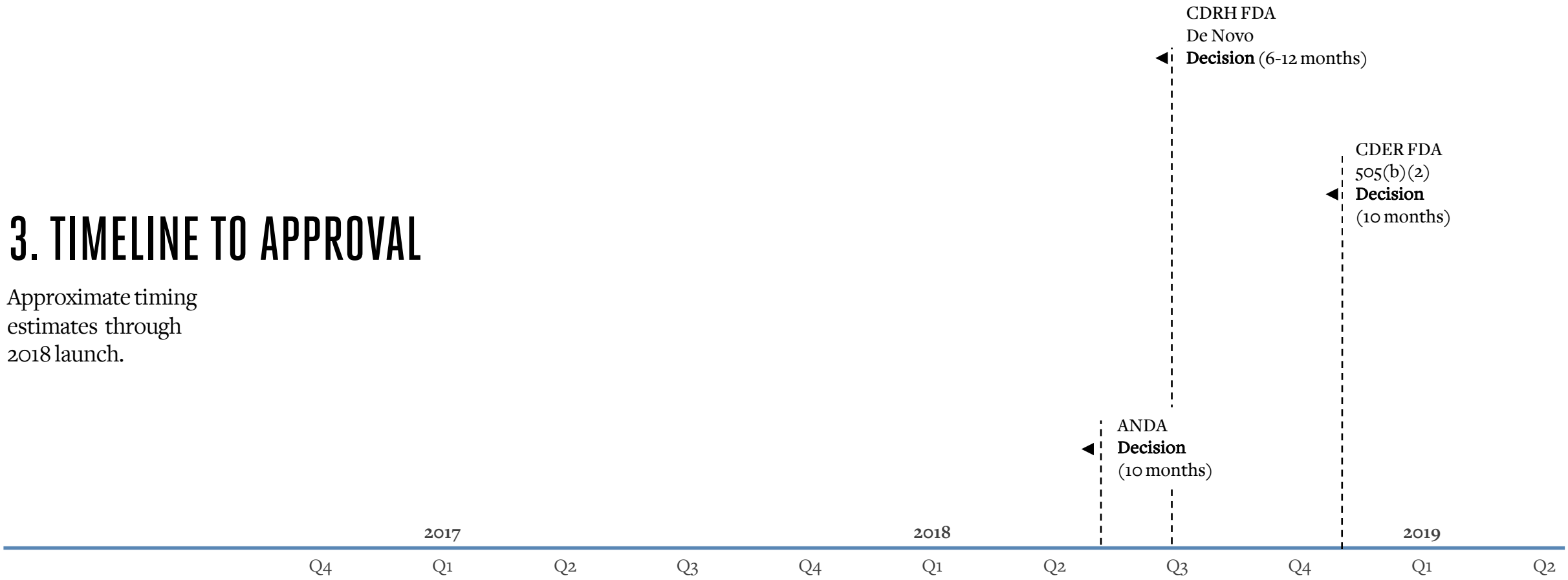
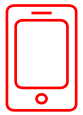
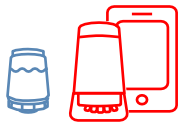
3. TIMELINE TO APPROVAL

Approximate timing estimates through 2018 launch.



"SYSTEM" DE NOVO REGULATORY STRATEGY

Platform "system" approach.

	Product	Regulatory Path (Individually)	Regulatory Path ("System")
In-office procedure device 	Micro-needling device + disposable sheath	6 month clinical study + **510(k) de novo** with special controls	**Combined "System" De Novo** **"System" 6 month clinical studies** (**n=200 TBC**) **Special controls** (e.g., follicular neogenesis)
At-home, connected device 	"Smart Dropper"	**510(k) exempt** (likely Class I)	
	Mobile app	**510(k) exempt**	
"Smart dropper" + Rx Cartridge 	Proprietary Minoxidil cartridges for use with "Smart Dropper"	**1) ANDA** *Men 5% vertex only; OTC* *Women 2% whole scalp; OTC* 6 month stability data; bioequivalence waiver **2) 505(b)(2) NDA** *Women 5% whole scalp* *Men 5% whole scalp* 6 month stability data; "System" clinical study (same study as above); IND filing for use of cartridge in "System" clinical study	Add cartridge approvals to labeling of "System" device via 30-day **"Special 510(k)"**

BASIS FOR REGULATORY STRATEGY

Developed with Precision for Medicine.

PRECISION FOR MEDICINE

Regulatory Strategy Developed in Context of Commercial Goals	- Manage the Combination Product regulatory environment as efficiently as possible - Create a coherent, positive user experience across products - Establish a product platform for use with a potential pipeline of APIs - Enable "smart" features, including medication reminders and patient engagement with mobile app - Optimize path to market while achieving target claims
Input 1 FDA Regulation of Microneedling & Hair Growth Medical Devices	- **Product Code GED:** Manual Dermabrasion Brush 21 CFR 878.4800 - Class 1 510(k) Exempt - **Product Code GFE:** Powered Dermabrasion Brush 21 CFR 878.4820 - Class 1 510(k) Exempt - **Product Code OAP:** Hair Laser Comb 21 CFR 890.5500 – Class 2 510(k) - **FDA Warning Letters to:** Dermaroller GmbH (3/1/2013), Derma Pen LLC (1/9/2015), Genesis Biosystems, Inc (9/21/15) and Eclipse Aesthetics (3/28/2016) - **FDA Guidance** – De Novo Classification Process (August 2014)
Input 2 FDA Regulation of Topical Drug Delivery, Medication Reminders & Mobile Apps	- **Product Code KYX:** Liquid Medication Dispenser 21 CFR 880.6430 Class 1 510(k) & GMP Exempt - **Product Code NXQ:** Medication Reminder 21 CFR 890.5050– Class 1 510(k) & GMP Exempt - **FDA Guidance** – Mobile Medical Applications (February 2015)
Input 3 FDA Regulation of Hair Growth Drugs	- **Minoxidil** 5% Men/ 2% Women Topical, 5% Men/Women Foam - **Finasteride** 1mg Tablet - **FDA Guidance** – Request for Waiver of In Vivo Bioequivalence Study Requirements for Minoxidil (2% topical, 5% topical, 5% foam) - **FDA Guidance** – Container Closure Systems for Packaging Human Drugs and Biologics (May 1999) - **FDA Guidance** – ANDA Submissions (June 2014) - **FDA Guidance** – Applications covered by 505(b)(2) (1999) - **FDA Draft Guidance** – Topical Dermatological Drug Product NDAs and ANDAs —In Vivo Bioavailability, Bioequivalence, In Vitro Release, and Associated Studies (1998)

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PROPOSED "SYSTEM" STUDY DESIGN

FOL-004, N=200+ (TBD)

RAIN System

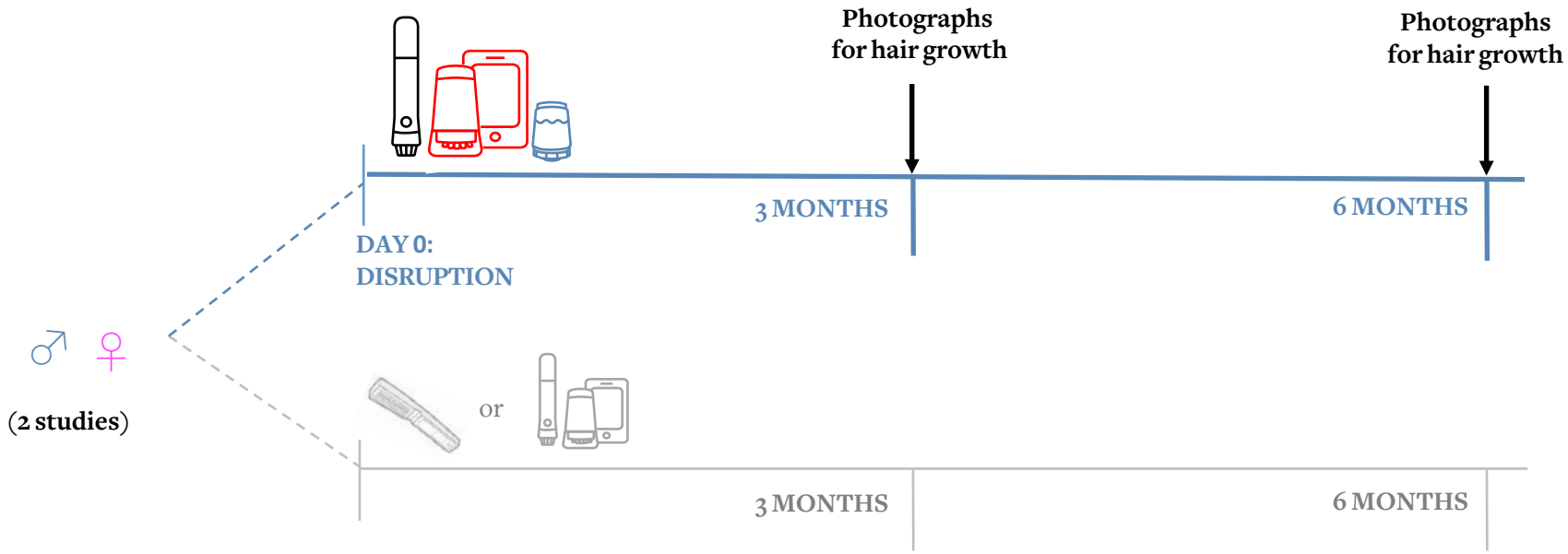
vs.

Sham devices or approved hair device (TBD)

vs.

Historical minoxidil control (published data)

.



Proposed General Design Features:

- Increase in **total hair count** as endpoint; evaluated by software and blinded expert
- Device-to-device non-inferiority comparison emphasizes **device** nature of product platform
- Use of proprietary Follica RAIN minoxidil **under IND**
- CDRH Pre-Submission Meeting + CDER Pre-IND (Type B) Meeting being pursued to optimize design / de-risk study program
- Sites will have appropriate **demographic / geographic diversity**
- Will coordinate with **human factors studies** for Smart Dropper + Mobile App

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BASIS FOR STUDY DESIGN

Developed with Precision for Medicine.

REVIEW OF PRIOR / ONGOING HAIR GROWTH STUDIES

- Search of Clinicaltrials.gov
- Thomson Reuters Alopecia studies list
- Minoxidil studies
- HairMax studies
- Microneedling studies

CONSULTATION WITH CLINICAL & PRODUCT ADVISORS

- Austin Speier (Precision for Medicine)
- Merry Lee Bain (Precision for Medicine)
- Alison Lawton (Advisor / Board Member)
- Meg Fitzgerald (Advisor / Board Member)
- Peter Hutt (Advisor)

REGULATORY CONSIDERATIONS

- Utilize established study design precedents where applicable
- Emphasize device-nature of the "system" platform (i.e., reinforce appropriate regulation as a device via *DE NOVO*)
- Basis for soliciting FDA feedback via Pre-Sub and Pre-IND process
- Designed to achieve target claims

DE NOVO CLASSIFICATION

System De Novo approach.

21 CFR 882.58## Targeted Cutaneous Perturbation and Smart Drug Delivery System for the Treatment of Androgenetic Alopecia:

DE NOVO DEVICE CLASSIFICATION

A Targeted Cutaneous Perturbation and Smart Drug Delivery System comprises (a) a microneedling device intended to perturb the skin in a manner that induces [follicular neogenesis / hair growth] and (b) a smart drug delivery device (including user software) designed to facilitate follow-on treatment to the area of [follicular neogenesis / hair growth], for use with FDA-approved drugs indicated to stimulate growth of terminal hairs. Combined, the System is intended to treat androgenetic alopecia by increasing terminal hair counts.

INDICATIONS FOR USE

"The Follica System is indicated to **promote hair growth** in males with androgenetic alopecia who have Norwood Hamilton Classifications IIa to V, and in females with androgenetic alopecia who have Ludwig-Savin Classifications I- II [**by stimulating the growth of new hair follicles** in areas of hair loss]."

SPECIAL CONTROLS

- Special Controls are established for the new classification as part of De Novo process. Special Controls are requirements to be met by any follow-on products. The exact requirements are developed by Follica in collaboration with FDA.
- Includes non-clinical and clinical testing, labeling, device information
- Can be crafted to match IP, unique features of Follica technology, or to simply create cost barriers for any follow-on products

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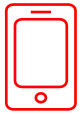
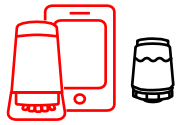
EUROPEAN REGULATORY STRATEGY

Developed with Precision for Medicine.

PRECISION FOR MEDICINE

	Product	Regulatory Path
In-office procedure device 	Micro-needling device + disposable sheath	**CE Mark** Active Medical Device Class IIa Clinical Data: US Pivotal Study
At-home, connected device 	"Smart Dropper"	**CE Mark** Active Medical Device Class IIa Clinical Data: US Pivotal Study
	Mobile app	Accessory to "Smart Dropper" (covered by same CE Mark)
"Smart dropper" + Rx Cartridge 	Proprietary Minoxidil cartridges for use with "Smart Dropper"	**Mutual Recognition Pathway** Generic / Hybrid Medicinal Product Abridged/Bibliographic Registration Procedure CE Mark for "Smart Dropper" included in application

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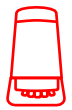
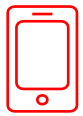
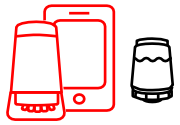
AESTHETIC-USE REGULATORY STRATEGY EXAMPLES

Developed with
Precision for Medicine.

	Product	Regulatory Path
In-office procedure device 	Micro-needling device + disposable "Precision Tip" sheath	**Class I 510(k)** Dermabrasion predicate device Clinical data: primarily third-party publications, plus small non-inferiority clinical study, if required by FDA
At-home, connected device 	"Smart Dropper"	**No FDA Review** Cosmetic
	Mobile app	Accessory to "Smart Dropper"
"Smart dropper" + Rx Cartridge 	Proprietary cartridge with cosmetic moisturizer	**No FDA Review** Cosmetic

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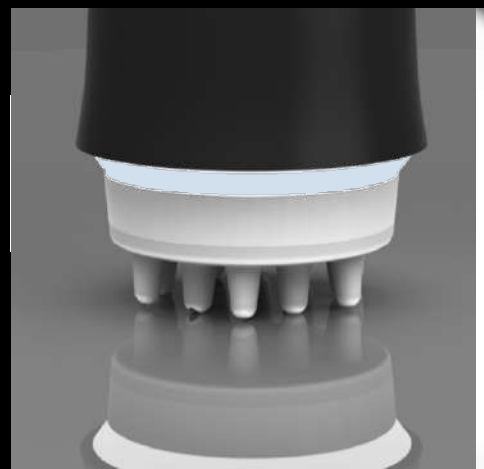

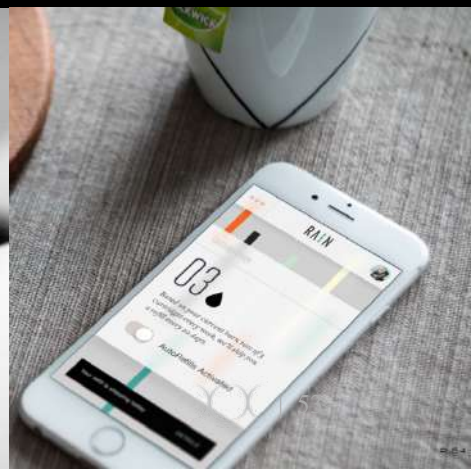

DISRUPTION IS OUR PORRIDGE

Induce neogenesis with a method practical for human use:

DA: "Too hot"

MDA: "Too cold"

Mechanical needling: "Just right"

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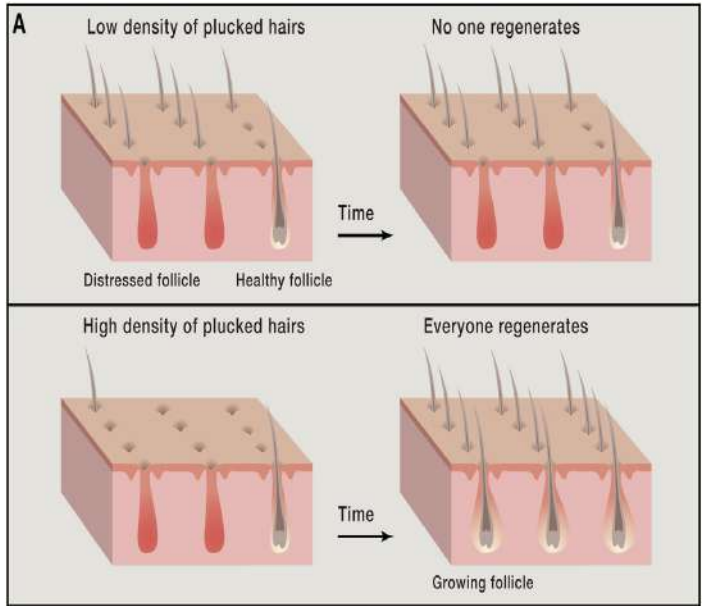
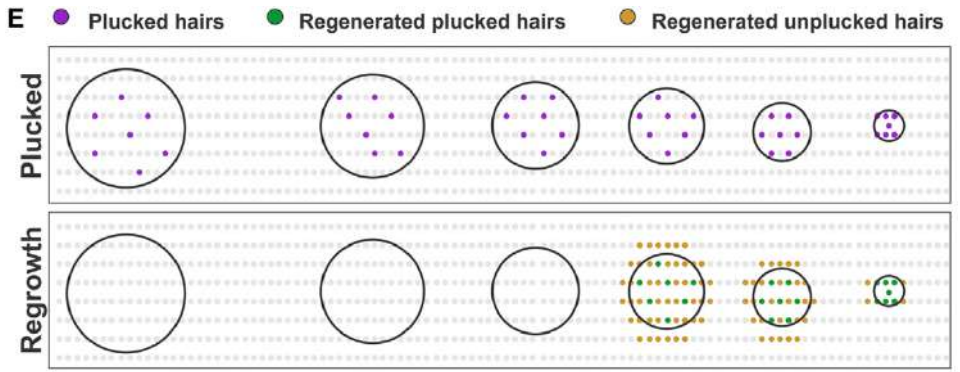
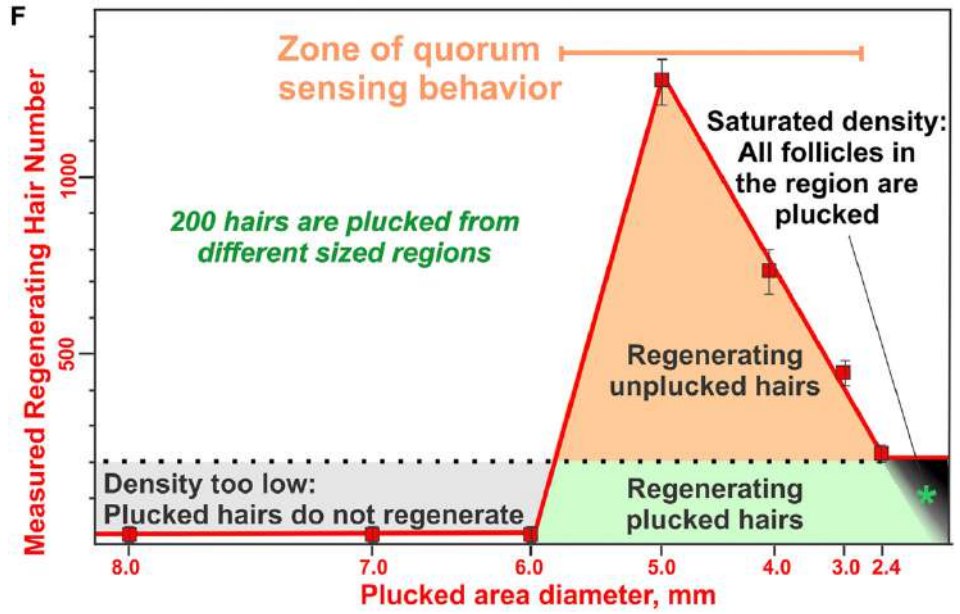
REGENERATION THRESHHOLD AS A DESIGN MODEL

Relationship between wounding density (aggressiveness) & area to induce regeneration.

Source: Chen CC, Wang L, Plikus MV, Jiang TX, Murray PJ, Ramos R, Guerrero-Juarez CF, Hughes MW, Lee OK, Shi S, Widelitz RB, Lander AD, Chuong CM. Organ-level quorum sensing directs regeneration in hair stem cell populations. Cell 161:277-290, 2015.







A (LOOSE) CONSERVED MODEL FOR OUR APPROACH?

Do humans need to meet a similar (inflammation) threshold to induce regeneration, but avoid scarring?