

 P.L.E.A.S.E.<sup>®</sup>  
P R O F E S S I O N A L

Sven Rohmann, BioEurope, Amsterdam

The breakthrough device  
for transdermal drug  
delivery

  
**pantec**  
biosolutions



# Disclaimer

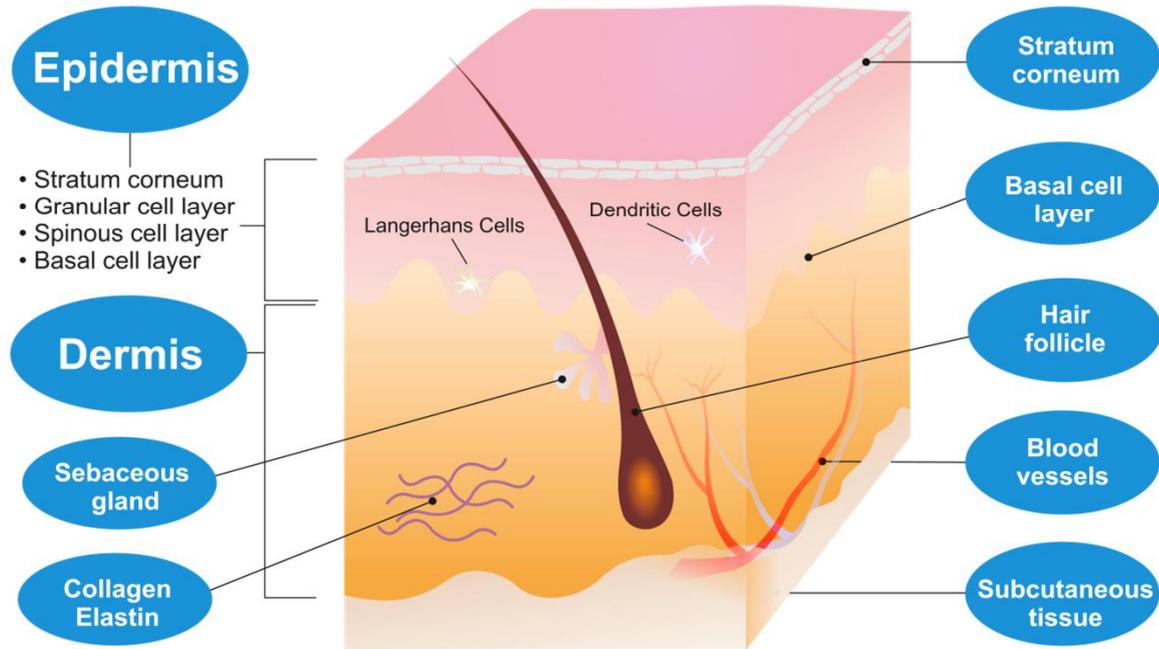
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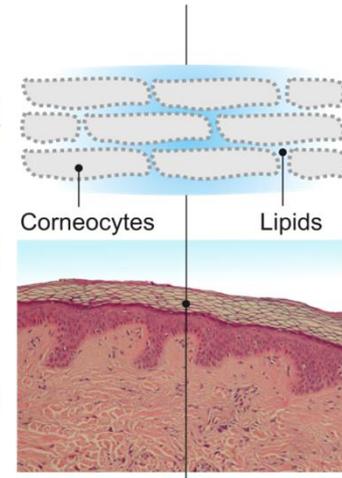
# Skin structure

## Skin structure and layers



Intra - and transdermal Drug Delivery

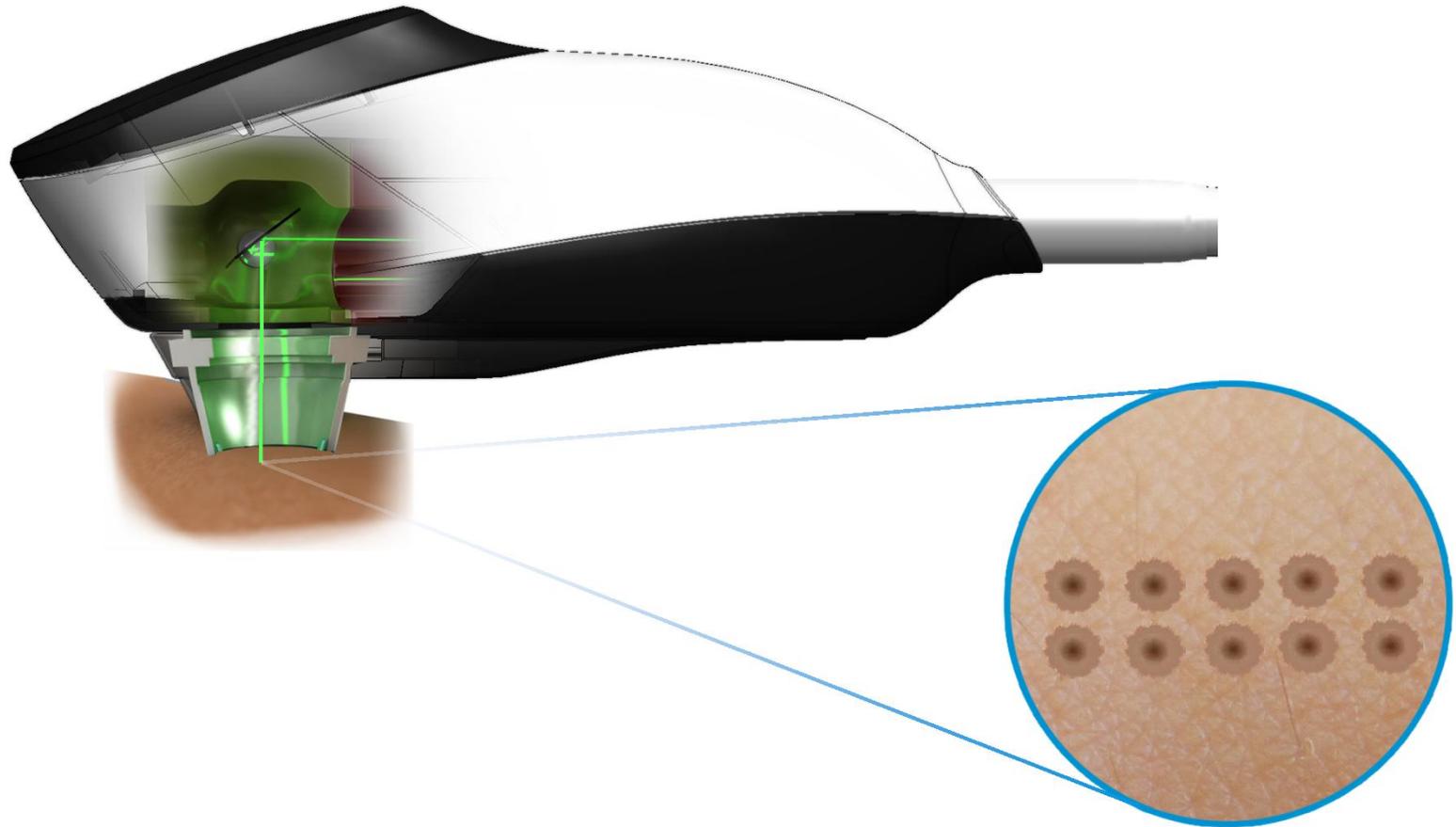
## The **SC** skin barrier



The stratum corneum layer is acting as a very strong barrier.

Physiochemical constraints effectively limit the passive permeation of many known therapeutics.

## Laser to create ultra-precise micropores

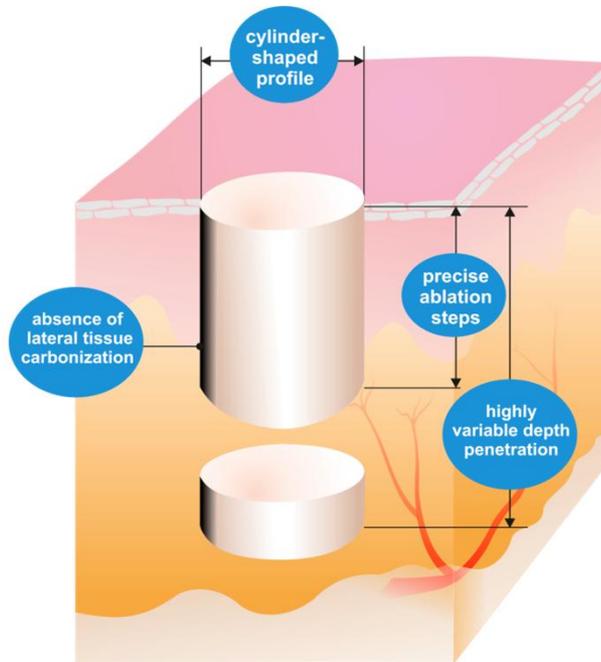


# Modifications of micropores

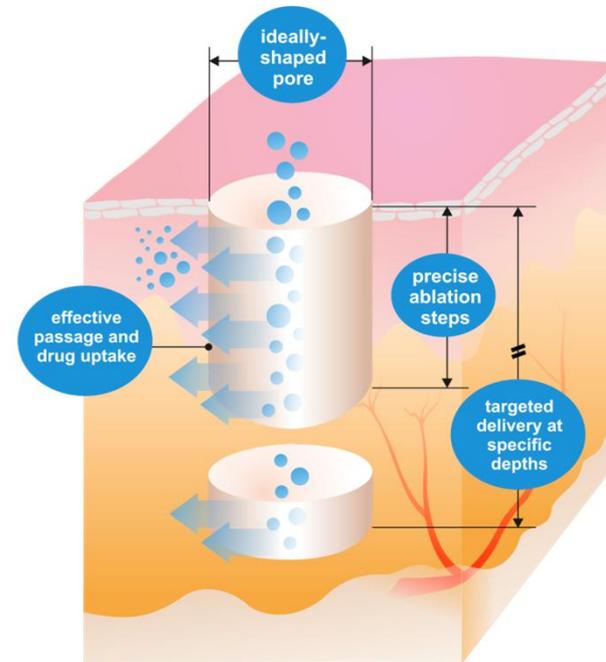
## Quality requirements:

Intra - and transdermal Drug Delivery

### High-precision pore geometry



### P.L.E.A.S.E.® Delivery of large molecular drugs

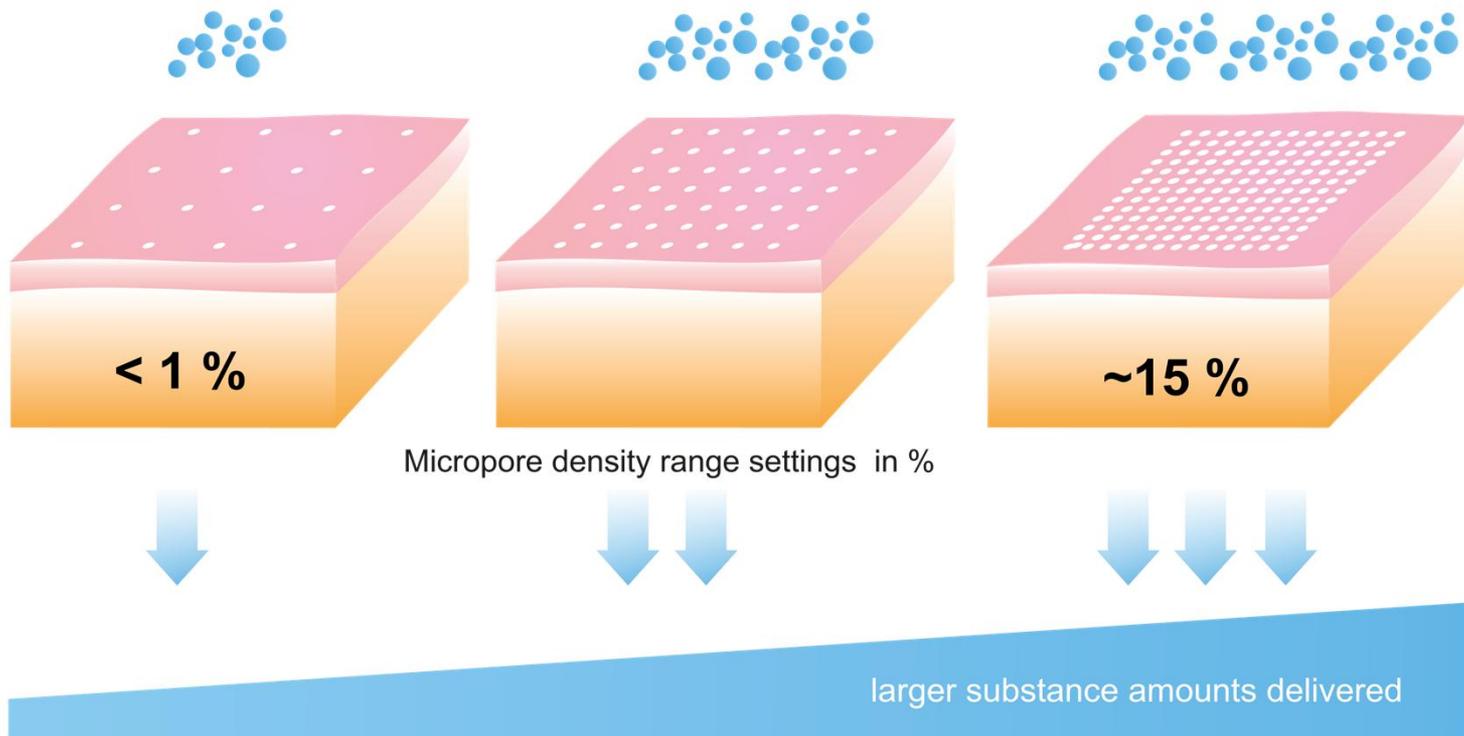


# Modifications of micropores

## Precisely controllable micropore density

Intra - and transdermal Drug Delivery

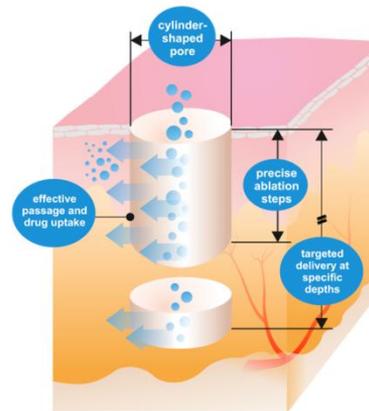
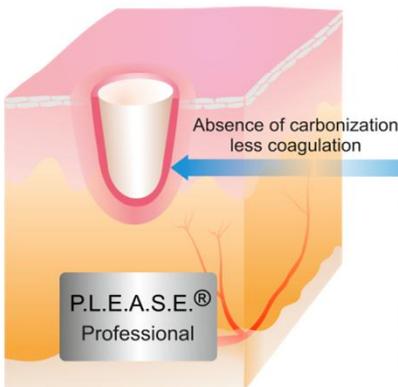
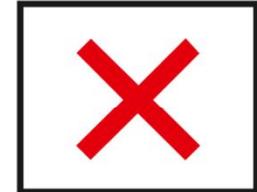
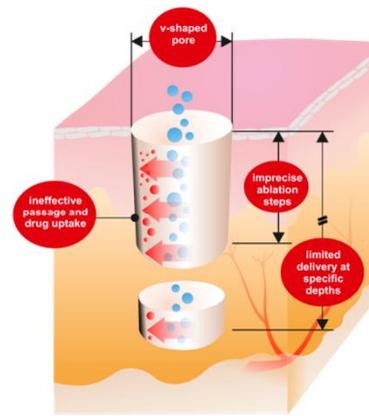
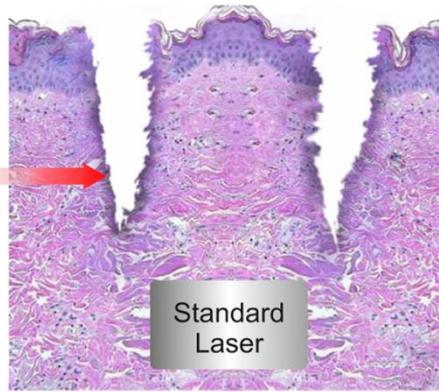
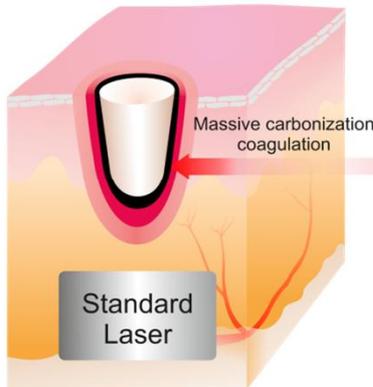
Adjustable skin permeation levels for precise amount control of substance delivered over time



# Modifications of micropores

## Standard ablative laser vs. P.L.E.A.S.E.® Professional

Ideally addresses intra- and transdermal drug delivery requirements

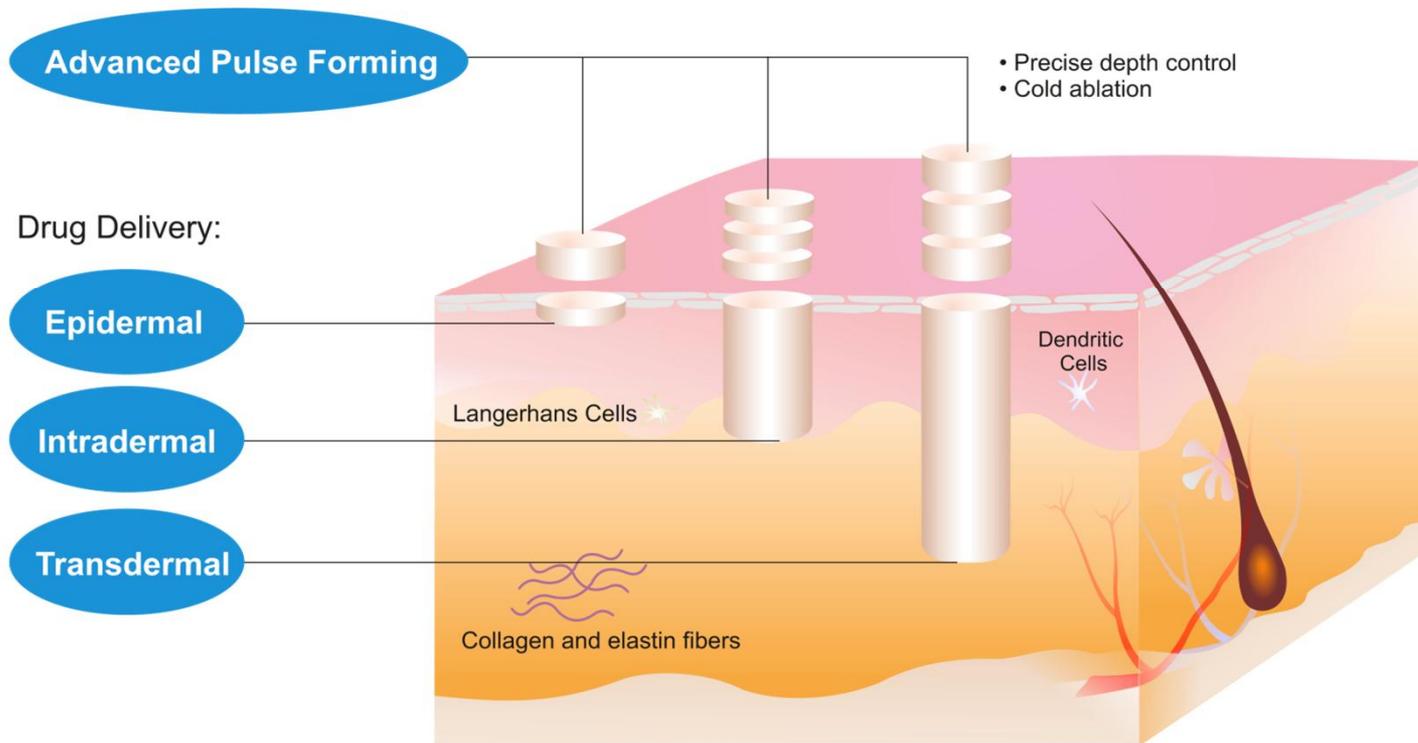


# Skin structure

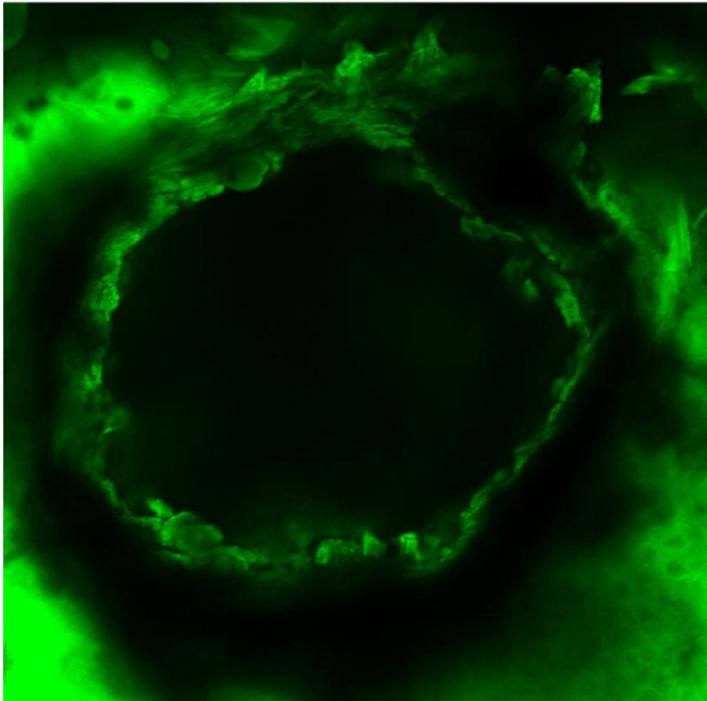
## P.L.E.A.S.E.® Professional

Intra - and transdermal  
Drug Delivery

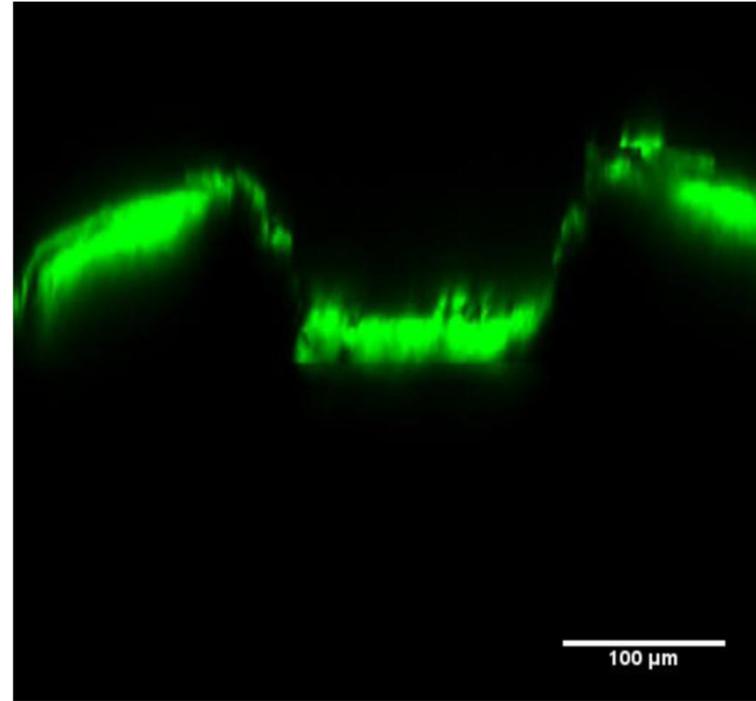
Modification of Micropores



## Skin structure



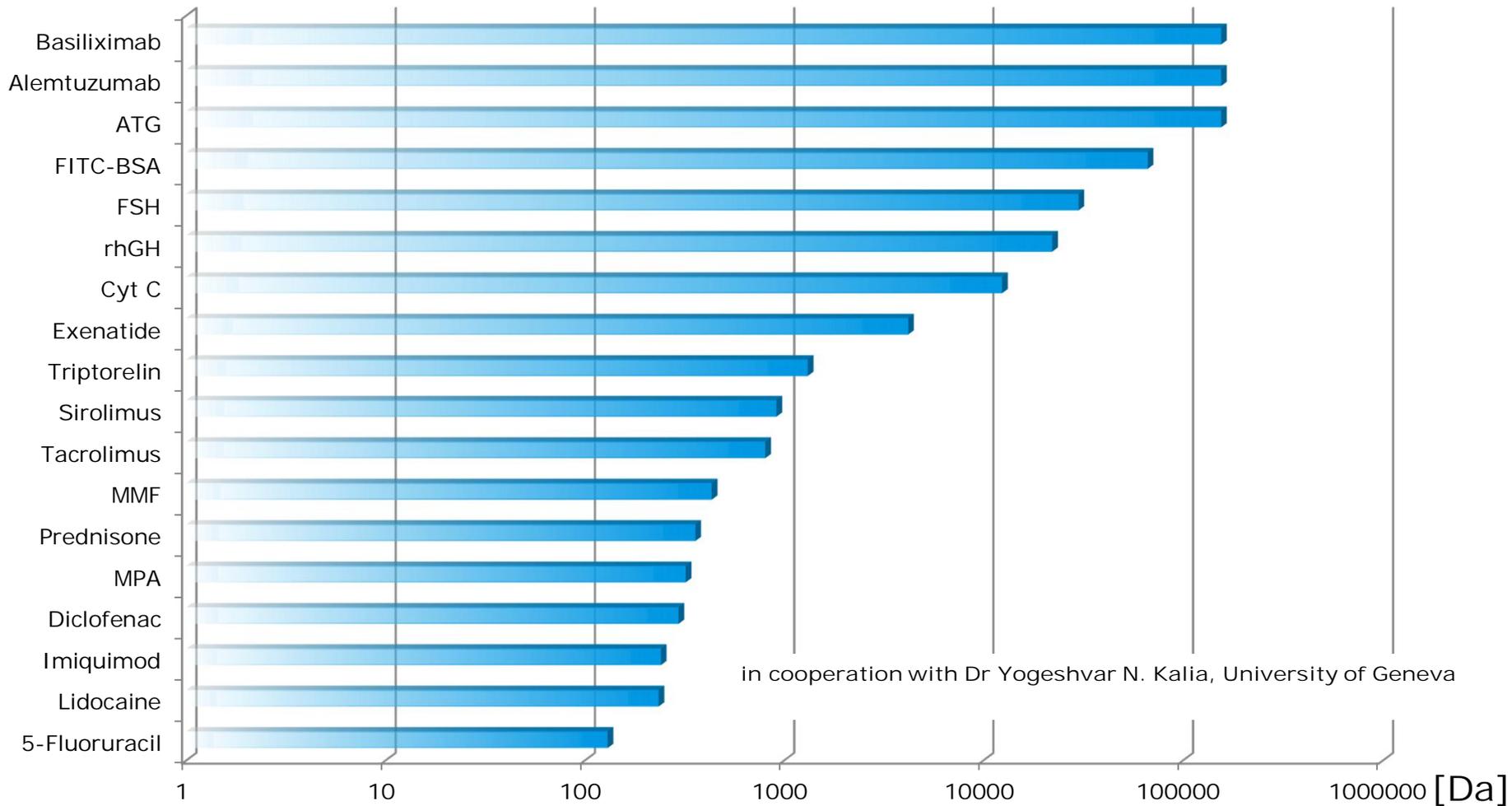
XY-image of the P.L.E.A.S.E.® micropore created in porcine skin.



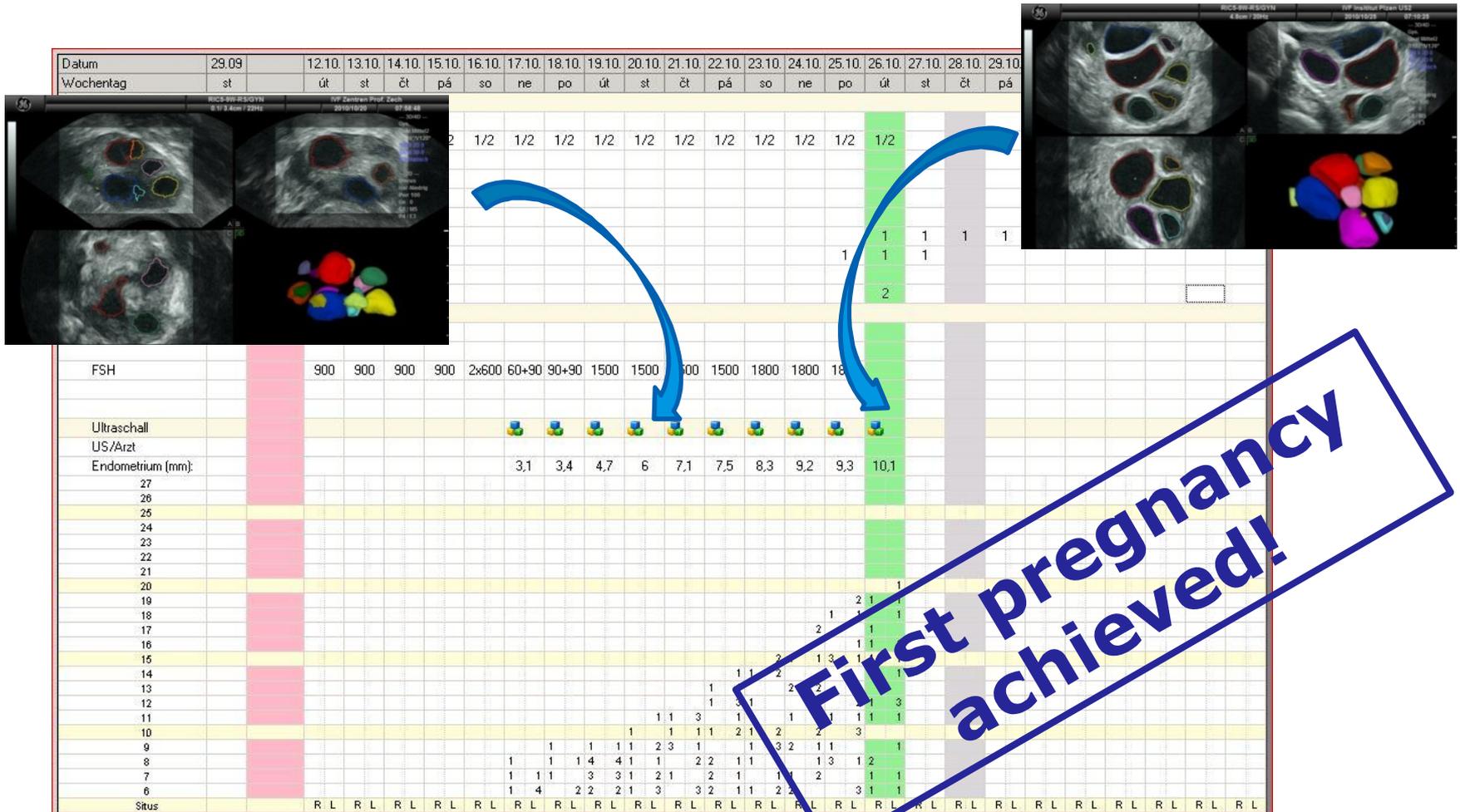
XZ-cross section of the P.L.E.A.S.E.® micropore created in porcine skin.

in cooperation with Dr Yogeshvar N. Kalia, University of Geneva

# Transdermal delivery without molecular size limitation



# Transdermal delivery of FSH in women (clinical POC)



in cooperation with LTS LOHMANN Therapie-Systeme AG  
and IVF Centres Prof. Zech

# Actinic keratosis

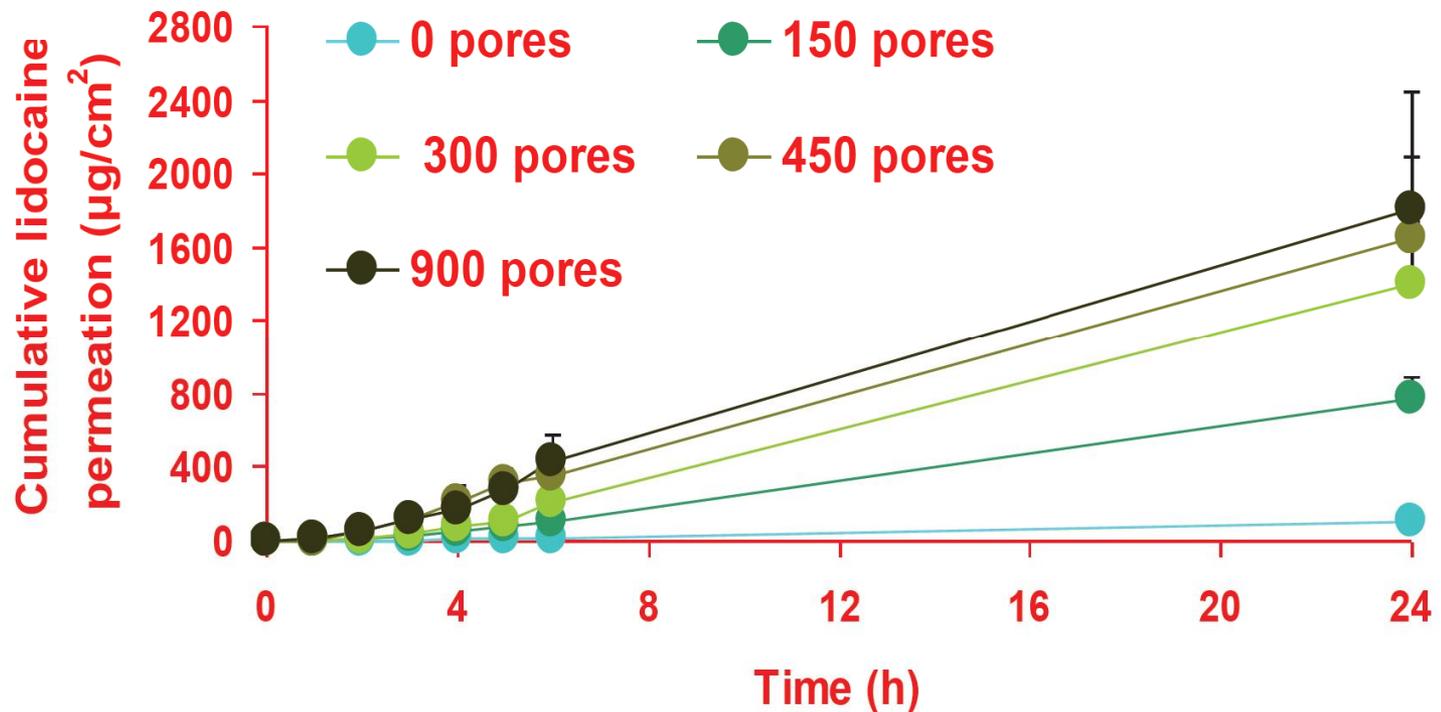


Before treatment with P.L.E.A.S.E.® and imiquimod



After 6 treatments with P.L.E.A.S.E.® and imiquimod during 20 days

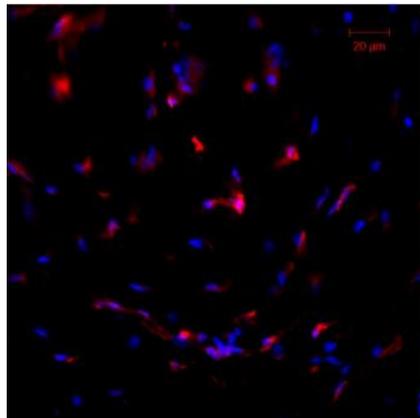
# Intradermal delivery



in cooperation with Dr Yogeshvar N. Kalia, University of Geneva

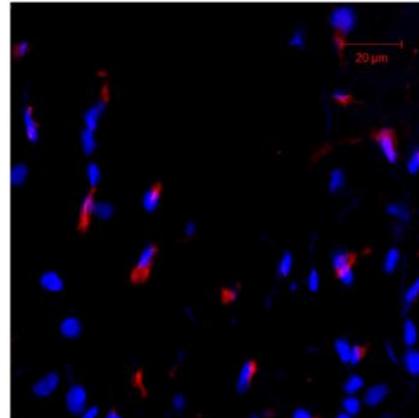
# Intradermal delivery – sd-rxRNA™

sd-rxRNA™ = novel, small asymmetric, hydrophobically modified RNAi compound developed by RXi Pharmaceuticals

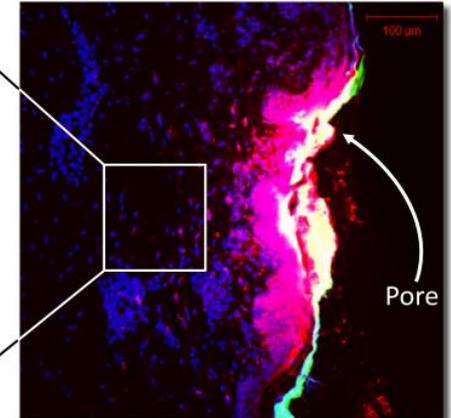


©2011 - I. Alberti - Study 6 - 5B(4) - Injected (2D-3x of 5B3)

**Pig skin ex vivo, fibroblast transfection following ID injection**



©2011 - I. Alberti - Study 6 - 3B(7) - Porated 5-250 (2D-3x of 3B5)



©2011 - I. Alberti - Study 6 - 3B(5)-Pored5-250(2D)

**Evidence of dermal fibroblast transfection in P.L.E.A.S.E.® microperated pig skin**

Skin scar keloids: dermal fibrosis due to excessive expression of a protein, CTGF (connective tissue growth factor)

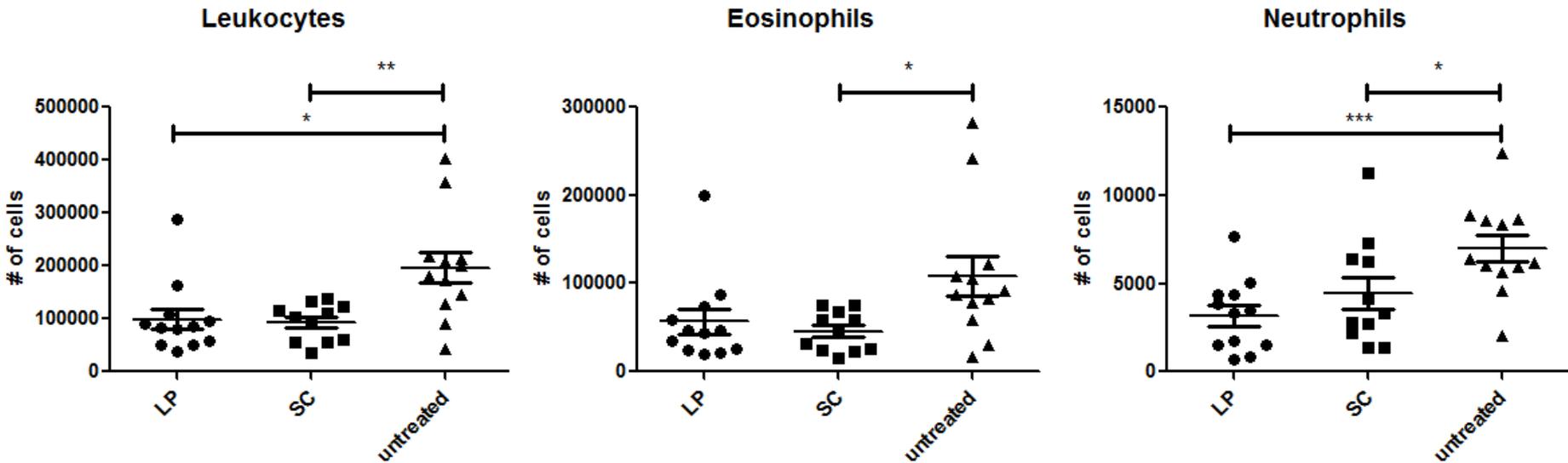
- Positive in vivo tests, siRNA uptake and gene silencing achieved by partner company
- Limitation: siRNA must currently be injected into scars
- P.L.E.A.S.E.® is a less invasive method of delivery
- US potential market: up to \$4 billion

Conclusions - in vitro skin

- There is qualitative evidence for dermal siRNA delivery following skin microperation
- Cellular transfection patterns appear comparable to those obtained by ID injection

**in cooperation with RXi Pharmaceuticals**

# Epidermal delivery (pre-clinical POC)



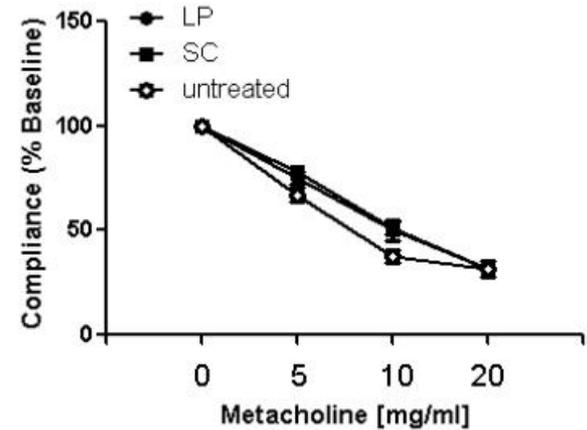
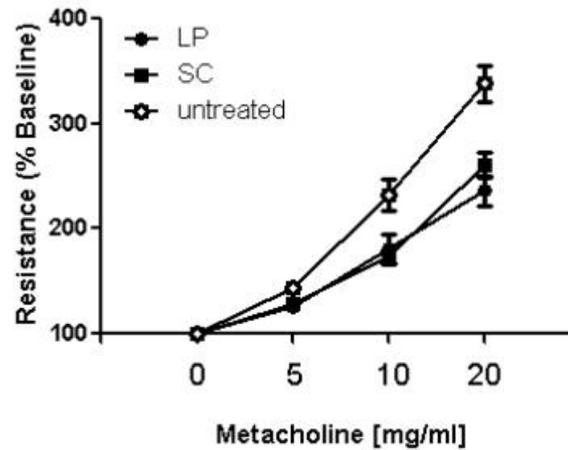
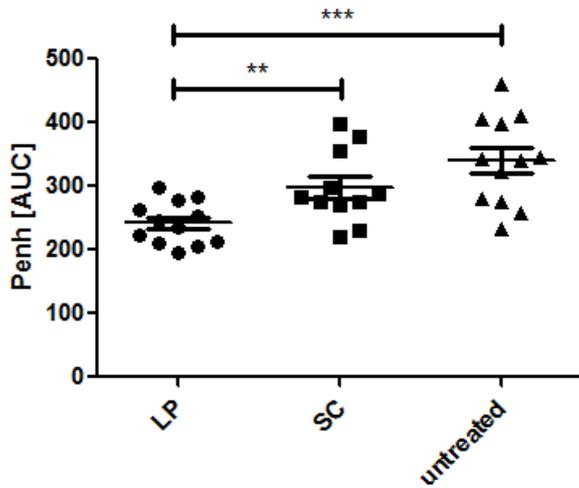
Mouse model of allergic asthma (rec. grass pollen) n=18 in 3 groups: control, 6 injections SCIT, 6 P.L.E.A.S.E.<sup>®</sup> treatments

## Results

- Transcutaneous Immunotherapy via P.L.E.A.S.E.<sup>®</sup> generated micropores equals SIT in efficacy
- Transcutaneous Immunotherapy induces a different systemic immune profile than SCIT
- P.L.E.A.S.E.<sup>®</sup> IT induces a decrease of pro-inflammatory cytokines
- SCIT induces an unwanted boost of Th2 cells

in cooperation with Biomay AG

# Epidermal delivery (pre-clinical POC)

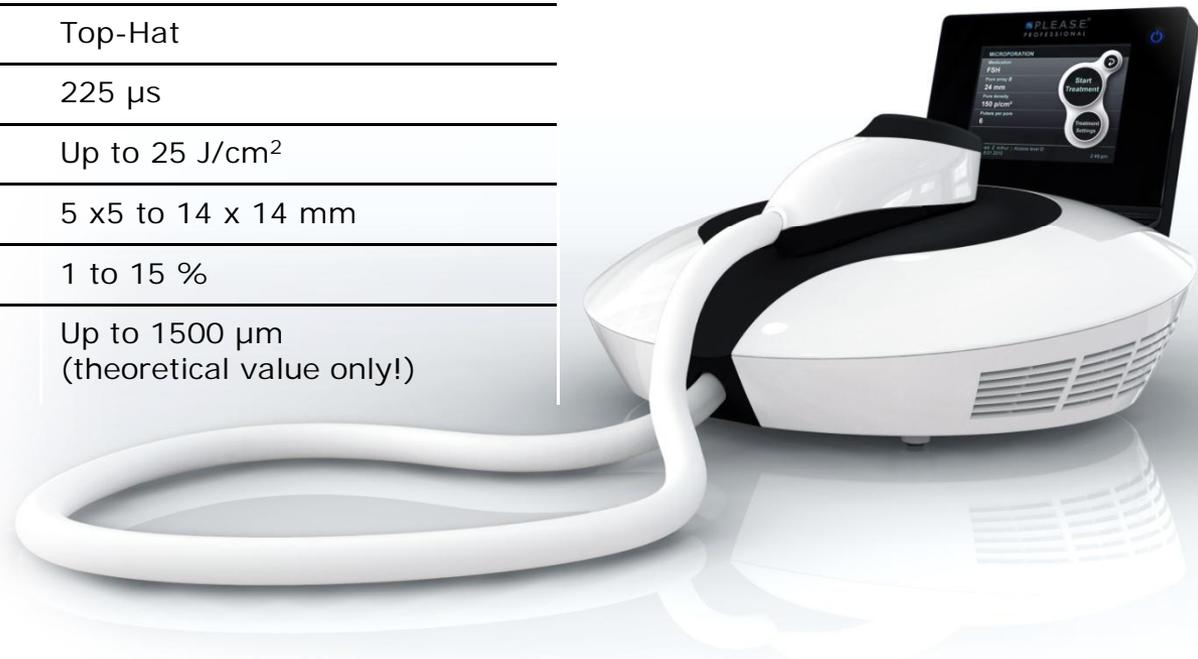


in cooperation with Biomay AG

# P.L.E.A.S.E.® Professional technical summary

## SYSTEM SPECIFICATIONS

Laser type:	Diode-pumped Er:YAG
Wavelength:	2940 nm
Pulse repetition rate:	100 to 500 Hz
Pulse duration:	50 to 225 $\mu$ s
Beam profile:	Top-Hat
Pore diameter:	225 $\mu$ s
Fluency:	Up to 25 J/cm <sup>2</sup>
Aperture:	5 x5 to 14 x 14 mm
Pore density, coverage:	1 to 15 %
Ablation depth:	Up to 1500 $\mu$ m (theoretical value only!)

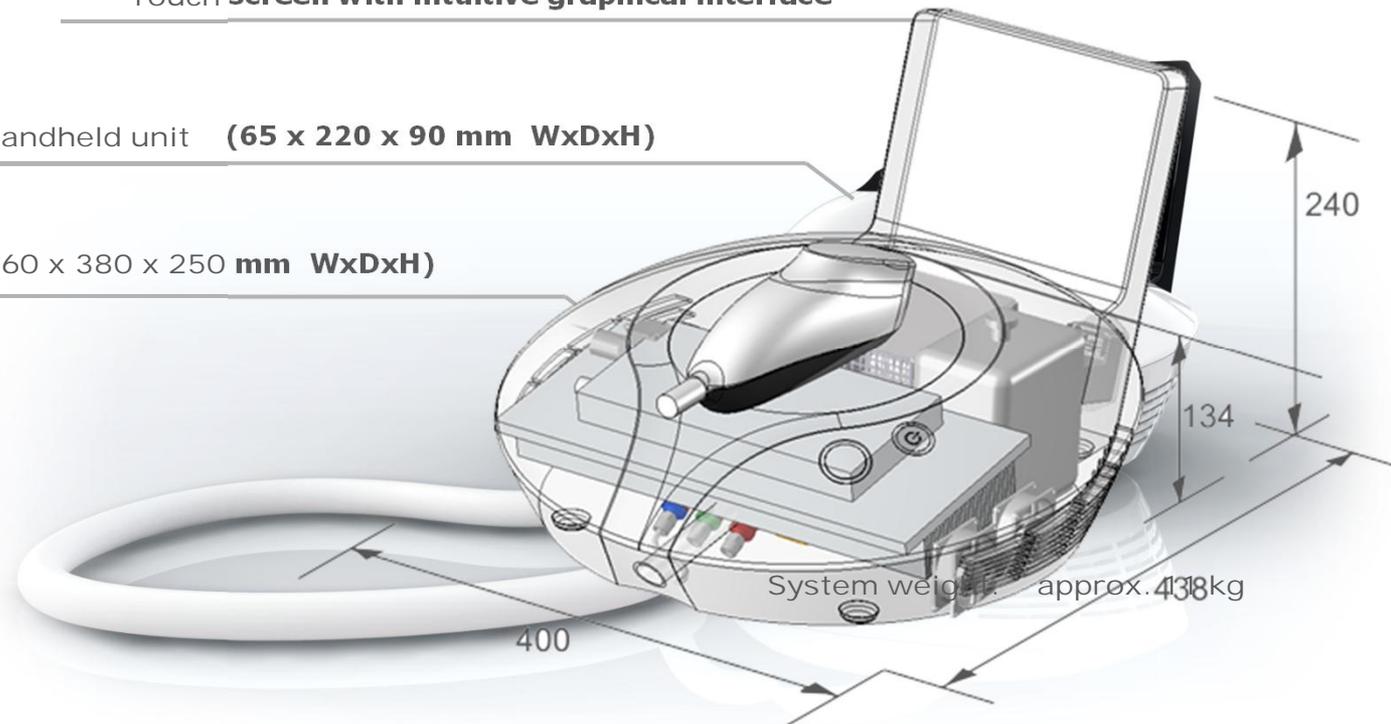


# P.L.E.A.S.E.® Professional technical summary

Touch **screen with intuitive graphical interface**

Handheld unit **(65 x 220 x 90 mm WxDxH)**

Tabletop unit **(460 x 380 x 250 mm WxDxH)**



## Pantec Biosolutions company profile

Location	Pantec Biosolutions AG Privately-owned Ruggell, Liechtenstein
Foundation	2005
Products	P.L.E.A.S.E. <sup>®</sup> Professional for dermatology applications P.L.E.A.S.E. <sup>®</sup> IVF (Hormone patches for IVF therapy in combination with P.L.E.A.S.E. <sup>®</sup> )
Employees	20 FTEs within Pantec Biosolutions, 10 FTEs in strategic partnerships



# Collaborations

- ✦ Global & Regional
- ✦ Transdermal
- ✦ Intradermal
- ✦ Epidermal

**You** have a molecule that profits from dermal delivery?

**We** add delivery, know-how, formulation expertise and a new patent position!

## P.L.E.A.S.E. Contact



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