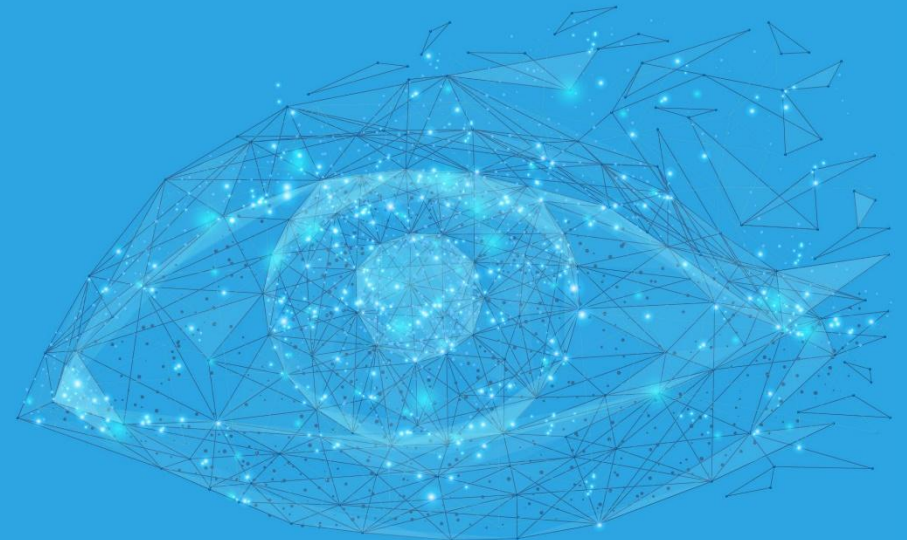


# Tacrosolv

A new Tacrolimus solution against  
ophthalmic inflammation

*February 2025*



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# Executive summary: Tacrosolv

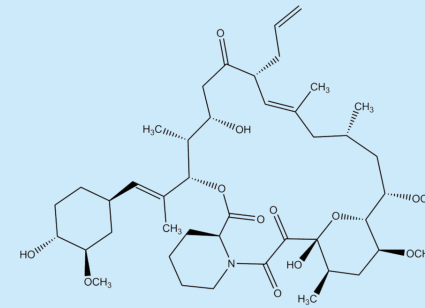
Novel low dose, preservative-free eyedrops targeting ocular inflammation

## Business model

- Classical license deal with downpayment, milestones and royalties
- Patent protected until 2036

## Tacrosolv

- **Low dose Tacrolimus formulation based on Marinosolv**
- **Preservative-free and clear solution**
- **Significant reduction of ocular symptoms after one week of treatment**



## Clinically proven

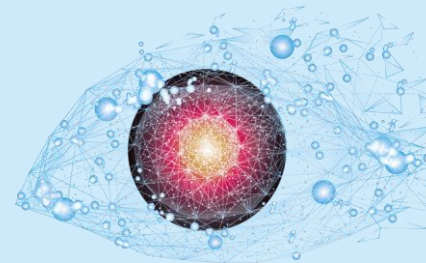
- In a clinical phase IIa 5µg/day Tacrolimus were effective

## Line extension

- Severe allergic conjunctivitis
- Herpetic stromal keratitis
- Vernal keratoconjunctivitis

## Safety

- Tacrolimus eyedrops are marketed in Japan and Korea at higher concentrations
- Preclinical safety of the formulation established



## Attractive market

- Tacrosolv addresses the Dry Eye Disease market
- The market is strongly growing with a CAGR of 7% until 2030

## Regulatory path

- Hybrid application in EU (Article 10(3), 2001/83/EC)

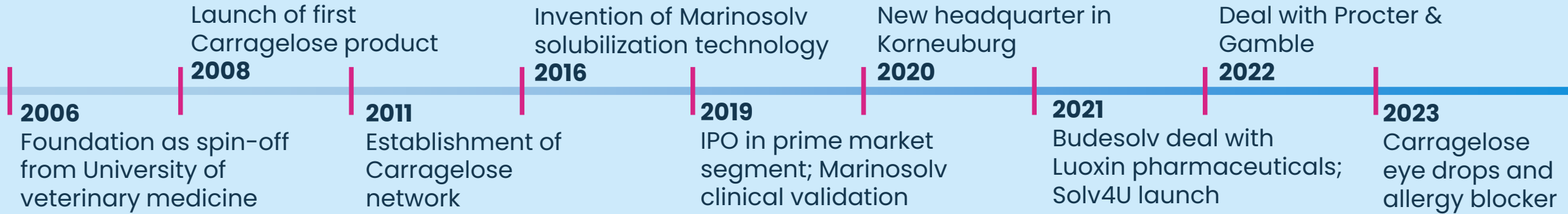


# Marinomed at a glance



# Marinomed at a glance

Publicly listed biopharmaceutical company located in Korneuburg, Austria



**Marinomed Headquarter in Korneuburg, Austria**



**Marinomed Management**

**Andreas Grassauer**  
Chief Executive Officer



**Eva Prieschl-Grassauer**  
Chief Scientific Officer



**Gabriele Ram**  
Chief Financial Officer



# Technologies & Therapeutic Areas

## Carragelose®

Universal **blocking of viruses and allergens** as well as moistening of mucosal tissues

### Cough & cold portfolio\*

Viral respiratory infections



### Allergy nasal spray\*

Mild allergic rhinitis



### Eye drops

Dry, irritated eyes



## Marinosolv®

**Solubilization** of poorly water-soluble compounds and improving **local onset of action**

### Budesolv

Allergic rhinitis



### Tacrosolv

Inflammatory eye diseases



### Solv4U Technology partnerships

## Solv4U

**VIROLOGY**



**IMMUNOLOGY**



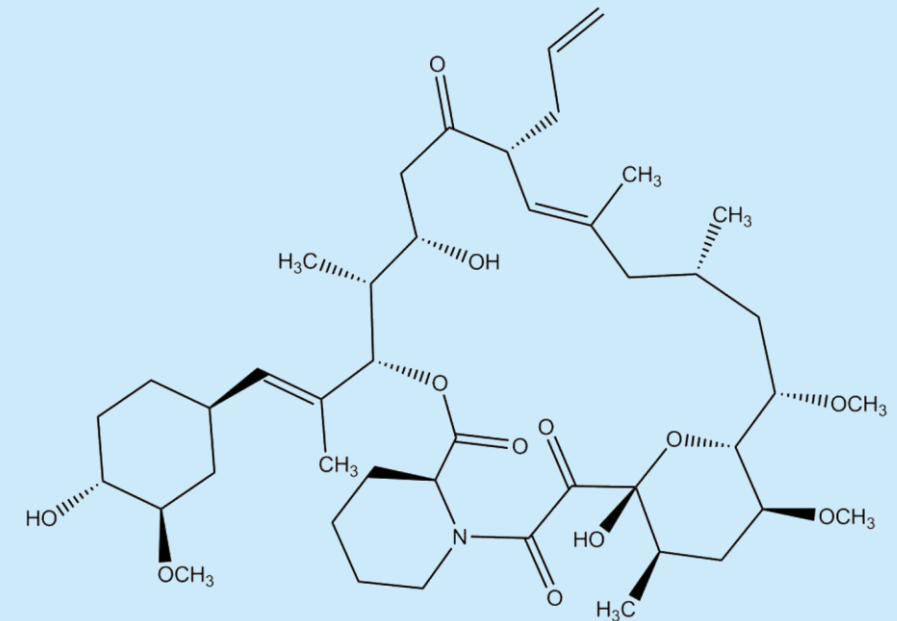
**SOLV4U**



# Tacrolimus: Highly potent macrolide immunosuppressant

A substance that could benefit so many more patients if solubilized

- **Highly hydrophobic** macrolide calcineurin inhibitor
- Immunosuppressive effect on T-cells and mast cells with indirect effects on many immune reactions
- **~100 times** more active than Cyclosporine
- Steroids usually should not be used longer than three weeks and are not routinely used in chronic inflammatory situations
- **Proof of concept** by a Tacrolimus containing drug marketed against vernal conjunctivitis in Japan and South Korea
- **No marketed product** in ophthalmology **available** outside Asia\*

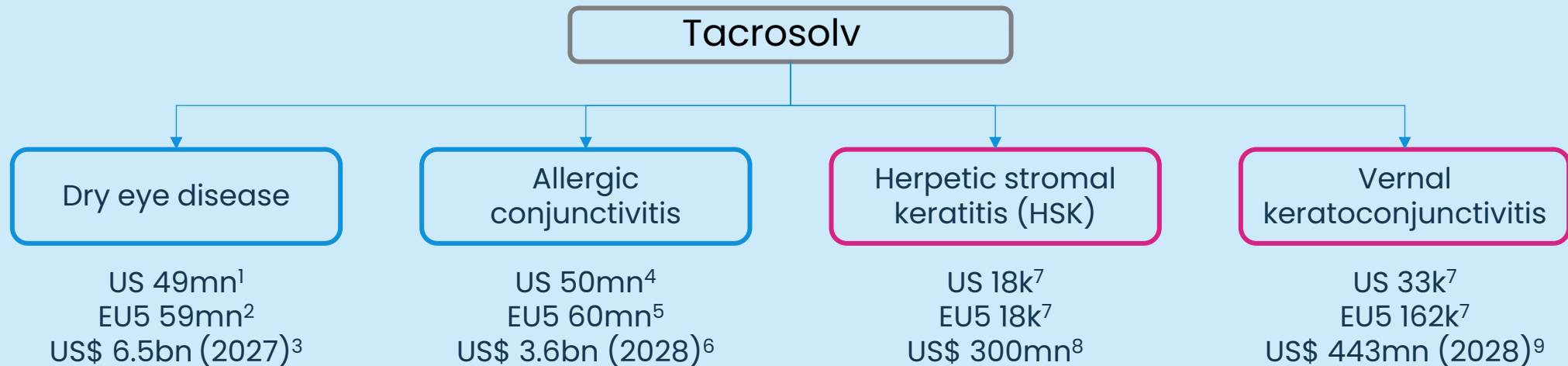


Potential to treat a multitude of ophthalmic inflammatory diseases



# Attractive ophthalmic market

## Total target populations & market sizes



Common disease

Rare disease

All numbers reflecting patients, except US\$

1 Paulsen AJ et al. Am J Ophthalmol 2014; 157:799e806

2 Ferrero A et al., Ocul Surf. 2018 16:112-119., Viso E et al., Ophthalmic Epidemiol 2009;16 Malet F, et al. Acta Ophthalmol 2014; 92:e429e36 Vehof J et al., Br J Ophthalmol 2014;98:1712e7.Vehof J, et al., Ophthalmology. 2017;124:505-511 Vehof J et al., Ocul Surf. 2021; 19:83-93.

3 Fortunebusinessinsights.com: Dry eye report, public information as of 12/2022

4 Fortunebusinessinsights.com: Allergic conjunctivitis report, public information as of 12/2022

5 Sources: Cibella FF et al., Allergy Asthma Immunol Res, 2015; 7:44-50 Klossek JM et al., Presse Med. 2009; 38:1220-9

6 Fortunebusinessinsights.com: Allergic conjunctivitis report, public information as of 12/2022

7 McCormick I et al.; Ophthalmic Epidemiology 2021; 8:1-1010

8 Internal calculation based on addressable patient numbers and estimated treatment costs

9 Coherent market insight: vernal keratoconjunctivitis market report, public information as of 12/2022





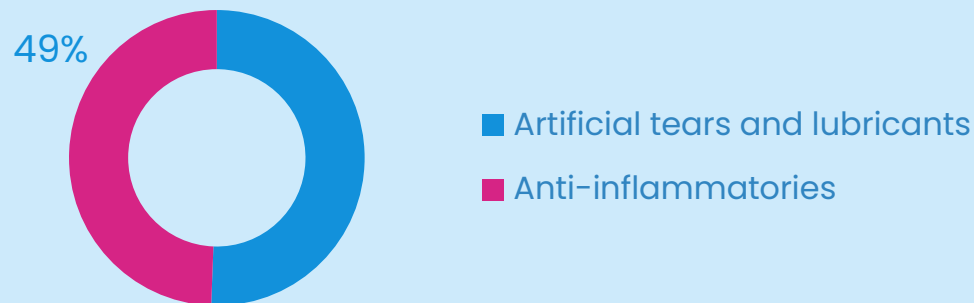
# Dry eye disease market

Tacrosolv eye drops target an underserved multi-billion Dollar market

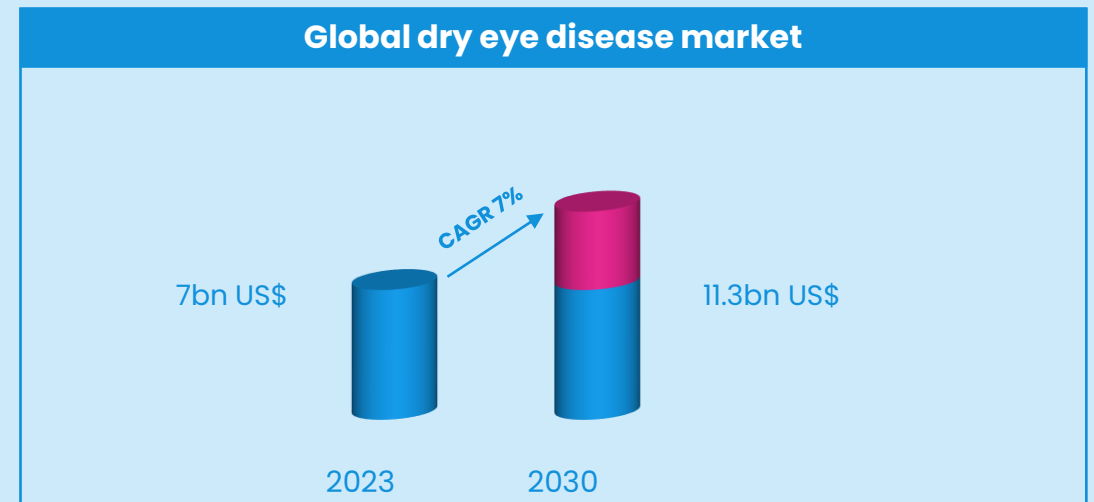
- Caused by either reduced production of tears or an increased evaporation of tears
- Symptoms: dryness, irritation, redness, fatigued eyes, and blurred vision
- Affects 360mn people with increasing prevalence due to growing use of screens and contact lenses increase in LASIK surgeries
- Up to 30% of the population is affected to some degree

- Markets expected to increase to **\$11.3bn** in 2027
- Largest market is the **US with \$3.1bn** in 2022
- Growth returning to pre-pandemic levels **CAGR 7%**
- Growth driven by huge **unmet medical need** and new products
- **Competitors:** Lubricants and pharmaceuticals

Global dry eye disease market share by product, 2019



Global dry eye disease market



# Tacrosolv: Exploratory phase 2a

## Allergic conjunctivitis as model indication

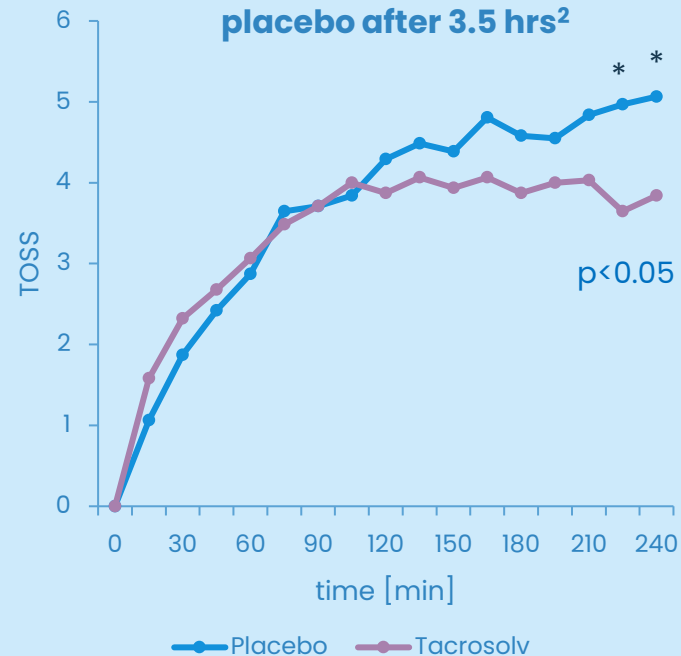
Study	Demonstration of safety and efficacy of two doses of Tacrosolv
Location	Vienna Challenge Chamber, Austria
Enrollment	64 participants
Design	Double blind, placebo-controlled, randomized, crossover Continuous allergen challenge over 4 hours
Treatment	Tacrosolv eye drops, 50µg/ml solubilized Tacrolimus (0.005%), Placebo eye drops, (buffer + propylene glycol)
Treatment regimen	1 or 2 eye drops (50µl) for 8 days (0.005%)
Primary Endpoint	Total Ocular Symptom Score (TOSS <sup>1</sup> ) on day 8 (12 max score), (baseline adjusted mean of TOSS during allergen challenge)
Secondary Endpoints	Change in ocular redness image score, Total Nasal Symptom Score (TNSS <sup>2</sup> ), Total Respiratory Symptom Score (TRSS <sup>3</sup> ), Nasal airflow
Ocular Safety Endpoints	Intra-ocular pressure, Cornea staining, Conjunctiva staining, Conjunctival chemosis, Eyelid edema, Conjunctival papillae



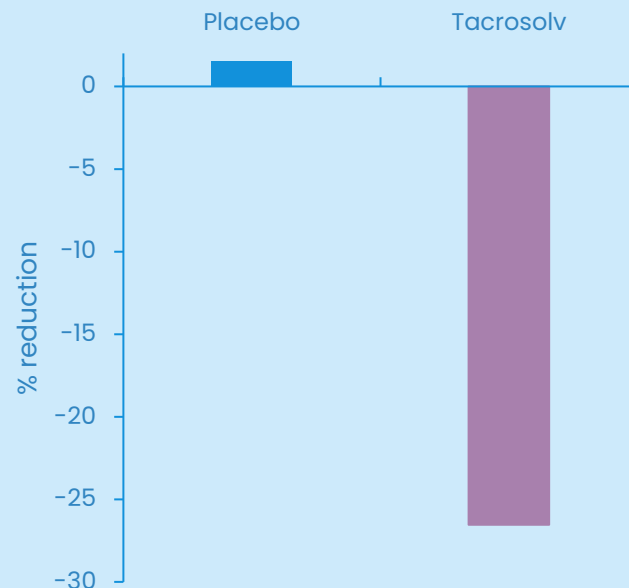
# Tacrosolv solution (0.005%): Exploratory phase 2a

Anti-inflammatory activity in model indication allergic conjunctivitis<sup>1</sup>

**HIGH DOSE: Significant reduction of TOSS on day 8 compared to placebo after 3.5 hrs<sup>2</sup>**



**HIGH DOSE: 26% reduction of TOSS\* on day 8 in Tacrosolv study group compared to day 1<sup>2</sup>**

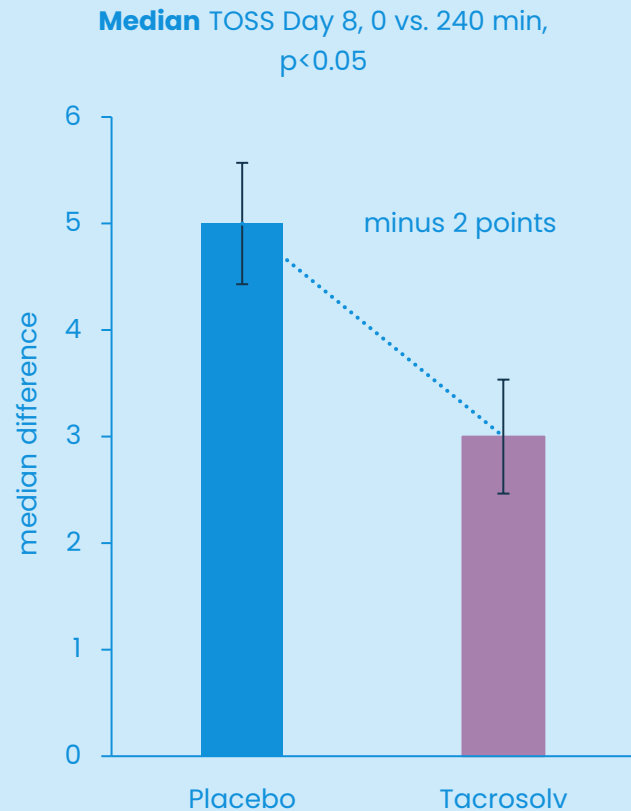
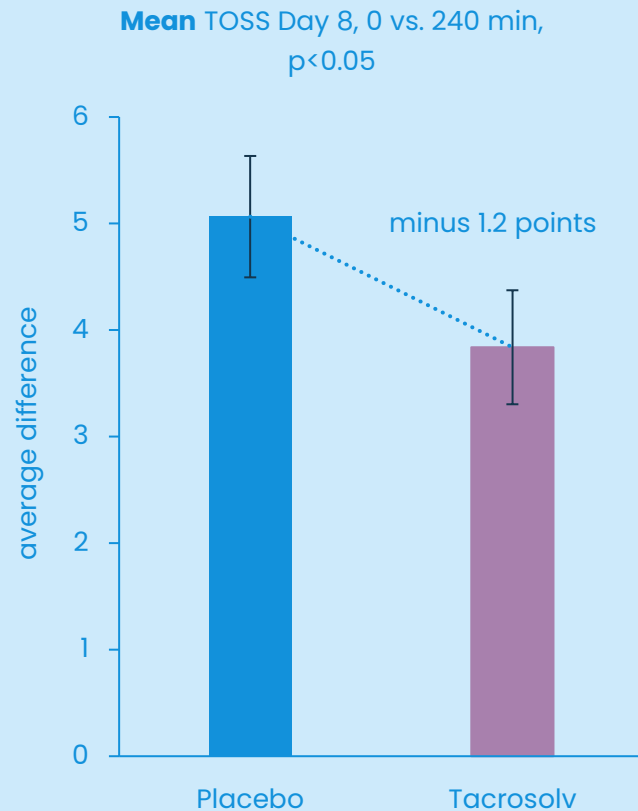


### Significant reduction<sup>3</sup>

- Ocular symptoms on day 8 of treatment compared to day 1
- Ocular symptoms after one week of treatment at 3.5 hours after challenge begin
- Nasal symptoms on day 8 of treatment

# Tacrosolv solution (0.005%): Exploratory phase 2a

Day 8 mean change from baseline TOSS under allergen challenge (high dose)



Difference of TOSS was calculated by subtracting TOSS at 0 minutes from TOSS at 240 minutes during continuous grass pollen challenge. Significance was tested with paired t-Test (nominal).  $n=31$  (all groups in cross-over design). Baseline adjusted.



# Background technology

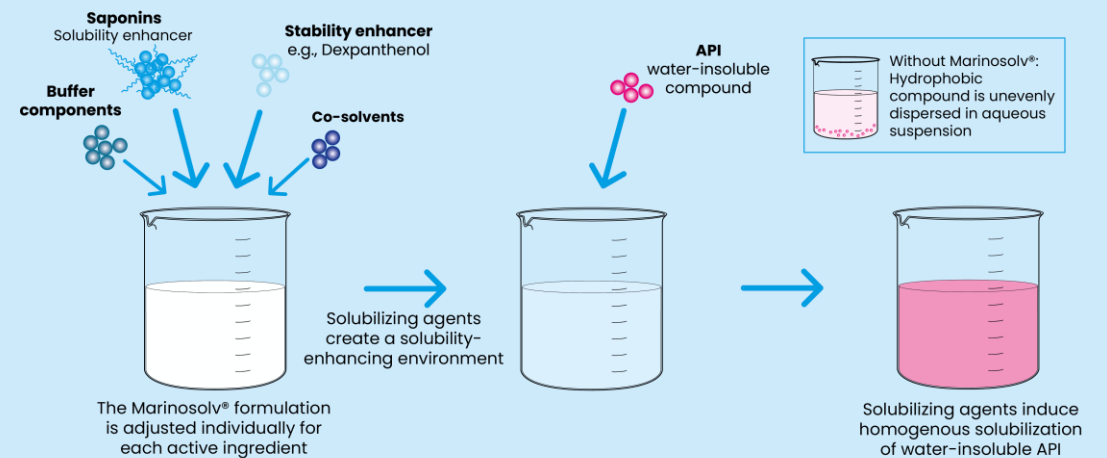
Marinosolv is a patent-protected technology to dissolve hardly soluble compounds

## Tacrosolv formulation development

- Tacrosolv is a **fully dissolved clear solution** of Tacrolimus based on the Marinosolv technology platform
- Marinosolv is a combination of water-soluble solvent, saponins, stability enhancer, and buffer
- Marinosolv is particularly suited to **increase the solubility** and consequently the **bioavailability** of hydrophobic pharmaceutical ingredients
- Tacrosolv contains a **significantly lower concentration** of the active pharmaceutical ingredient compared to marketed products in Japan and Korea
- Tacrosolv is **clinically tested** and patent protected

## Formulation technology

### Marinosolv® formulation & solubilization of water-insoluble API



Marinosolv allows a complete dissolution of Tacrolimus



# Tacrolimus: Suspension versus solution

Marinosolv allows 600-fold increased solubility of Tacrolimus<sup>1</sup>

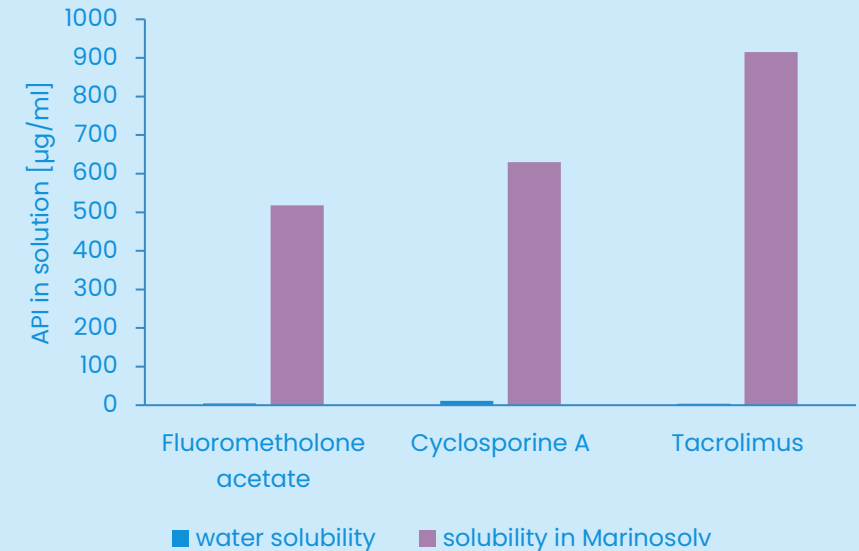
**Marketed product Talymus (Asia): Tacrolimus suspension\***



**Tacrosolv: Tacrolimus solution**



**Effect of Marinosolv on solubility**



# Quotes from Medical Experts

Key opinion leaders confirm the medical need for fully solubilized Tacrolimus

*"Tacrosolv could be a breakthrough."*

**Expert at Tufts University, Boston USA**

**Expert at Institut de la Vision, Paris France**

*Marinomed is in a "very good field of activity that is under-appreciated," and "formulations are important."*

*"There is definitely a need for it. There is nothing compared with steroids in terms of safety and efficacy and that could be used as steroid-sparing."*

*"You don't have to convince me that tacrolimus works."*

**Expert at University of Cologne, Cologne Germany**

**Expert at Tufts University, Boston USA**

**Expert at Wilmer Eye Institute USA**

*"It is quite unheard of to have a signal of efficacy in just 8 days."*



# Tacrosolv

A new Tacrolimus solution against  
ophthalmic inflammation



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