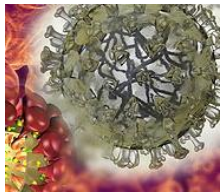
The Marinosolv® Technology Platform

Enables novel aqueous formulation of hardly soluble compounds

Solve the un(dis)solvable






Company highlights

Innovative biopharmaceutical company focused on respiratory, allergy and ophthalmic OTC and Rx therapies

1 Established biopharmaceutical company with a global presence

- Unique, asset-light business model with significant growth potential
- Significant pipeline with multiple, derisked and near to market assets
- Strong experience in bringing products to market

2 Marinosolv®: an innovative drug delivery platform focused on allergy and eye diseases

- Enabling novel stable aqueous formulations of hardly soluble compounds
- Budesolv finished Phase III for allergic rhinitis, Tacrosolv in Phase II for allergic conjunctivitis
- Potential for additional indications through proprietary programs and/or Pharma licensing deals

3 Carragelose®: a powerful OTC platform focused on respiratory diseases

- Clinically proven efficacy against over 200 viral strains
- Six products on the market, generating approximately €30m in retail sales in over 40 countries
- Significant growth potential with additional near term (new) product launches in major markets

4 Experienced leadership team backed by high quality boards

- Strong track record in the pharmaceutical industry and scientific community
- Over €65m in total equity and non-dilutive funding raised to date

Marinosolv® optimises local drug delivery

Technology platform for novel aqueous formulations of virtually any drug

An improved way of formulating poorly soluble compounds for sensitive tissues

- **Faster onset of action**
- **Improvement of local activity**
- **Reduction of administered dose**
- **Better patient adherence**

Marinosolv® enables the solubilisation of hardly soluble compounds, unlocking new possibilities in treating a multitude of diseases.

Marinosolv®

Platform technology for formulation of insoluble locally applied drugs

Increase of solubility of compounds due to Marinosolv®

Shown in multiple experiments

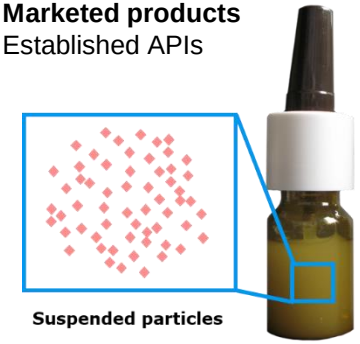
Compound	fold-increase of solubility compared to water
Steroid	
Budesonide	> 10-fold
Fluticasone propionate	50-100-fold
Mometasone fuorate	100-fold
Macrolide immunosupressant	
Cyclosporin A	30-fold
Pimecrolimus	80-fold
Tacrolimus	200-fold
Others	
Paclitaxel	> 10-fold
Curcumin	> 1000-fold

Marinosolv® Platform Technology for Formulation of Pharmaceutical Ingredients Hardly Soluble in Water

A versatile delivery system that could improve bioavailability for potent compounds

- Marinosolv® is a **patent-protected technology platform** enabling novel well tolerated **aqueous solutions** of relatively to highly insoluble compounds
- First aqueous steroid **solutions** offer **increased bioavailability**
- First developments concentrate on **intranasal and ocular applications**, further use such as for lungs to be tested
- Marinosolv® is a preservative-free formulation based on **micelles**

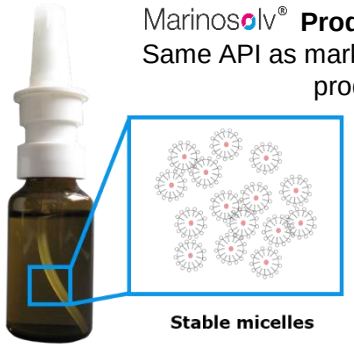
Marketed products
Established APIs



Suspended particles

Technology Platform	Potential to facilitate delivery of **any compound** with solubility issues in aqueous solutions, e.g. corticosteroids
Increased bioavailability	**Faster** onset of action More local and lower systemic availability
Dose reduction	**Lower** possible **side effects** Lower production costs
Aseptic filling	**Preservative free** formulation Lower production costs (steroids)

Marinosolv® **Products**
Same API as marketed products



Stable micelles in solution

Marinosolv® enhances bioavailability

Preclinical studies strongly suggest increased bioavailability in a variety of organs

Increased permeability of fluorescently labelled dissolved estradiol compared to a suspension

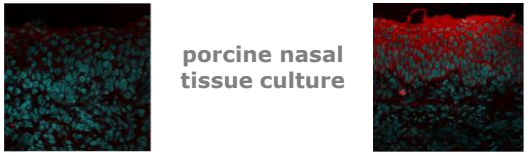
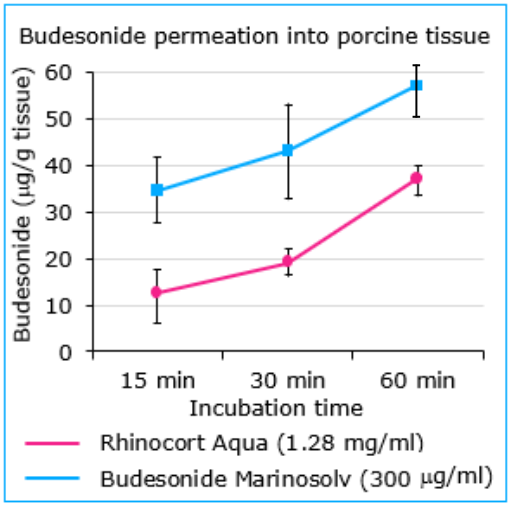


Photo: Rhinocort Aqua (Astra Zeneca) nasal spray (left) and Marinosolv® enabled Budesonide nasal spray (right).
Source: Marinomed

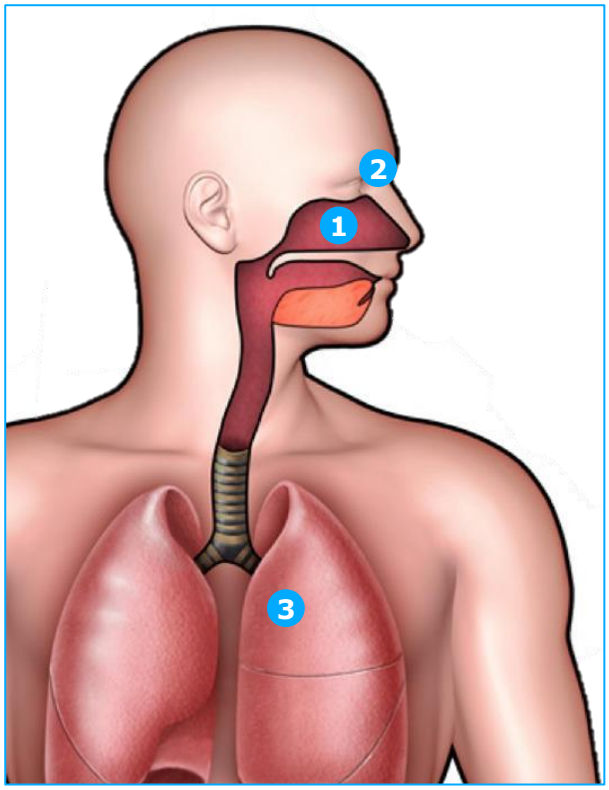


- **Marinosolv®** enables **novel stable aqueous formulations** of hardly soluble compounds
- Technology is not limited to a specific compound and has the potential to facilitate delivery of **any compound** with solubility issues, e.g. corticosteroids or others
- Compatible with **ocular and intranasal applications or sensitive tissues in general**
- **Dose reduction** of the active compound, thus lowering possible side effects and production costs

Source: Company data

Marinosolv® portfolio overview

Budesolv finished clinical phase III and Tacrosolv ready for phase II



1 Nasal products

- **Budesolv** 10µg nasal spray for allergic rhinitis
- **Flutisolv** nasal spray for allergic rhinitis
- Nasal formulation of macrolide immunosuppressant for non-steroid treatment of allergic rhinitis and other nasal conditions

2 Ophthalmic products

- **Tacrosolv** immunosuppressant for allergic conjunctivitis, dry eye and other inflammatory eye diseases
- Undisclosed projects

3 Lung products

- Inhalation products for lung diseases such as COPD

The Marinosolv® products focus on sensitive mucosal tissues of the respiratory tract and the eyes

Budesolv will be very competitive

Budesolv, a strong competitive edge in allergic rhinitis

Rhinocort Aqua 64 µg nasal spray

(suspension of Budesonide, 64 µg per dose/spray)

- Sub-optimal treatment for allergic rhinitis
- Clinical improvement usually takes multiple days
- Reaching maximum benefit takes approximately 2 weeks
- Contains a preservative

Budesolv 10 µg nasal spray

(solution of Budesonide, 10 µg per dose/spray)

- ✓ **Reduced dose** → 10% of the original dose
- ✓ **Faster onset of action** → hours versus days
- ✓ **Immediate relief** of symptoms
- ✓ **100% preservative-free**

- Budesolv 10 µg nasal spray will have a **very strong competitive advantage** over Rhinocort Aqua, the current leading Budesonide nasal spray for allergic rhinitis
- McNeil Consumer Healthcare, a subsidiary of Johnson & Johnson, acquired the US rights to Rhinocort Aqua in 2014 for an undisclosed amount and launched the OTC version in Feb 2016 in the US
- Cilag GmbH International, a subsidiary of Johnson & Johnson, acquired the rights to Rhinocort Aqua outside of the US in Oct 2016 for a total of $330 million in cash

Budesolv will be the first product from the Marinosolv® platform, validating its strong competitive edge.

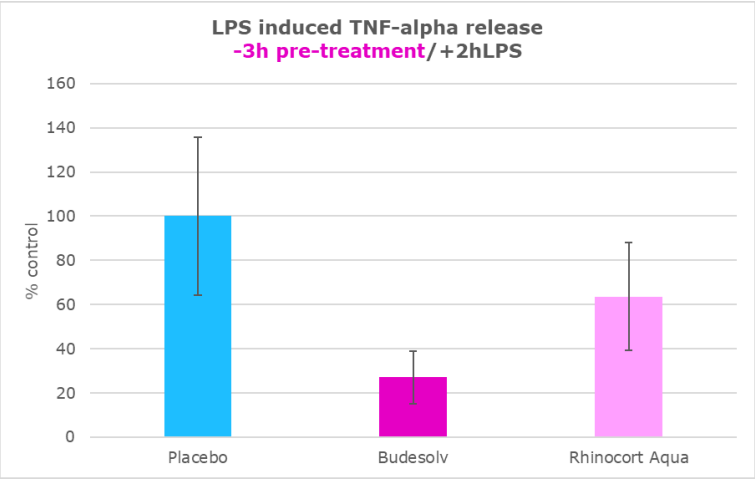
Source: Rhinocort Aqua Patient information leaflet USA, press releases AstraZeneca, press releases Johnson & Johnson

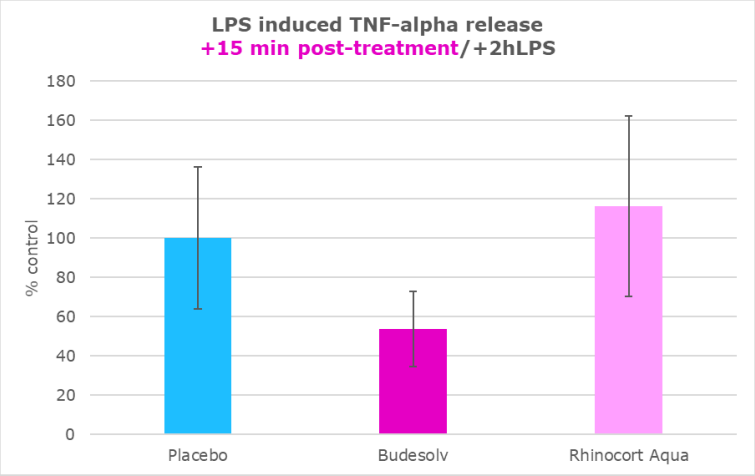
STEROIDS EXEMPLIFIED BY BUDESONIDE

Efficacy of dissolved Budesonide versus suspensions in a murine lung inflammation model

Strong decrease of TNF-alpha production in a murine inflammatory lung model

A dose of 300 µg/ml dissolved Budesonide is more effective in reducing TNF-alpha release than the marketed product with 1.28 mg/ml suspension when applied 3 hours before challenge or 15 minutes after challenge.





Budesolv demonstrates superiority of a Marinosolv® enabled corticosteroid compared to marketed product

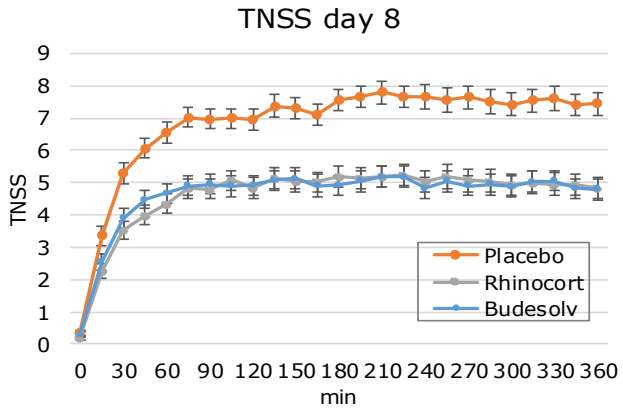
Successful Phase III supports clinical efficacy and fast onset of action

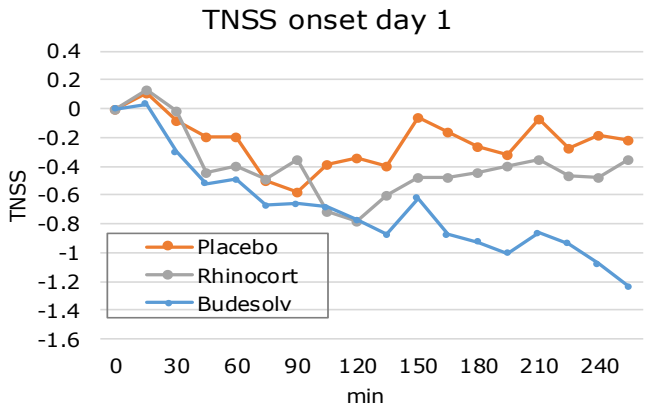
Primary endpoint of non-inferiority met

- Result to demonstrate a reduction of TNSS* score non-inferior equivalent to the originator on **Day 8**
- Both active treatments show **significant superiority** compared to placebo on Day 8

Key secondary endpoint of fast onset met

- Result to demonstrate a **significant reduction of TNSS score** by Budesolv on **Day 1** after first dose
- Other allergy-related symptom scores measured may support additional claim for further differentiation





Budesolv can effectively control AR nasal symptoms

Demonstrated clinical benefit 3 hours after the first Budesolv treatment on Day 1

More detailed results of the study can be found at
https://www.marinosolv.com/en/publications

AR: Allergic Rhinitis

*TNSS: Total Nasal Symptom Score – Higher scores correlate to more severe conditions

IMMUNOSUPPRESSANTS
TACROLIMUS

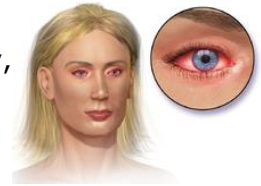
Tacrosolv - optimised eye therapies

Marinosolv®-enabled novel formulation of Tacrolimus

Enabling Tacrolimus to reach its full potential…

- Macrolide immunosuppressants such as Tacrolimus and Cyclosporine A show **activity on allergically stimulated mast cells**, suggesting an application in conditions such as **allergic conjunctivitis** as alternative for antihistamine or steroid based eye drops
- These substances are also **clinically proven** to be effective against inflammatory and Sjögren's Syndrome related **dry eye disease**, with Cyclosporin A being the only approved drug for dry eye in the US (*Restasis* by Allergan)
- In eye related treatment, Tacrolimus is typically applied as a **dispersion with limited efficacy and bioavailability**, especially as the majority of the drug particles is quickly cleared in case of ocular applications
- **The Marinosolv® platform is exceptionally well suited to develop effective treatments with solubilized Tacrolimus for these large and underserved indications**

…for treating largely unmet medical needs

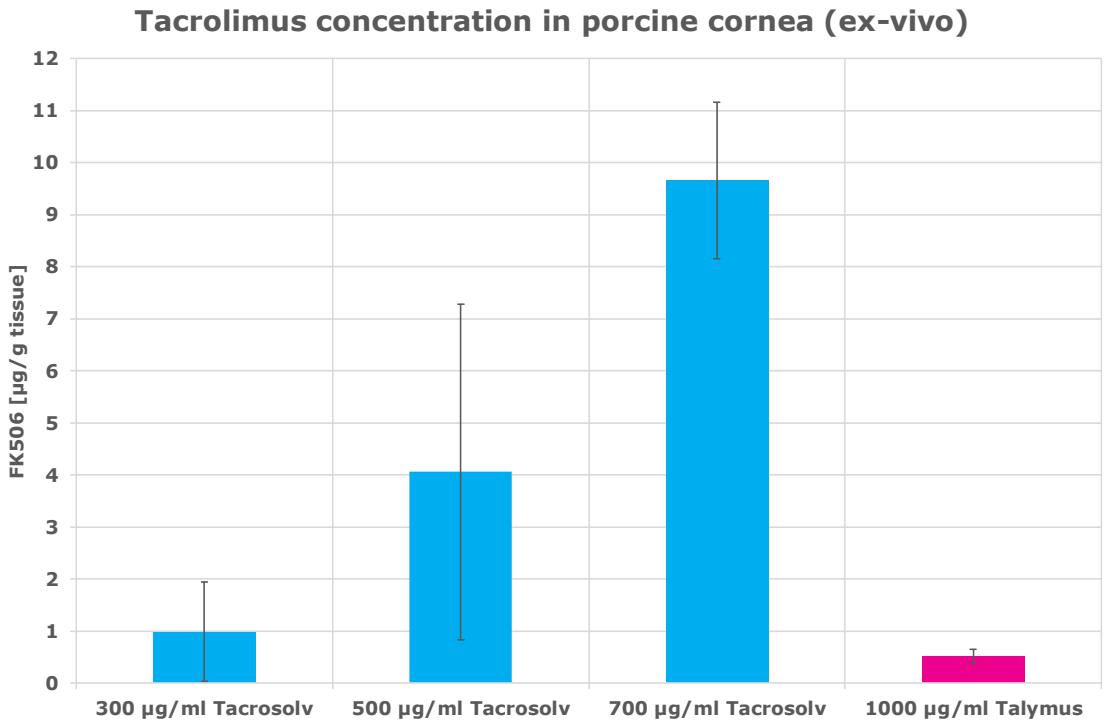


- **Allergic conjunctivitis** is an inflammation of the conjunctiva of the eye due to allergy, affecting ~20% of the population annually
- Mild cases are usually treated with antihistamines, whereas more serious cases are treated with corticosteroids and immunotherapy → **target market for Tacrosolv**
- **Dry eye disease** is a common condition of insufficient or poor-quality tear production, leading to inflammation and affects 10-30% of the population. Next to that patients with Sjögren's syndrome suffer from dry due to an autoimmune reaction. Approx. 1% of the population suffers from Sjörgen's syndrome.
- *Restasis* by Allergan and *Ikervis* by Santen (both Cyclosporin) and *Xiidra* by Novartis (Lifitegrast) are the only drugs approved for dry eye with *Restasis* reaching $1.47bn in 2017 sales in US alone

Tacrosolv is ready to start Phase II clincal trial for allergic conjunctivitis.

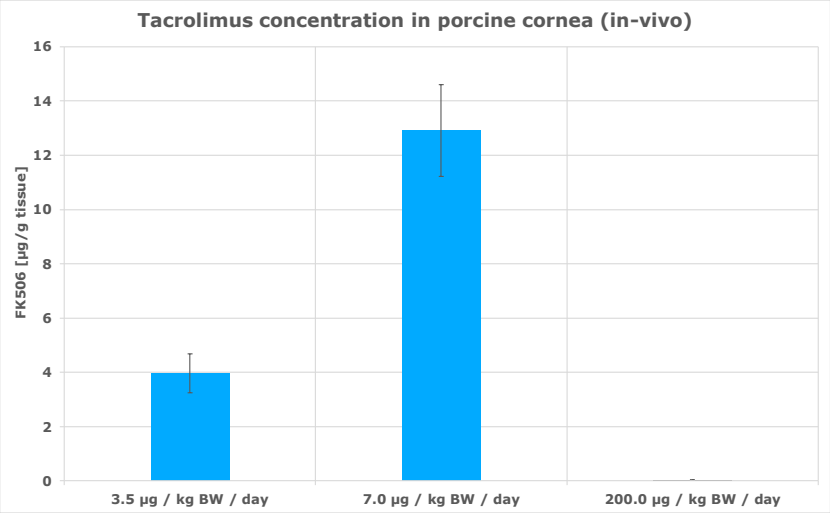
Source: Cont Lens Anterior Eye. 2015 Oct;38(5):373-8; "Punctal occlusion for dry eye syndrome". The Cochrane Database of Systematic Reviews. 6: CD006775; Primer on the rheumatic diseases (13th ed.). New York, NY: Springer. p. 389.

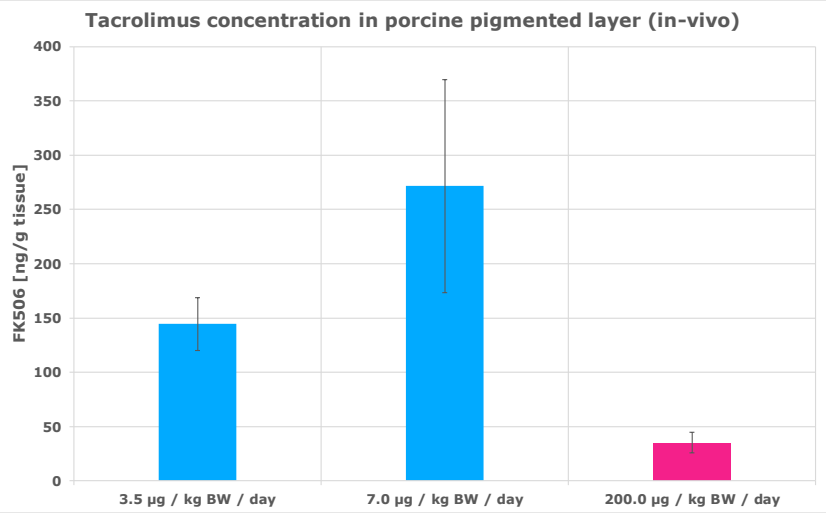
Increased tissue concentration of Tacrolimus due to Marinosolv®



Different Marinosolv enabled Tacrolimus formulations (Tacrosolv) including the marketed suspension product (Talymus) were applied onto porcine eyes and afterwards the concentration of Tacrolimus was determined with HPLC-MS

Increased tissue concentration of Tacrolimus due to Marinosolv®





Marinosolv enabled Tacrolimus formulation (Tacrosolv) in different dosages (3.5 and 7.0 µg / kg BW / day) were applied onto porcine eyes and compared to an oral treatment (200.0 µg / kg BW / day) of a marketed product (Prograf). The concentration of Tacrolimus was determined with HPLC-MS.

Marinosolv®

Solve the un(dis)solvable

Contact BD&L
bd@marinomed.com
www.marinomed.com