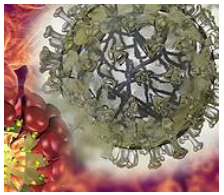
The Marinosolv® Technology Platform

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 in Phase III for allergic rhinitis, Tacrosolv in Phase II for allergic conjunctivitis/dry eye
- 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 €25m in retail sales in over 30 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®, the basis for better therapies

Technology platform for novel aqueous formulations of virtually any drug

- Based on plant derived saponins
- Enables novel stable formulations of practically insoluble compounds such as corticosteroids
- Allows for faster onset of action, elimination of harmful solvents, better bioavailability, high local activity and thus reduction of the API dose
- Budesolv (Budesonide formulation) is the most advanced asset, currently in Phase III
  Tacrosolv (Tacrolimus formulation) is ready to start Phase II
- Marinosolv® platform provides countless opportunities for Marinomed and Pharma partners
- Supported with a strong patent family (novel use) providing protection until at least 2036

Marinosolv®

Platform technology for formulation of insoluble locally applied drugs

Increase of solubility of compounds due to Marinosolv®

Shown in multiple experiments

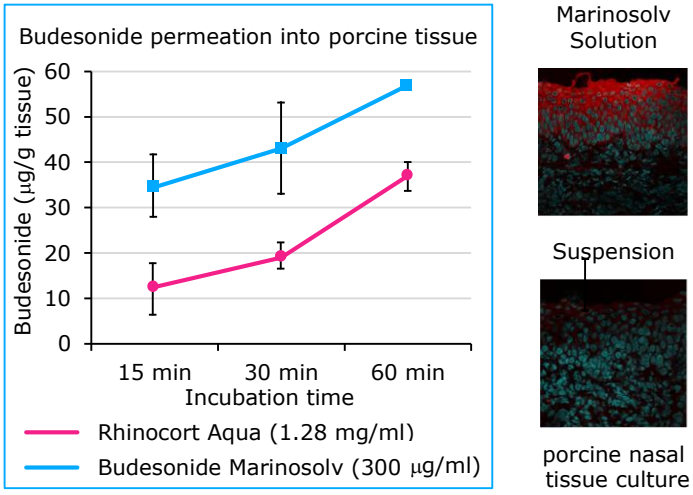
Compound	fold-increase of solubility compared to water
Steroid	
Budesonide	> 10-fold
Fluticasone propionate	50-100-fold
Mometasone fuorate	100-fold
Macrolide immunosupressant	
Cyclosporin A	30-fold
Pimecrolimus	80-fold
Tacrolimus	200-fold
Others	
Paclitaxel	> 10-fold
Curcumin	> 1000-fold

Marinosolv® enhances bioavailability

Preclinical studies strongly suggest increased bioavailability in a variety of organs

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

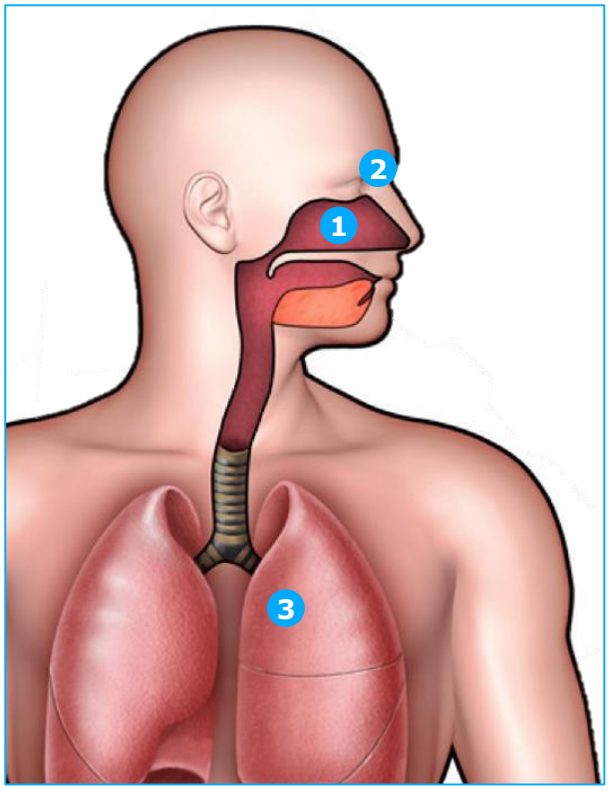
Increased permeability of dissolved budesonide / labelled esteradiol compared to a suspension[1]



- 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
- Compatible with ocular and intranasal applications
- Dose reduction of the active compound, thus lowering possible side effects and production costs

Marinosolv® portfolio overview

Budesolv in clinical phase III and Tacrosolv ready for phase II



1 Nasal products

- **Budesolv** 10mcg 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 the allergic conjunctivitis, dry eye and other conditions
- 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, launched in 2016 as OTC product
- Clinical improvement usually takes 1-2 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 → less than 20% of the original dose
- Potential faster onset of action → minutes versus days
- Potential 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

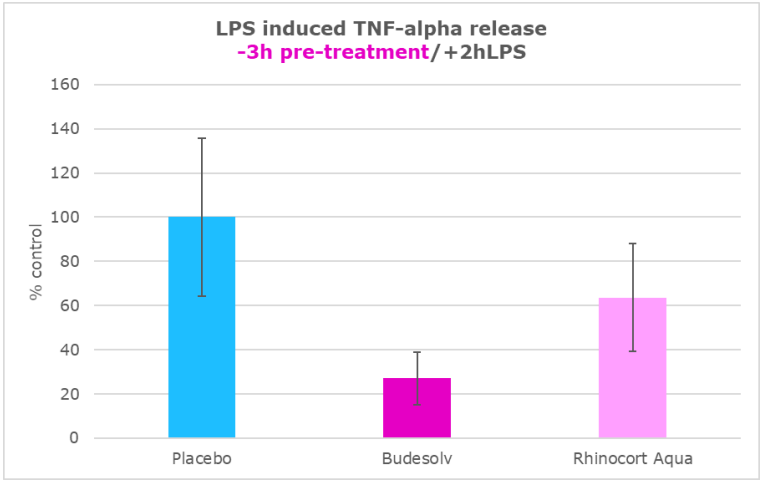
Budesolv will be the first product from the Marinosolv® platform, validating its strong competitive edge.

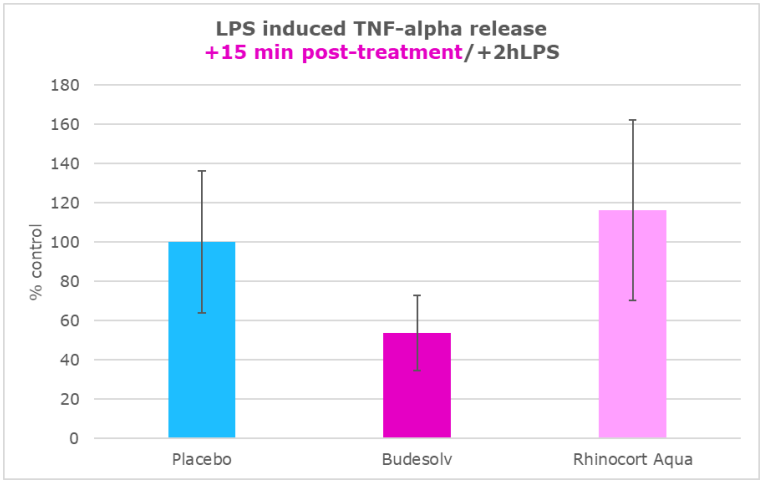
Source: Rhinocort Aqua Patient information leaflet USA, press releases AstraZeneca, press releases Johnson & Johnson

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 than the marketed product with 1.28 mg/ml suspension when applied 3 hours before challenge or 15 minutes after challenge





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 have been developed for organ transplantation due to their activity on T-cells
- These compounds also 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
- Next to that, macrolide immunosuppressants 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, a topical 0.03% eye ointment in the case of allergic conjunctivitis
- Therapeutic efficacy of dispersions is generally limited, especially as the majority of the drug particles is quickly cleared in case of ocular applications
- **Marinosolv® platform is exceptionally well suited to develop effective treatments with Tacrolimus for these large and underserved indications**

…for treating large unmet medical needs

- **Allergic conjunctivitis** is an inflammation of the conjunctiva of the eye due to allergy

~20% of the population is affected annually

- Mild cases are usually treated with antihistamines, whereas more serious cases are treated with corticosteroids and immunotherapy → target market for Tacrosolv
- **Dry eye syndrome** is the common condition of having dry eyes. It is caused by either reduced production of tears or an increased evaporation of tears. Next to that patients with Sjögren's syndrome suffer from dry due to an autoimmune reaction

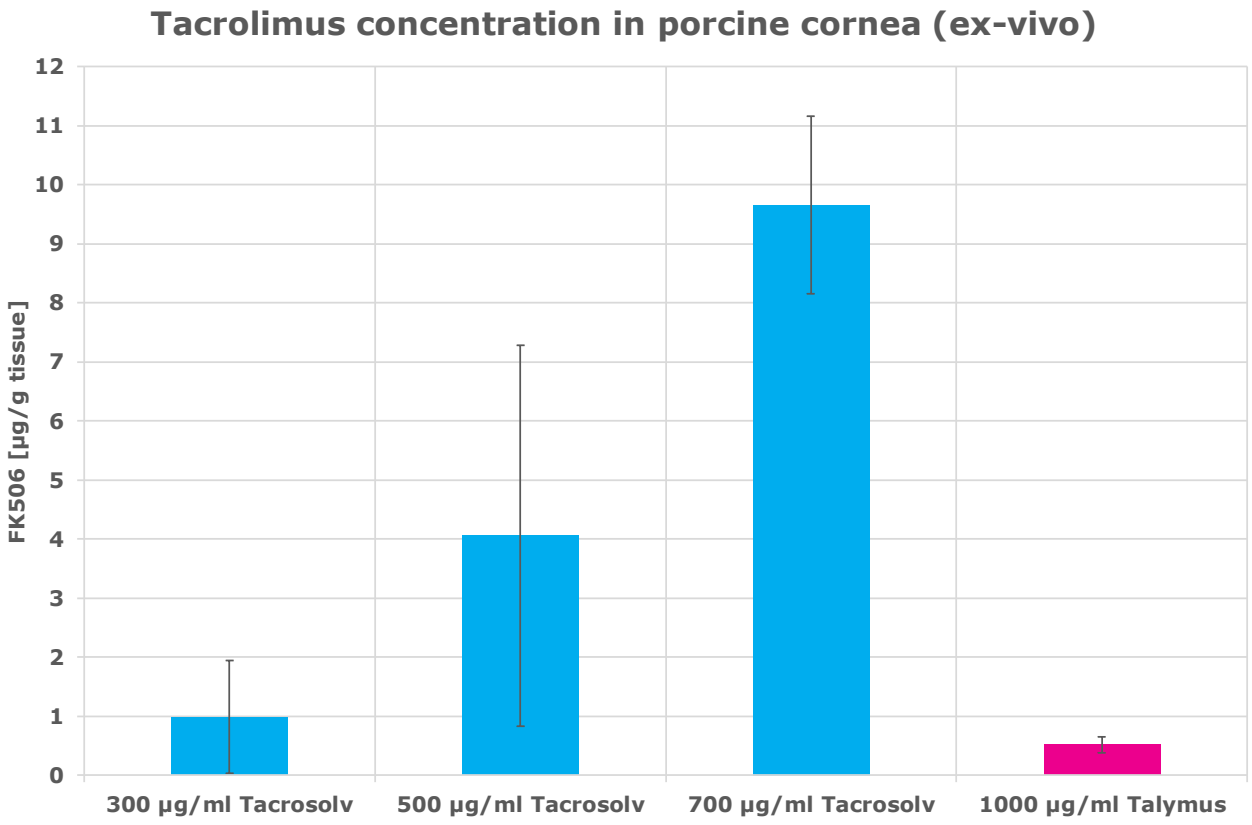
10-30% of the population is affected to some degree

~1% of the population suffers from Sjögren's syndrome

- Restasis by Allergan and Ikervis by Santen (both Cyclosporin) and Xiidra by Shire (Lifitegrast) are the only drugs approved for dry eye with Restasis reaching $1.47bn in 2017 sales in US alone

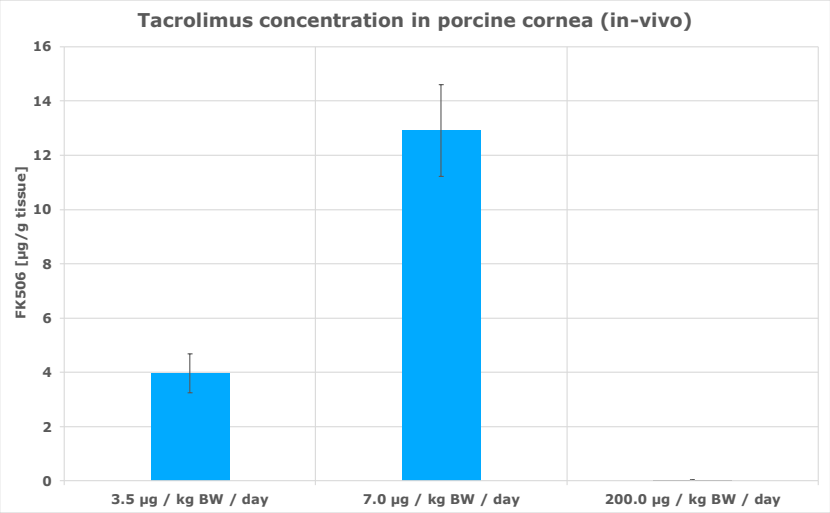
Source: Cont Lens Anterior Eye. 2015 Oct;38(5):373-8; "Punctal occlusion for dry eye syndrome". The Cochrane Database of Systematic Reviews. 6: CD006775; Primer on the rheumatic diseases (13th ed.). New York, NY: Springer. p. 389.

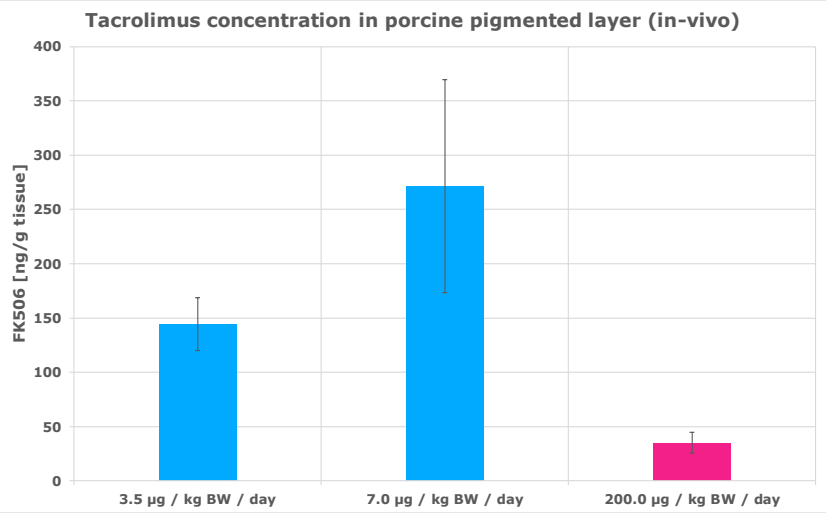
Increased concentration of Tacrolimus due to Marinosolv®



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

Increased concentration of Tacrolimus due to Marinosolv®





Tacrolimus formulation 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

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