



# RealM Therapeutics Corporate Presentation

July 2018

NASDAQ/AIM:RLM

# Important Information

This presentation contains information pertaining to Realm Therapeutics plc ("Realm"), and has been prepared by Realm solely for your information and for use at a presentation for the purpose of providing background information on Realm, its business and the industry in which it operates. For the purposes of this notice, "presentation" means this document, any oral presentation, any question and answer session and any written or oral material discussed or distributed during the presentation meeting. This presentation has not been independently verified and no representation or warranty, express or implied, is made or given by or on behalf of Realm or any of its parent or subsidiary undertakings, or the subsidiary undertakings of any such parent undertakings, or any of such person's respective directors, officers, employees, agents, affiliates or advisers, as to, and no reliance should be placed on, the accuracy, completeness or fairness of the information or opinions contained in this presentation and no responsibility or liability is assumed by any such persons for any such information or opinions or for any errors or omissions. All information presented or contained in this presentation is subject to verification, correction, completion and change without notice. In giving this presentation, none of Realm or any of its parent or subsidiary undertakings, or the subsidiary undertakings of any such parent undertakings, or any of such person's respective directors, officers, employees, agents, affiliates or advisers, undertakes any obligation to amend, correct or update this presentation or to provide the recipient with access to any additional information that may arise in connection with it, nor makes any representation or warranty, express or implied, as to the accuracy or completeness of any of the information contained in this presentation or any other information transmitted or made available to the viewer or recipient hereof, whether communicated in written or oral form. This presentation does not constitute or form part of, and should not be construed as, an offer to sell or issue or the solicitation of an offer to buy or acquire securities of Realm in any jurisdiction or an inducement to enter into investment activity, nor shall there be any sale of securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction. No part of this presentation, nor the fact of its distribution, should form the basis of, or be relied on in connection with, any contract or commitment or investment decision whatsoever. This presentation does not purport to contain all of the information that may be required to evaluate any investment in Realm or any of its securities and should not be relied upon to form the basis of, or be relied on in connection with, any contract or commitment or investment decision whatsoever. This presentation is not intended to provide complete disclosure upon which an investment decision could be made. The merit and suitability of an investment in Realm should be independently evaluated and any person considering such an investment in Realm is advised to obtain independent advice as to the legal, tax, accounting, financial, credit and other related advice prior to making an investment. Matters discussed in this presentation may constitute forward-looking statements, including those relating to Realm's projected financial results and trends, business plans and prospects, and the development of product candidates in Realm's pipeline, including clinical trial results and the status of regulatory review thereof. The forward-looking statements contained in this presentation reflect Realm's views as of the date of this presentation about future events and are subject to risks, uncertainties, assumptions, and changes in circumstances that may cause Realm's actual results, performance or achievements to differ significantly from those expressed or implied in any forward-looking statement. Some of the key factors that could cause actual results to differ from Realm's expectations include Realm's plans to develop and potentially commercialize Realm's product candidates; Realm's clinical trials and preclinical studies for Realm's product candidates; the timing of and Realm's ability to obtain and maintain regulatory approvals for Realm's product candidates; the clinical utility and market acceptance of Realm's product candidates; Realm's commercialization, marketing and manufacturing capabilities and strategy; Realm's intellectual property position; and Realm's ability to identify, acquire and in-license additional product candidates. For further information regarding these risks, uncertainties and other factors that could cause Realm's actual results to differ from Realm's expectations, you should read Realm's Annual Report for the year ended December 31, 2017 posted on <http://ir.realmtx.com/>. No reliance should be made on such forward-looking statements. While Realm may elect to update the information in this presentation, including any such forward looking statements, in the future, Realm undertakes no obligation to do so on account of new information, future events or otherwise, except as required by applicable law or applicable stock exchange regulations if and when circumstances arise that will lead to changes compared to the date when these statements were provided. This presentation concerns products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. Their use in the United States is currently limited by federal law to investigational use, and no representation is made as to their safety or efficacy for the purposes for which they are being investigated. To the extent available, the data contained in this presentation has come from official or third party sources. Third party industry publications, studies and surveys generally state that the data contained therein have been obtained from sources believed by Realm to be reliable, but that there is no guarantee of the accuracy or completeness of such data. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size, growth, and other data about Realm's industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of Realm's future performance and the future performance of the markets in which Realm operates are necessarily subject to a high degree of uncertainty and risk. While Realm believes that each of these publications, studies and surveys has been prepared by a reputable source, Realm has not independently verified the data contained therein. In addition, certain of the data contained in this presentation come from the Realm's own internal research and estimates based on the knowledge and experience of Realm's management in the market in which Realm operates. While Realm believes that such research and estimates are reasonable and reliable, they, and their underlying methodology and assumptions, have not been verified by any independent source for accuracy or completeness and are subject to change without notice. Accordingly, undue reliance should not be placed on any of the data contained in this presentation.

# Investment Highlights

## Proprietary Immunomodulatory Platform

- Ability to modulate key cytokines implicated in multiple therapeutic areas
- Initial focus on dermatology
- Portfolio of granted patents extending into 2032

## Potential First-in-Class Topical IL4 / IL13 Inhibitor

- Demonstrated immunomodulatory and anti-inflammatory effects
- Potentially advantageous safety profile
- Phase 2 study in atopic dermatitis underway; data expected 3Q 2018

## Attractive Market Opportunity

- Large target markets with significant unmet need
- Initially addressing growing dermatology markets with a targeted topical gel for atopic dermatitis as our lead product candidate

## Institutional Support

- Backed by leading specialist investors: OrbiMed, BVF, Invesco, RA Capital, and Abingworth

# Strong Management Team and Investors

Alex Martin  
CEO



Marella Thorell  
CFO /COO



Christian Peters, M.D., Ph.D.  
CMO



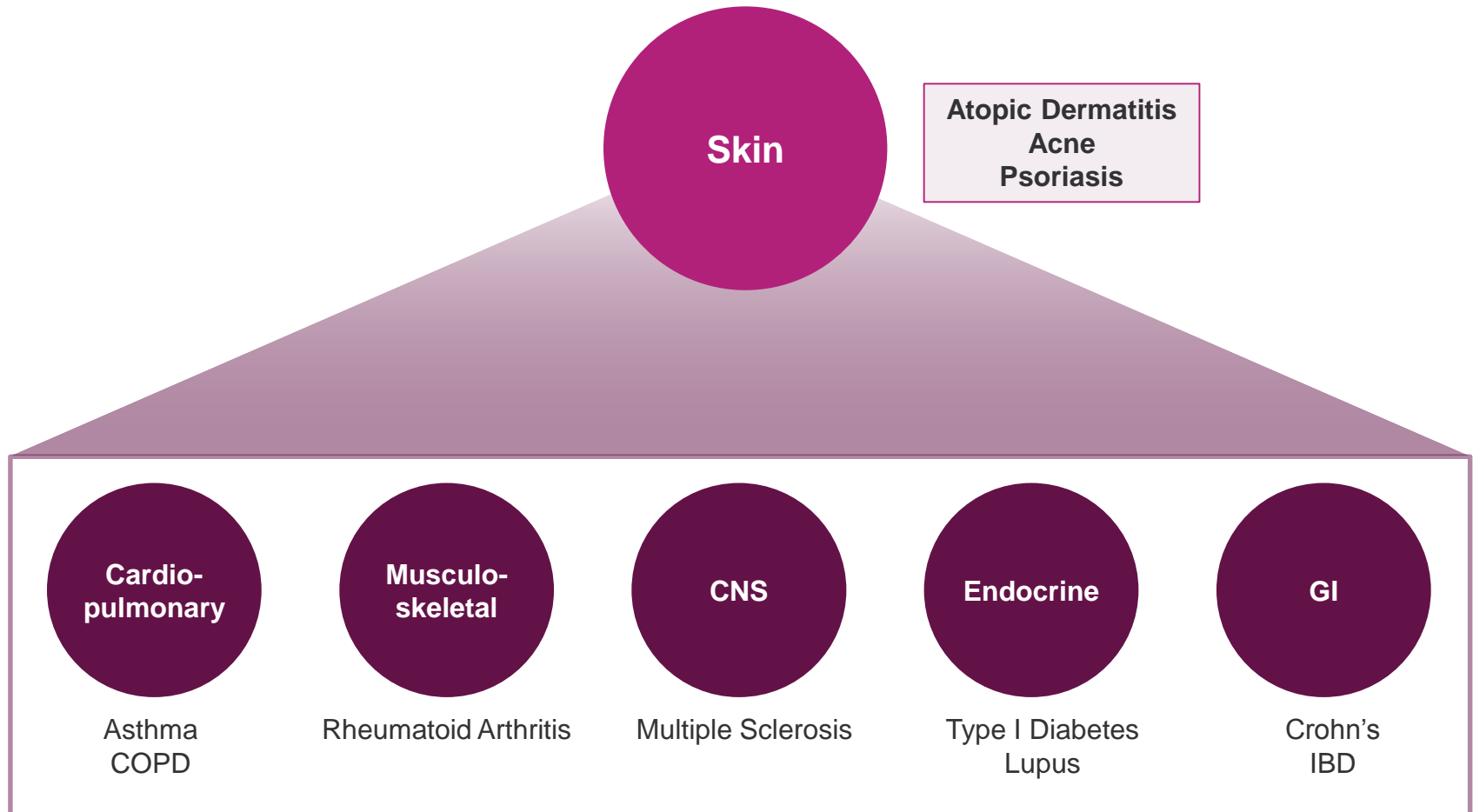
Mark Sampson, Ph.D.  
VP, Research & Development



Cary Schockemoehl  
VP, Business Development



# Building an Immune-Mediated Disease Company



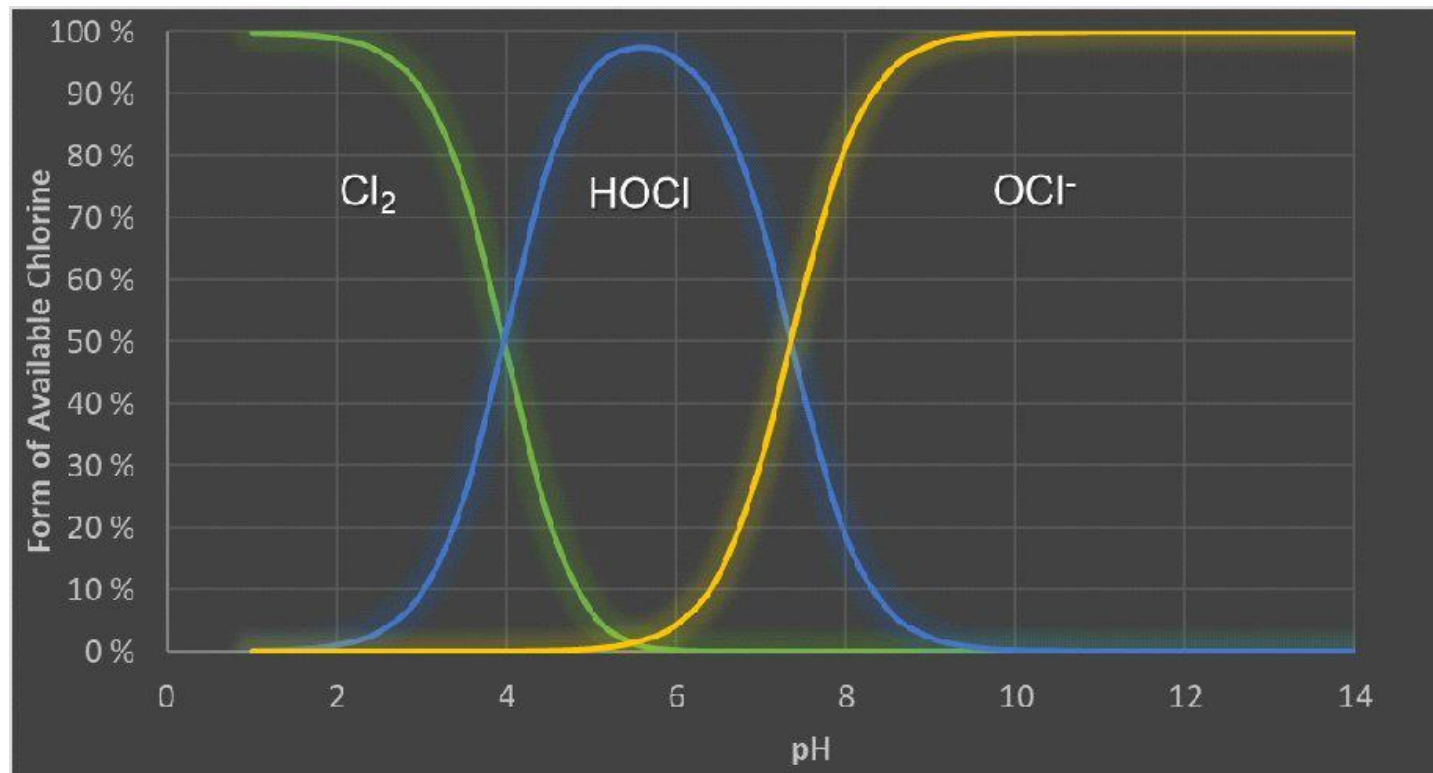
# Current Pipeline

Candidate	Indications/Target	Preclinical	Phase I	Phase II	Phase III	Anticipated Milestones
<b>PR022</b> (topical gel)	Atopic Dermatitis					AD: Phase 2 top-line data expected to be reported in Q3 '18
	Psoriasis					Psoriasis: IND filing expected in Q1 '19
<b>RLM023</b> (topical gel)	Acne					Acne: IND filing expected in Q4 '18, Phase 2 initiation expected in Q1 '19*

\*Pending FDA clearance of IND, we anticipate being able to proceed directly to a Phase 2 trial.

# High Concentration pH Specific Formulation

*Drives immunomodulatory effects and safety profile*



**Specialized manufacturing of high purity HOCl results in high-concentration formulations for drug development**

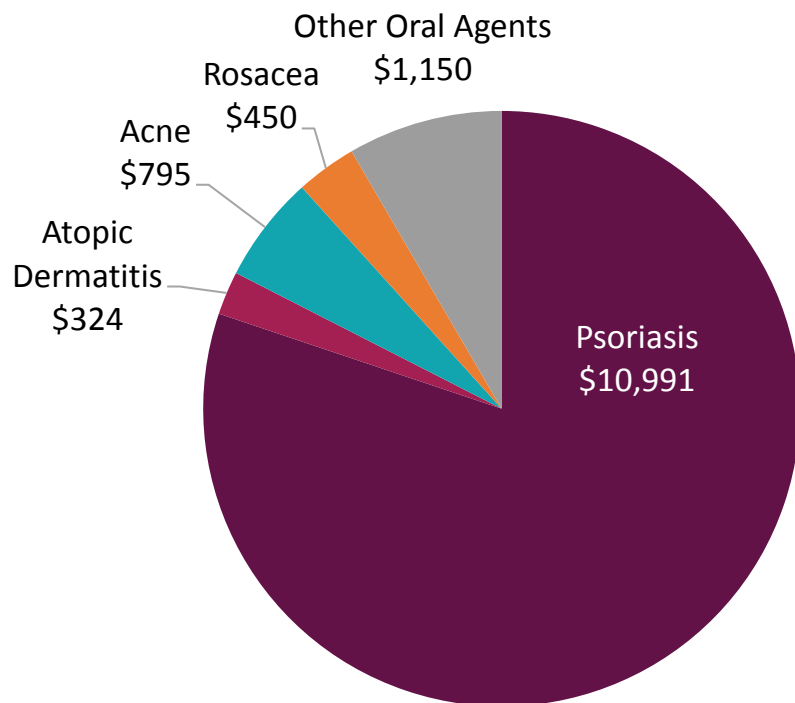
Source: Study prepared by NovaChem Laboratories, Inc.

# Initial Target Market: Dermatology

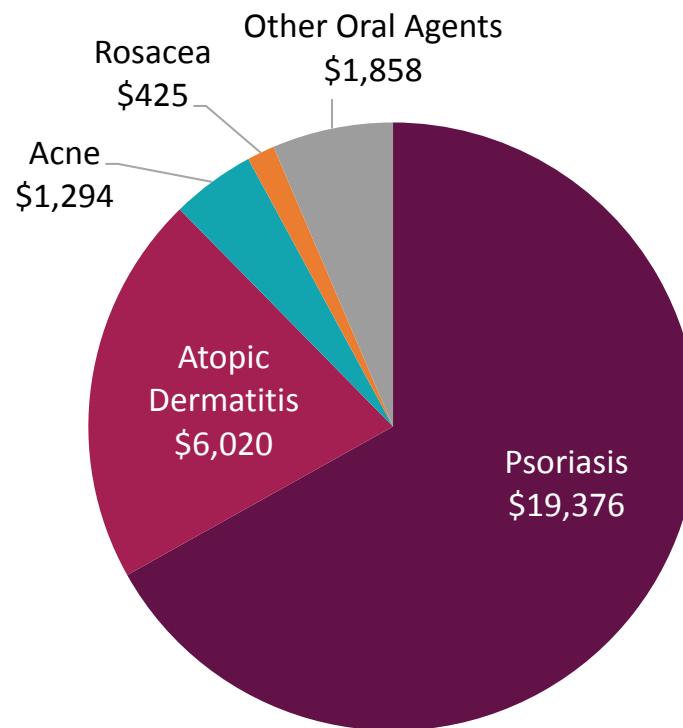
*Fast-Growing Market for Novel AD Drugs Expected to Exceed \$6 Billion in 2022*

## Worldwide Market for Select Branded Dermatology Therapeutics

2017 ~13.7B



2022 ~29.0B



Source: Cowen & Company estimates. Key products for Atopic Dermatitis include dupilumab and crisaborole; for Acne include Aczone, Solodyn, and Retin A; for Psoriasis include Otezla, Remicade, and Humira.



# PR022 for Atopic Dermatitis

# Atopic Dermatitis: Significant Unmet Medical Need

*Estimated \$5 billion in US sales by 2022*

## Disease Overview

- Chronic inflammatory skin disease arising from genetic and environmental factors
- Characterized by acute and chronic breakouts
- Scratching is a major factor of the acute and chronic skin lesions and can lead to secondary infection
- Can occur at any age, but most often begins in infancy or childhood
- ~60% of cases are diagnosed by age 1 and ~85% before age 5

Primarily treated by topical steroids and calcineurin inhibitors



# PR022 Targeted Topical for Mild to Moderate AD

## Novel Mechanism

- First-in-class topical IL-4 / IL-13 inhibitor

## Validating Data

- Pre-clinical anti-inflammatory and immunomodulatory results similar to steroids, reducing lesions and itch
- Delivers anti-microbial effects

## Safety Profile

- Potential improvement over standard of care and suitable for infants

## Favorable Administration

- Cosmetically elegant, easy to spread gel formulation
- Dries fast, no burning / stinging demonstrated to date

# Aurstat (0.045% HOCl) in Atopic Dermatitis Patients

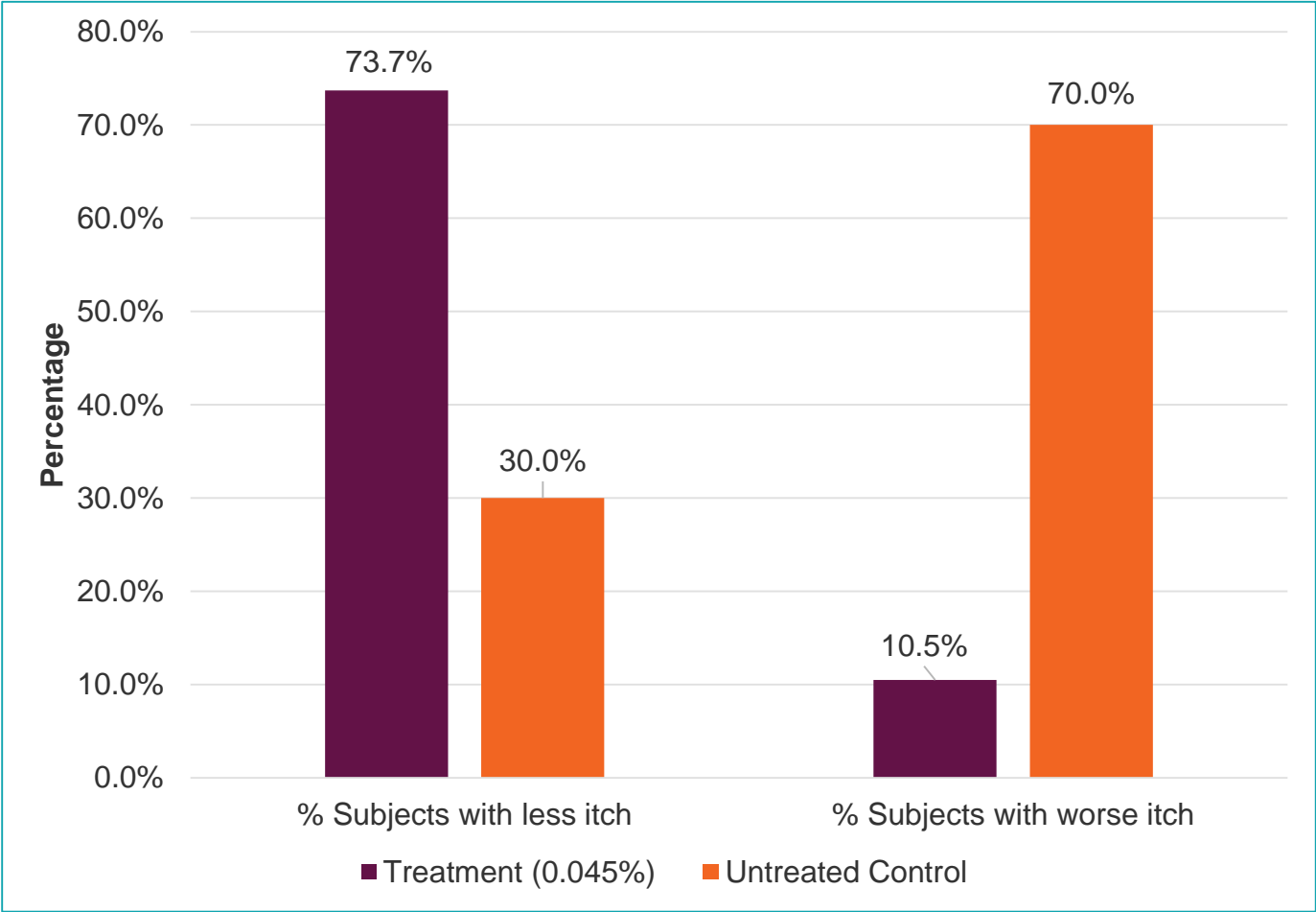


- Cleared by FDA as a medical device for management and relief of pain, burning, and itching associated with various dermatoses
- Out-licensed and launched in 2013; 20,000 Rx in first 18 months
- Terminated out-licensing agreement in 2014 in order to develop topical HOCl formulation into a drug

## Aurstat Investigator Study

- Dr. Brian Berman conducted a blinded, randomized trial using Aurstat in 30 subjects with mild to moderate AD
- Evaluated the effects of Aurstat on pruritis vs untreated control
- Assessed pruritis and tolerability at baseline through Day 3:
  - VAS Scale used to measure pruritis
  - Investigator and subject assessment of tolerability

# Itch Reduction in 74% of Subjects With 0.045% HOCl Hydrogel



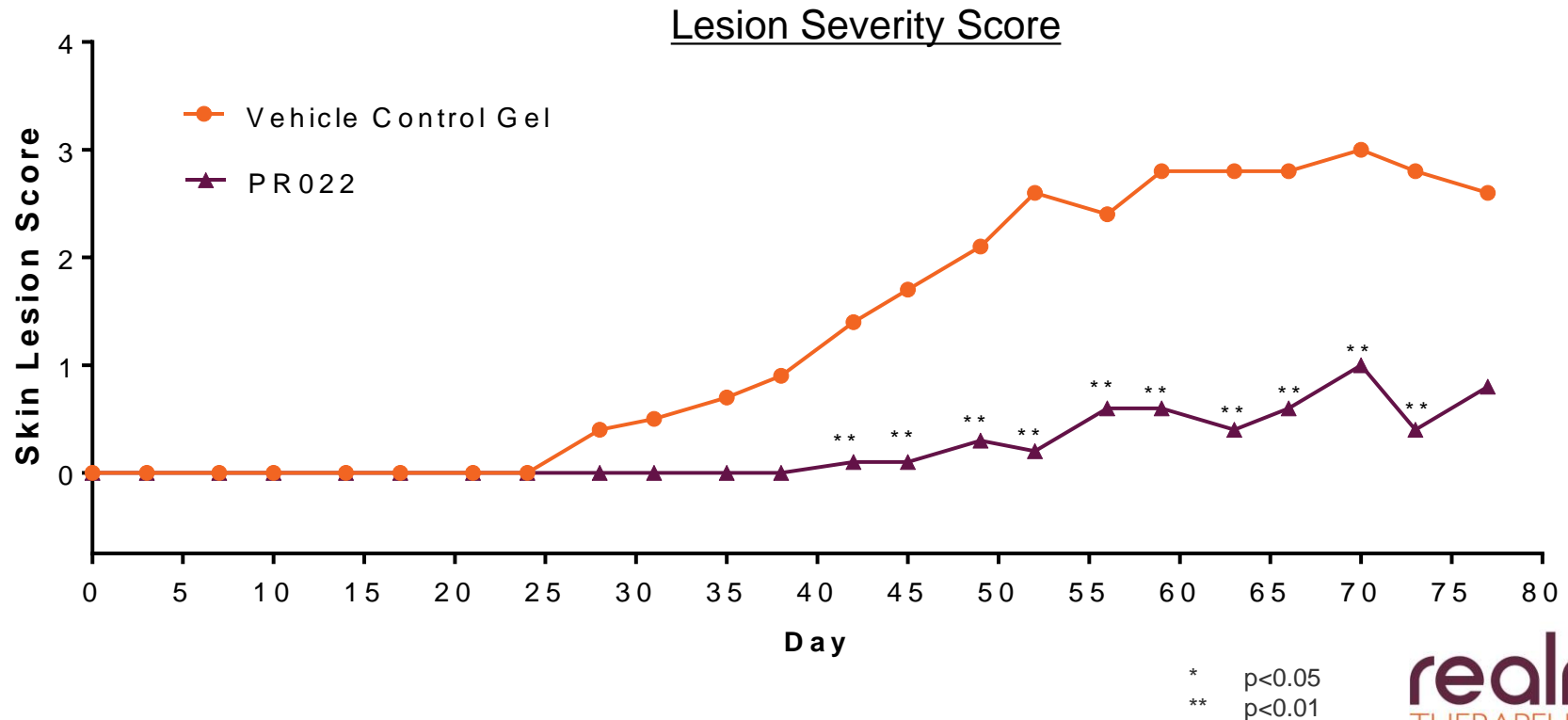
$p=0.007$

Berman, B., Cash, K., Frisina, A., Swenson, N., Kollman, E., Nestor, M. (2013). Evaluation of an Anti-Itch Hydrogel Containing 0.045% HOCl versus Untreated Control in the Treatment of Atopic Dermatitis Associated Pruritus. *Fall Clinical Dermatology Conference*, Las Vegas, NV.



# PR022 Delays Onset and Minimizes Lesions

Topical application of PR022 delayed the onset of lesions and reduced the severity of lesions compared to the vehicle group over 12-weeks

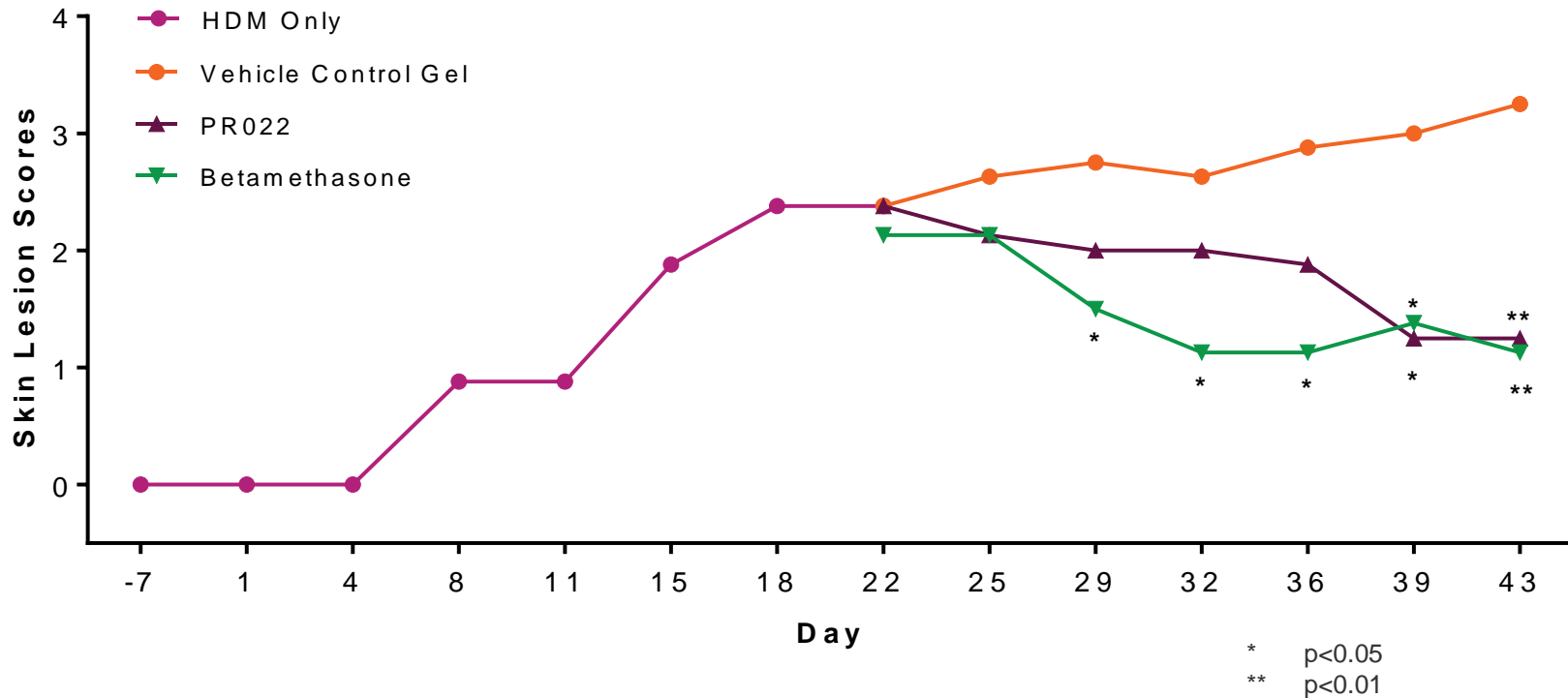


Studies completed by NC State University, College of Veterinary Medicine.

# PR022 Efficacy Comparable to Steroids

Steady decrease in lesion severity in the PR022 treatment group, comparable to immunosuppressive steroids

Lesion Severity Score



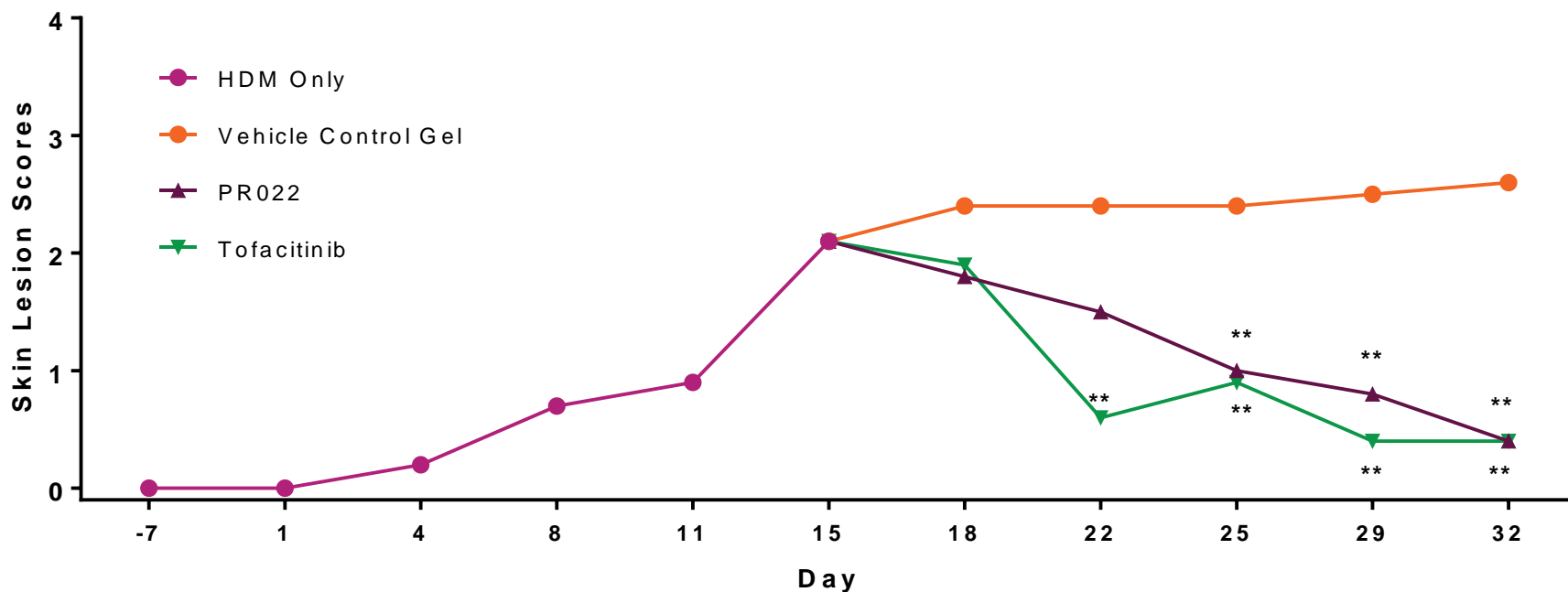
\* p<0.05  
\*\* p<0.01



# PR022 Efficacy Comparable to JAK inhibitors

PR022 decreased lesions and scratching comparable to tofacitinib

Lesion Severity Score



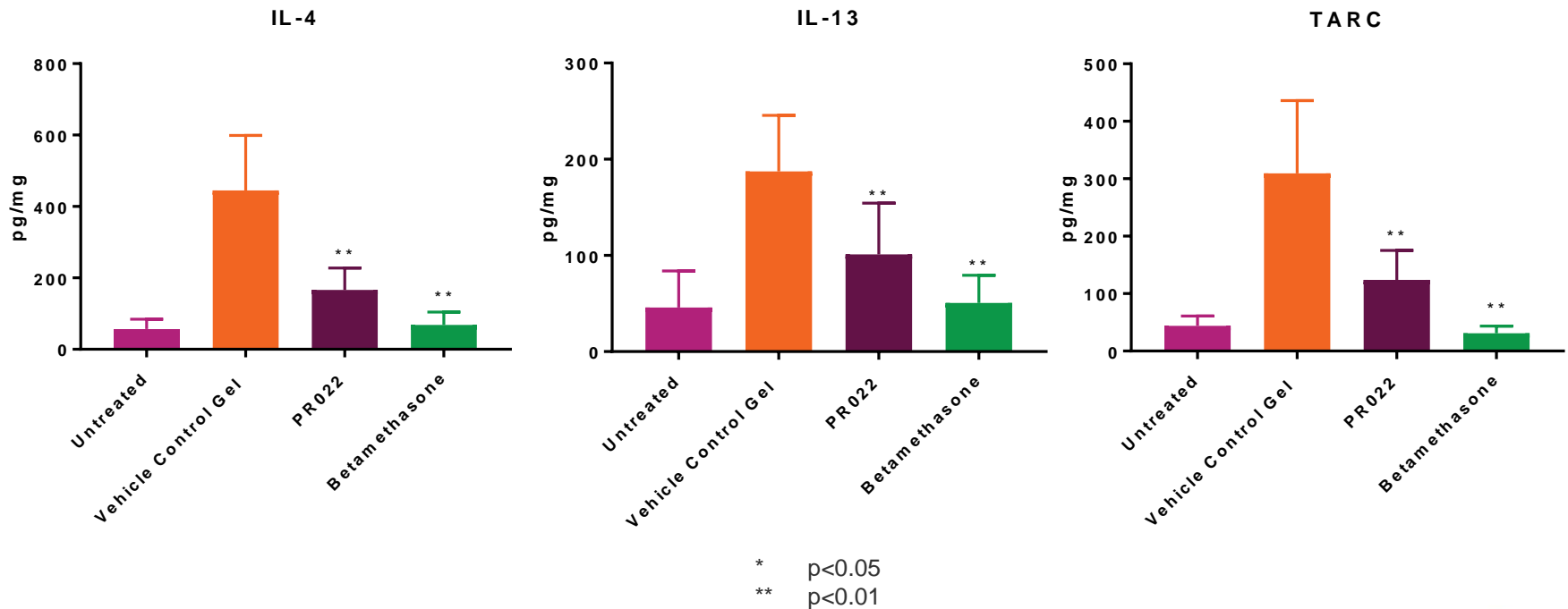
\*\* p<0.01



# PR022 Reduces IL-4, IL-13 and TARC

Levels of relevant pathogenic cytokines associated with atopic dermatitis significantly reduced by treatment with PR022

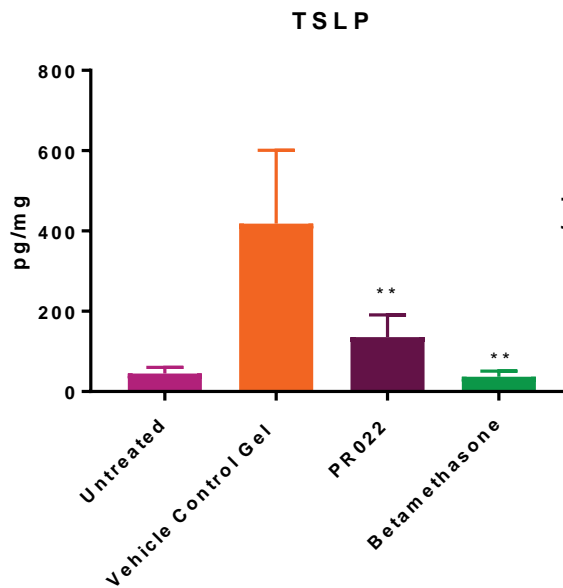
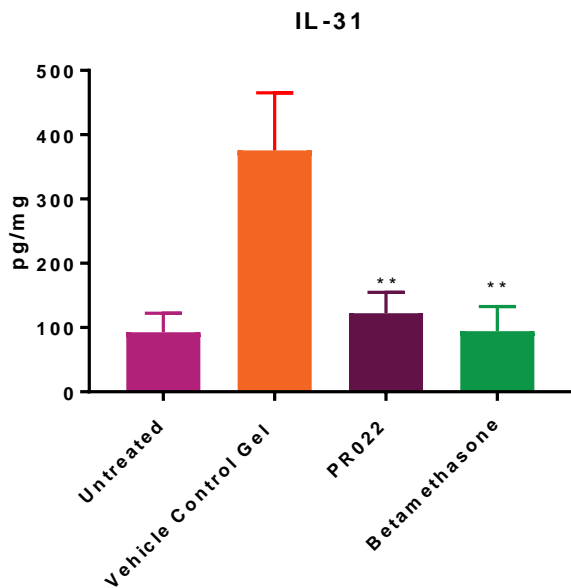
## Cytokine Concentration in Back Skin



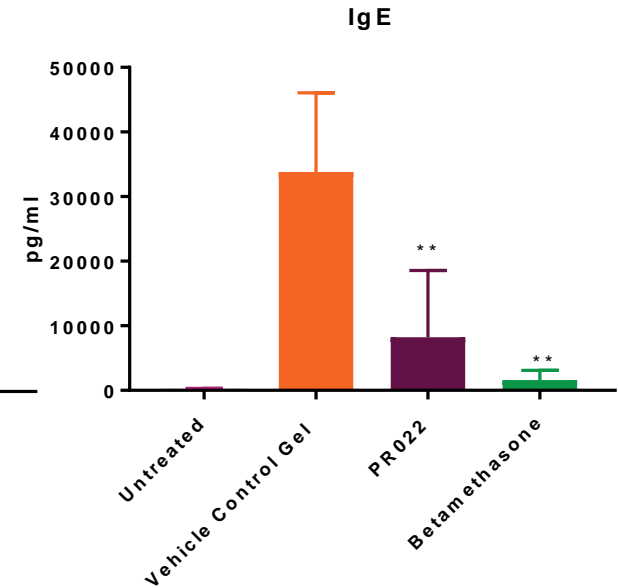
# PR022 Reduces IL-31, TSLP and Serum IgE

Levels of relevant cytokines associated with pruritus and IgE in serum significantly reduced by treatment with PR022

Cytokine Concentration in Back Skin



Serum IgE Levels



\* p<0.05  
\*\* p<0.01

# Phase 2a Clinical Study for Atopic Dermatitis

- **Study Design**

- 3 arm, randomized, double-blind, vehicle-controlled, parallel-group study

- **Dosage and Administration**

- PR022 topical gel 0.05% and 0.1%, 2x day, for 28 days

- **Patients**

- 122 patients with mild-to-moderate Atopic Dermatitis
- Total affected Body Surface Area (BSA) of 5% to 20%

- **Efficacy Endpoints**

- EASI (Eczema Area and Severity Index)
- IGA, SCORAD, NRS, DLQI, 5-D Itch Scale

- **Safety Endpoints**

- AE incidence and severity, local tolerability

**Enrollment complete; Expect topline data this quarter**

# RLM023 for Acne

# Acne: Significant Unmet Medical Need

Estimated ~\$5 billion in US sales in 2017

## Disease Overview

- Chronic inflammatory skin disease notable for comedones and inflammatory lesions
- Colonization of the follicles with *P. acnes* plays a critical role in the development of inflammatory acne
  - *P. acnes* stimulates the production of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$  and IL-12.
- Acne affects about 14% of the population
- **Ideal treatment is an agent with potent antimicrobial and anti-inflammatory properties**

## Types and Diagnosis

- Physicians recognize both non-inflammatory acne and inflammatory acne
- Diagnosis by history-taking and visual assessment



Source: Up to Date – Acne Beyond the Basics; Bhate K, Williams HC. Epidemiology of acne vulgaris. The British journal of dermatology 2013;168:474-85.; Guidelines of care for the management of acne vulgaris: February 2016; Global Acne Markets (www.asdreports.com)

# RLM023 Novel Topical Treatment for Acne Vulgaris

## Novel Mechanism

- Proprietary formulation with potent anti-inflammatory and immunomodulatory effects being developed
- Antimicrobial agent with no known resistance

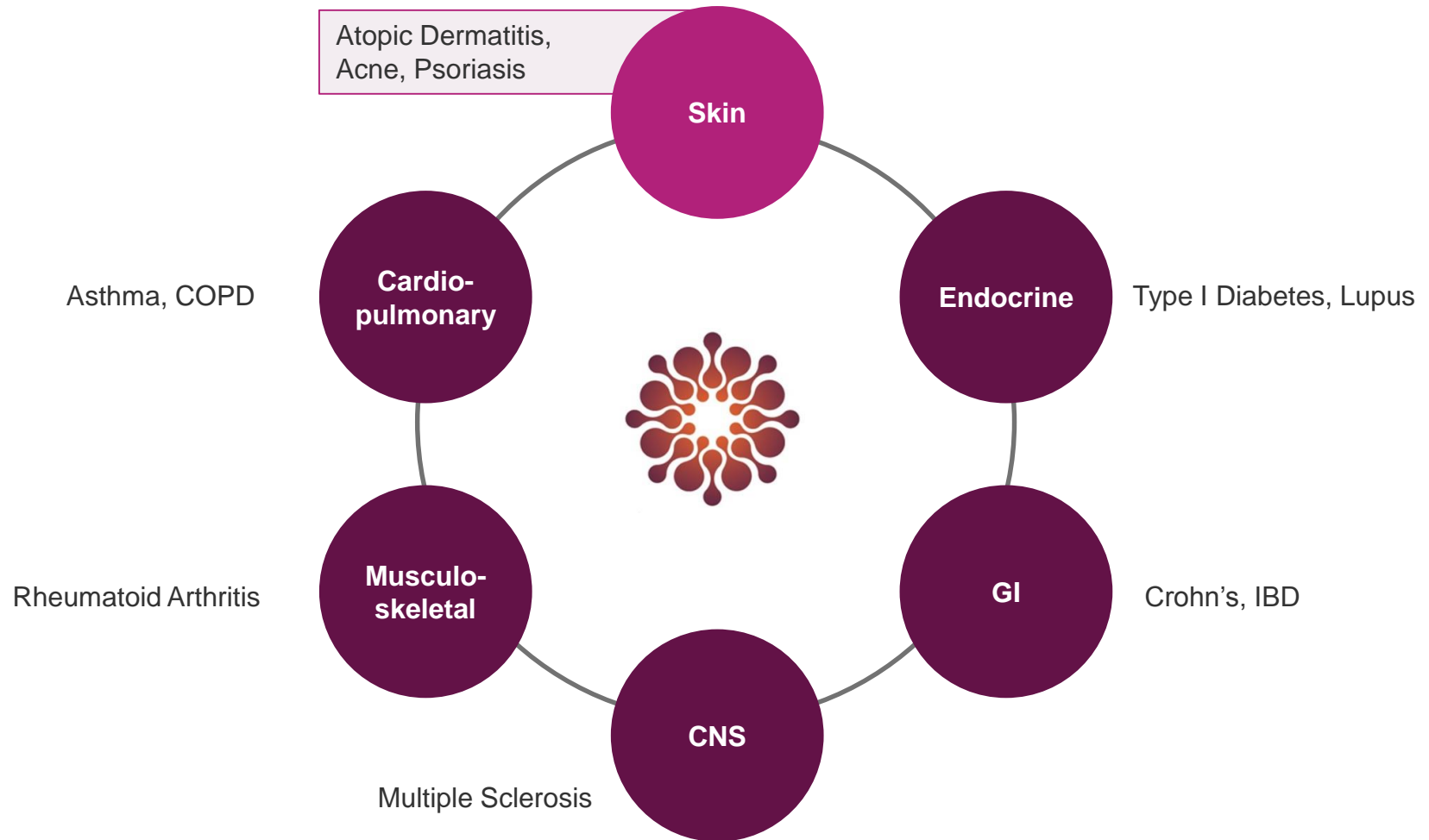
## Preclinical Proof-of-Mechanism

- Inhibition of IL-1 $\beta$ , TNF $\alpha$  and IL-12 *in vitro* and *in vivo* models

## Clinical Development

- Tox studies underway in support of IND
- IND filing planned for early Q4 2018
- Expect to initiate Phase 2 study in Q1 2019, may use different concentration of PR022 to expedite entry into clinic

# Building an Immune-Mediated Disease Company



**Platform with broad-spectrum immunomodulatory effects;  
seeking to acquire additional assets**

# Cash Position and Runway

- **\$29.0 M ~ Cash, Cash Equivalents and Short-term investments at March 31, 2018**
- **On current plans and timelines, cash expected to be sufficient to fund:**
  - Completion of Atopic Dermatitis Phase 2 study
  - Tox studies and other work necessary to support Acne IND
  - Acne Phase 2 (proof-of-concept) study (*assuming FDA clearance to directly enter Phase 2*)
  - General R&D efforts
- **Runway into H2 2019**







# Key Milestones



- Phase 2a Atopic Dermatitis data Q3 '18
- IND filing for Acne Vulgaris Q4 '18
- Phase 2a Acne Vulgaris initiation Q1 '19
- IND filing for Psoriasis Q1 '19

# Appendix

# Select KOLs for Atopic Dermatitis Clinical Trials

Name	University	Position
Jonathan Silverberg, MD, PhD, MPH *	 Northwestern University	Assistant Professor of Dermatology
Emma Guttman-Yassky, MD, PhD	 Icahn School of Medicine at Mount Sinai	Professor of Dermatology and Clinical Immunology
Lisa A. Beck, MD	 UNIVERSITY of ROCHESTER	Professor of Dermatology
Thomas Leung, MD, PhD	 Penn UNIVERSITY of PENNSYLVANIA	Assistant Professor of Dermatology, Cell and Molecular Biology Immunology

\* Primary investigator

# Current Dermatologic Treatment Landscape

Indication	Current Treatment Option	Current Treatment Option Limitation(s)
<b>Atopic Dermatitis</b>		
	Corticosteroids	Systemic side effects like adrenal suppression, weight gain, thinning of the skin
	Calcineurin inhibitors	Often carry a boxed warning for a possible link to cancer
	Antihistamines	Limited efficacy / typically only used as adjunct therapies
	Antibiotics	Concerns of resistance
	Injectables	Inconvenient and costly
<b>Acne</b>		
	Antibiotics and antibacterials	Concerns of resistance
	Retinoids	Dryness, erythema, irritation photosensitivity side effects in addition to a Category C pregnancy medication risk
	Oral contraceptives	Cardiovascular risk and contraindicated in pediatric and male patients
<b>Psoriasis</b>		
	Corticosteroids	Systemic side effects like adrenal suppression, weight gain, thinning of the skin
	Vitamin D analogs	Skin irritation and expensive
	Phototherapy	Increased risk of skin cancer with increased sensitivity to sunlight

# Issued Patents Offer Broad IP Coverage

*Combines with significant know-how given years of experience with the molecule*

- **Composition of Matter**

- 8,871,278: Stabilized hypohalous acid solutions – 2032
- 9,414,584: Stabilized hypohalous acid solutions – 2032

- **Method of Use**

- 9,381,214: Method of treating irritation of the skin – 2032
- 8,877,257: Method and compositions for treating conditions associated with infection and/or inflammation – 2031

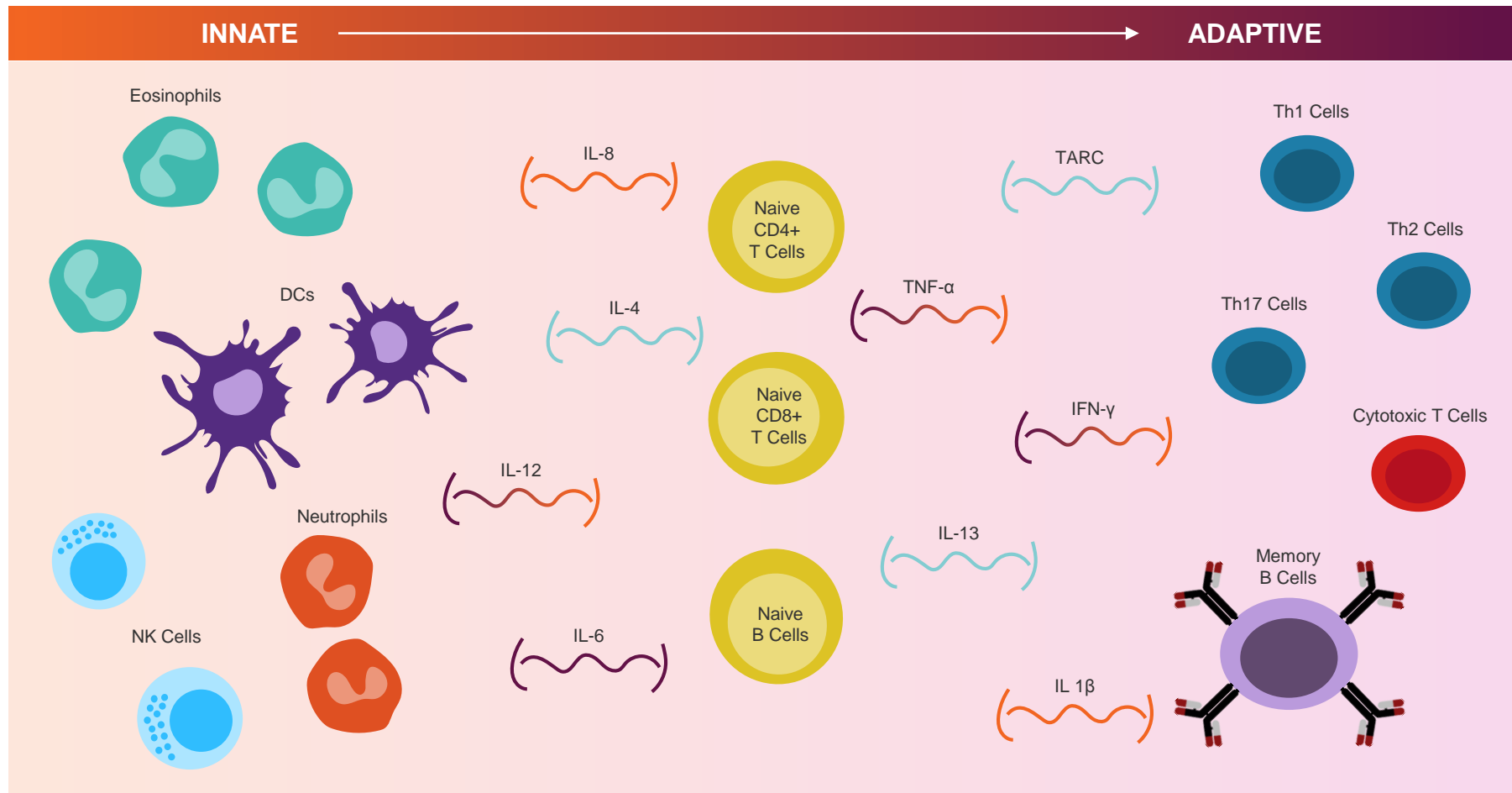
- **Method of Manufacture**

- 7,897,023: Device for producing anodic oxidation products of an alkali or alkali-earth metal chloride solution - 2028

# An Introduction to Immunity

- Immunity is the equilibrium between immune activation and immune suppression
- Cytokines are small cell signaling proteins that regulate immune and inflammatory responses
- Immunomodulatory therapeutics can ameliorate a dysregulated immune response by impacting cytokines
- Cytokines represent an important frontier in medicine specifically in the fields of inflammation and immunology
- We believe our platform technology's ability to modulate key cytokines will have broad-spectrum impact on both the innate and adaptive arms of the immune system

# Cytokines Orchestrate the Body's Immune Responses



KEY CYTOKINES		
	Atopic Derm.	
	Acne	
	Psoriasis	