ROIVANT SCIENCES

Roivant R&D Day

September 28, 2021

Statement of Limitations (1/2)

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This Presentation It is not intended to form the basis of any investment decision or any other decisions with respect of the proposed transactions (the "Business Combination") contemplated by the Business Combination Agreement, by and among Montes Archimedes Acquisition Corp. (the "SPAC"), and the Company and should not be relied upon in connection with any investment decision. The information contained herein does not purport to be all-inclusive and none of the SPAC, the Company or any of their respective affiliates, directors or officers makes any representation or warranty, express or implied, as to the accuracy, completeness or reliability of the information contained in this Presentation.

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This Presentation may contain forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. Forward-looking statements include, without limitation, statements regarding the estimated future financial performance, financial position and financial impacts of the Business Combination, the satisfaction of closing conditions to the Business Combination and any related financing, the level of redemption by the SPAC's public stockholders, the timing of the completion of the Business Combination, anticipated ownership percentages of the combined company's stockholders following the potential transaction, and the business strategy, plans and objectives of management for future operations, including as they relate to the potential Business Combination. Future results are not possible to predict. Opinions and estimates offered in this Presentation constitute the Company's judgment and are subject to change without notice, as are statements about market trends, which are based on current market conditions. This Presentation contains forward-looking statements, including without limitation, forward-looking statements that represent opinions, expectations, beliefs, intentions, estimates or strategies regarding the future of the SPAC and the Company and its affiliates, which may not be realized. Forward-looking statements can be identified by the words, including, without limitation, "believe," "anticipate," "continue," "estimate," "may," "project," "expect," "plan," "potential," "target," "intend," "seek," "will," "would," "could," "should," or the negative or plural of these words, or other similar expressions that are predictions or indicate future events, trends or prospects but the absence of these words does not necessarily mean that a statement is not forward-looking. Any statements that refer to expectations, projections or other characterizations of future events or circumstances, including strategies or plans as they relate to the Business Combination, are also forward-looking statements. In addition, promising interim results or other preliminary analyses do not in any way ensure that later or final results in a clinical trial or in related or similar clinical trials will replicate those interim results. The product candidates discussed herein are investigational and not approved and there is no assurance regarding any possible progress in the clinical trials, timing and results of the clinical trials, potential drug profile and points of differentiation for the potential drug candidates, the safety and efficacy of the potential drug candidates, the timing and commercial success of the product candidates, strategies for completion and likelihood of success for our business and activities, development plans, target product profiles, regulatory activities, competitive position, market opportunity, potential pricing and reimbursement claims, potential growth opportunities or that any product candidates will ever receive regulatory approval or be successfully commercialized.

All forward-looking statements are based on estimates and assumptions that are inherently uncertain and that could cause actual results to differ materially from expected results. Many of these factors are beyond the SPAC's and the Company's ability to control or predict. These risks include, but are not limited to: (1) the occurrence of any event, change or other circumstances that could result in the failure to consummate the Business Combination; (2) the outcome of any legal proceedings that may be instituted against the SPAC and the Company regarding the Business Combination; (3) the inability to complete the Business Combination due to the failure to obtain approval of the stockholders of the SPAC or to satisfy other conditions to closing in the definitive agreements with respect to the Business Combination; (4) changes to the proposed structure of the Business Combination that may be required or appropriate as a result of applicable laws or regulations or as a condition to obtaining regulatory approval of the Business Combination; (5) the ability to meet and maintain Nasdaq's listing standards following the consummation of the Business Combination; (6) the risk that the Business Combination disrupts current plans and operations of the Company as a result of the announcement and consummation of the Business Combination; (7) costs related to the Business Combination; (8) changes in applicable laws or regulations; (9) the possibility that the Company may be adversely affected by other economic, business, and/or competitive factors, including risks related to (i) the Company's limited operating history and the inherent uncertainties and risks involved in biopharmaceutical product development, (ii) the outbreak of the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19, and could adversely impact the Company's business, including its clinical trials and pre-clinical studies. (iii) the Company's ability to successfully identify new product candidates to develop, acquire or in-license and its drug discovery efforts, which may not be successful, (iv) the regulatory approval process for new drugs, and ongoing regulatory obligations for approved product candidates, (v) regulatory and legislative developments in the healthcare industry, (vi) the Company's ability to attract and retain key personnel, (vii) the Company's international operations and (viii) the Company's ability to obtain and maintain intellectual property protection for its technology and product candidates; (10) the risk that we may not be able to raise financing in the future; (11) the risk that we may not be able to retain or recruit necessary officers, key employees or directors following the Business Combination; (12) the risk that our public securities will be illiquid; (13) the effect of COVID-19 on the foregoing, including the SPAC's ability to consummate the Business Combination due to the uncertainty resulting from the COVID-19 pandemic; and (14) other risks and uncertainties indicated from time to time in filings made with the SEC, including those risk factors described under "Risk Factors" of the Form S-4/A filed with the SEC on August 9, 2021, under "Item 1A. – Risk Factors" of the Company's Quarterly Report on Form 10-Q filed with the SEC on September 21, 2021 and, where applicable, the most recent Annual or Quarterly Reports on Form 10-K or 10-Q, as applicable, filed with the SEC by our SEC registered affiliates, including Arbutus Biopharma Corp., Sio Gene Therapies Inc. and Immunovant, Inc. Should one or more of these risks or uncertainties materialize, they could cause our actual results to differ materially from the forward-looking statements. We are not undertaking any obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise. You should not take any statement regarding past trends or activities as a representation that the trends or activities will continue in the future. Accordingly, you should not put undue reliance on these statements in deciding how to make any investment decisions.

You are cautioned not to place undue reliance upon any forward-looking statements. Any forward-looking statement speaks only as of the date on which it was made, based on information available as of the date of this Presentation, and such information may be inaccurate or incomplete. The Company undertakes no obligation to publicly update or revise any such statements, whether as a result of new information, future events or otherwise, except as required by law.

Statement of Limitations (2/2)

Key Performance Indicators
This Presentation may include certain key performance indicators ("KPIs"). Management regularly reviews these and other KPIs to assess the Company's operating results. Realized return on our investments in Vants and technology sold to Sumitomo Dainippon Pharma Co., Ltd. ("DSP") reflect the value realized directly from the DSP transaction. The Company measures its return on publicly traded Vants by comparing the value of its ownership stake in the public Vants against its aggregate investment in those entities. The Company believes these KPIs are useful to investors in assessing operating results and returns on historical investments. These KPIs should not be considered in isolation from, or as an alternative to, financial measures determined in accordance with GAAP. There is no assurance the future investments will achieve similar results

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Industry and Market Data
In this Presentation, the Company may rely on and refer to certain information and statistics obtained from third-party sources which they believe to be reliable. The Company has not independently verified the accuracy or completeness of any such third-party information. No representation is made as to the reasonableness of the assumptions made within or the accuracy or completeness of any such third-party information.

Additional Information
The Company has filed a proxy statement / prospectus on Form S-4/A with the SEC relating to the proposed Business Combination, which has been mailed to the SPAC's stockholders. This Presentation does not contain all the information that may be considered concerning the proposed Business Combination and is not intended to form the basis of any investment decision or any other decision in respect of the Business Combination. The SPAC's stockholders and other interested persons are advised to read the proxy statement / prospectus and the amendments thereto and other documents filed in connection with the proposed Business Combination, as these materials contain important information about the Company, the SPAC and the Business Combination. Stockholders are able to obtain copies of the definitive proxy statement / prospectus and other documents filed with the SEC, without charge at the SEC's website at www.sec.gov.

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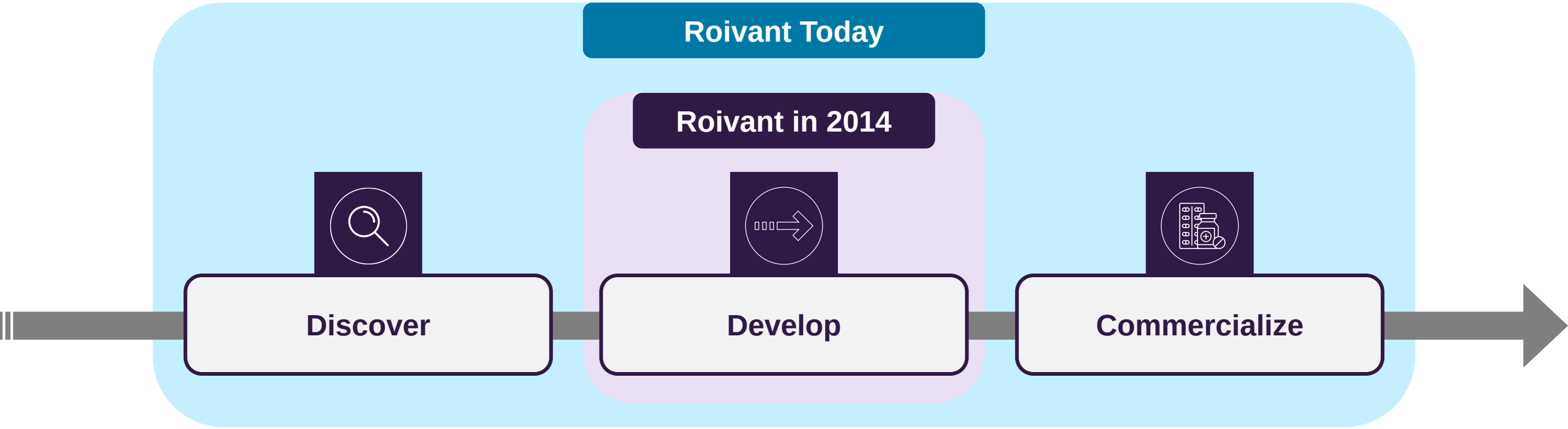
Roivant: Redefining “Big Pharma” from End to End



Our Principles

1. Create Value
2. Be Contrarian
3. Climb the Wall
4. Sweat the Details
5. Evolve or Die

How We've Executed on Our Vision

Clinical Achievements

- ✓ **8** positive Phase 3 trials of 9 total[1]
- ✓ **3 FDA approvals** from Vants launched by Roivant and owned by Sumitovant[1]
- ✓ **>40 medicines** brought into development[1]
- ✓ NDA for tapinarof accepted for filing; first expected Roivant product launch

Small Molecule Discovery Engine

- ✓ Leading computational drug discovery platform, with proprietary tools for **atom-by-atom simulations** and a team to continue to push the frontier
- ✓ Broad discovery pipeline of programs designed or optimized *in silico* to address challenging, high-value targets

Strong Financial Track Record

- ✓ **$3BN upfront** transaction with Sumitomo Dainippon Pharma (DSP), yielding **4.3x return** on Vants and technology sold[2]
- ✓ **$2BN** consolidated cash balance as of June 30
- ✓ **$320M** in cash and minority equity stake in Datavant, following merger with Ciox Health[3]

Cited figures and associated investment multiples are Key Performance Indicators. Please refer to the information included on Slide 3 with respect to our KPIs.

1. Medicine, Vant launch, and approval figures include Alliance Vants transferred to Sumitovant, a wholly-owned subsidiary of Sumitomo Dainippon Pharma ("Sumitomo"), in December 2019. SPIRIT 1 and SPIRIT 2 were completed subsequent to Myovant's transfer to Sumitovant. 2. Based on aggregate Roivant investments in tech assets and in the five transferred Vants from Vant inception to transaction close, and aggregate proceeds received at closing of the Sumitomo Transaction, excluding (i) a $1BN allocation to Sumitomo's purchase of Roivant equity and (ii) $99.1M initial liability related to Option Vants. Excludes investment in Sinovant and proceeds received from the termination of Sumitomo's options to purchase Roivant's ownership interests in the Option Vants. 3. The implied enterprise value of the combined company at the conversion price cap of the new preferred equity investment made concurrently with the merger was $7.0 billion. This enterprise value implies an equity value of $6.1 billion (after netting out approximately $900 million of debt and other adjustments). No assurance can be given that the implied enterprise or equity value is an accurate reflection of the value of the combined business at closing or in the future. At closing of the merger and assuming a $7.0 billion enterprise value, Roivant's ongoing, fully diluted equity ownership in the combined entity was approximately 12% (without giving effect to certain liquidation preferences held by the preferred equity shareholders).

8 Consecutive Positive Phase 3 Studies

Study	Drug	Indication	Patients Enrolled	Geography	Topline Results		Primary p-value
PSOARING 1	Tapinarof	Psoriasis	510		August 2020	✓	P < 0.0001
PSOARING 2	Tapinarof	Psoriasis	515		August 2020	✓	P < 0.0001
SPIRIT 1*	Relugolix	Endometriosis	638		June 2020	✓	P < 0.0001
SPIRIT 2*	Relugolix	Endometriosis	623		April 2020	✓	P < 0.0001
HERO	Relugolix	Prostate Cancer	934		November 2019	✓	P < 0.0001
LIBERTY 2	Relugolix	Uterine Fibroids	382		July 2019	✓	P < 0.0001
LIBERTY 1	Relugolix	Uterine Fibroids	388		May 2019	✓	P < 0.0001
EMPOWUR	Vibegron	Overactive Bladder	1,530		March 2019	✓	P < 0.001
MINDSET	Intepirdine	Alzheimer's Disease	1,315		September 2017	✗	P > 0.05

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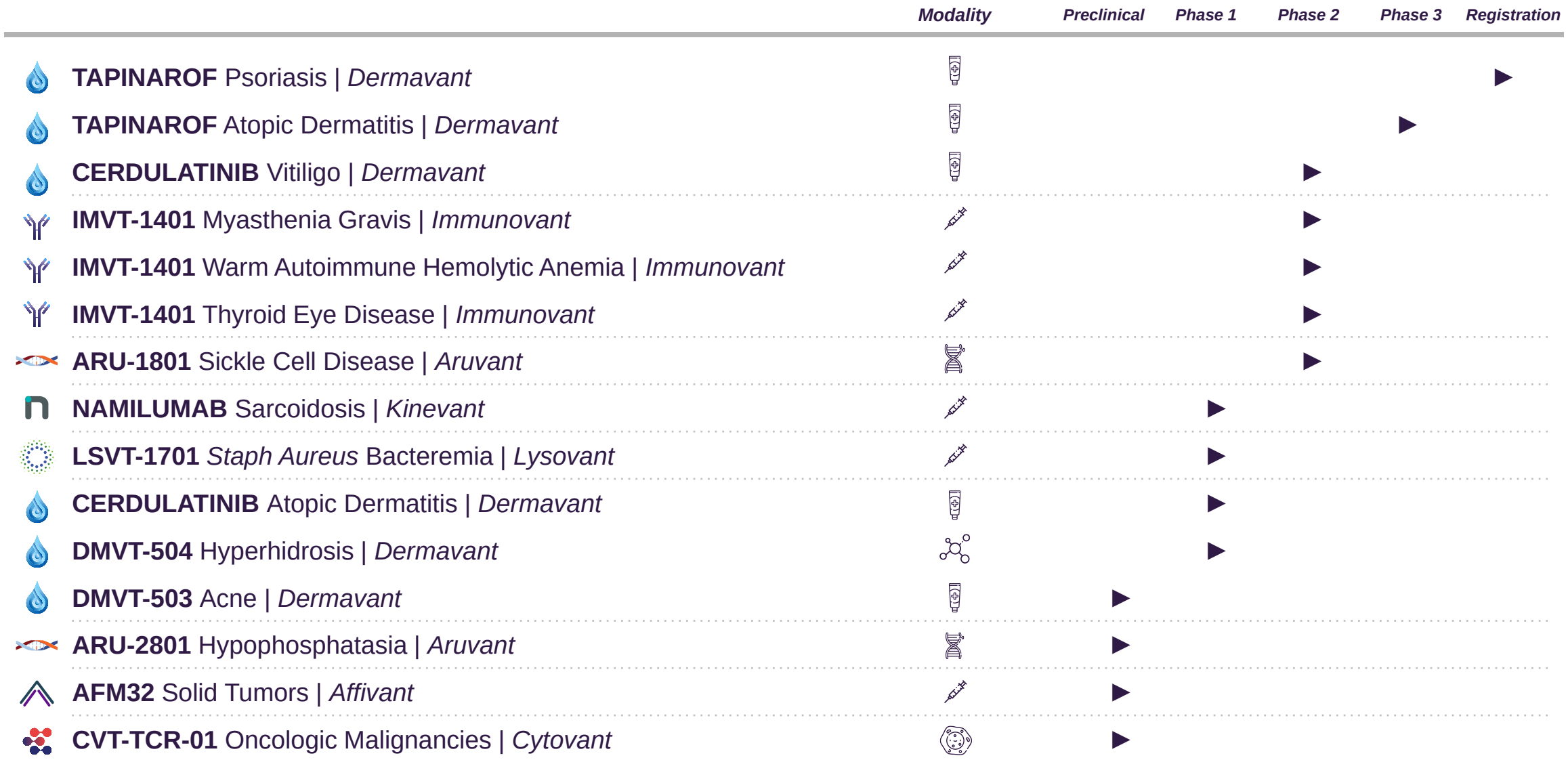
Note: The FDA has approved relugolix for the treatment of adult patients with advanced prostate cancer and for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. The FDA has approved vibegron for the treatment of adult patients with overactive bladder. Otherwise, the drugs noted above in current pipeline are investigational and subject to health authority approval. Topline results dates are based on corresponding Vant press releases. Relugolix and vibegron are being developed by Myovant and Urovant, two Vants that were transferred to Sumitovant, a wholly-owned subsidiary of Sumitomo Dainippon Pharma, in December 2019.
*SPIRIT 1 and SPIRIT 2 were completed subsequent to Myovant's transfer to Sumitovant. Trial geography maps indicate continents with trial sites and do not represent all countries within a given continent.

Development Pipeline



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Note: All drugs in current pipeline are investigational and subject to health authority approval.

Gene Therapy | Cell Therapy | Topical | Biologic | Small Molecule

dermavant™

Novel steroid-free topical tapinarof, if approved, could be uniquely positioned to transform two of the largest global immuno-dermatology markets

Value Added by Roivant Platform

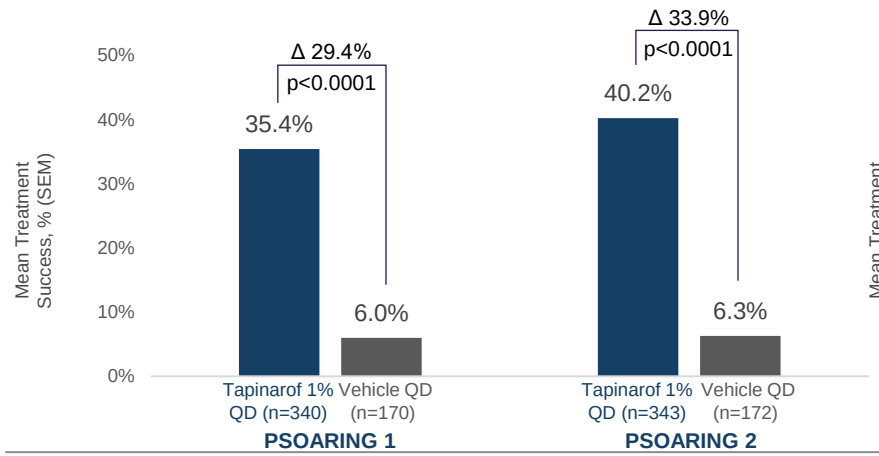
- Leveraged platform expertise to expand IP with multiple patents expected to provide protection until at least 2036
- Hired leadership and provided investment that together delivered Phase 3 success

Potential To Transform the Treatment of Psoriasis and Atopic Dermatitis

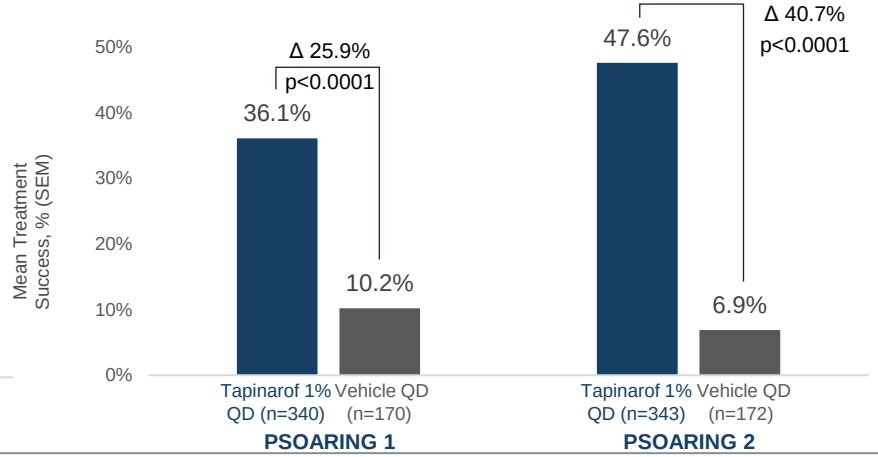
- Once-daily, cosmetically elegant, non-steroidal cream that, if approved, could offer a favorable combination of treatment effect, safety, durability on therapy, and remittive effect
- Psoriasis and atopic dermatitis affect an estimated 8M and 26M patients in the US, respectively
- Potential to be used across mild, moderate & severe plaque psoriasis, including sensitive areas

Psoriasis Phase 3: Statistically significant improvement in PGA score of clear or almost clear with a minimum 2-grade improvement compared to vehicle from baseline (p<0.0001)[1]

Primary Endpoint: PGA Response[2]



Key Secondary Endpoint: PASI75[3]



Positive Data from Long-Term Extension Study:

- *39.2% (299/763) of subjects included in interim analysis achieved complete disease clearance (PGA=0)*
- *In an integrated analysis including the pivotal trials and extension, 63.5% of subjects achieved PASI75 and 44.2% achieved PASI90[4]*
- *Remittive benefit of approximately four months observed following treatment discontinuation[5]*

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Note: All drugs in current pipeline are investigational and subject to health authority approval.
1. In both PSOARING 1 and PSOARING 2, adult patients with plaque psoriasis were randomized in a 2:1 ratio to receive once daily (QD) treatment with tapinarof cream, 1% or vehicle cream. 2. Proportion of subjects who achieved a Physician Global Assessment (PGA) score of clear (0) or almost clear (1) with a minimum 2-grade improvement from Baseline at Week 12. 3. Proportion of subjects with ≥75% improvement in Psoriasis Area and Severity Index (PASI) from Baseline at Week 12. 4. Proportion of subjects with ≥90% improvement in Psoriasis Area and Severity Index (PASI) from Baseline at any time point. 5. For subjects entering the extension study with a PGA score of 0, median time to disease worsening (PGA score ≥2).

ARUVANT

Only one-time potentially curative gene therapy for sickle cell disease with demonstrated ability to engraft with reduced intensity conditioning (RIC)

Value Added by Roivant Platform

- Longstanding Roivant relationship with CCHMC enabled initial asset license and strong academic-industry partnership
- Manufacturing process improvements have enabled increased hemoglobin F expression and vaso-occlusive event (VOE) reduction

Well-Positioned Against Competitors[1]

GBT	CRISPR THERAPEUTICS	bluebirdbio
~$2BN market cap	~$10BN market cap	~$1BN market cap
Oxbryta approved Chronic therapy	*Developing CTX001 Requires myeloablation*	*Developing LentiGlobin Requires myeloablation*

ARU-1801 is <u>only</u> product candidate clinically shown to engraft with only an RIC regimen

Preliminary clinical data from ongoing Phase 1/2 trial of ARU-1801 demonstrate potential to deliver durable, meaningful VOE reductions to patients with sickle cell disease[2]

Updated manufacturing →

	Hospitalized VOEs			Total VOEs		
	Pre-treatment (24 mo)	Post-treatment (24 mo)	***Reduction (%)***	Pre-treatment (24 mo)	Post-treatment (24 mo)	***Reduction (%)***
Patient 1	7	**1**	***86%***	41	**3**	***93%***
Patient 2	1	**0**	***100%***	20	**3**	***85%***
Patient 3	6	**0 at 18 mos**	***100%***	12	**0 at 18 mos**	***100%***
Patient 4	8	**0 at 12 mos**	***100%***	12	**0 at 12 mos**	***100%***

- **Durable engraftment to 36+ months in Patients 1 and 2**
- **No VOEs to date in most recent patients**

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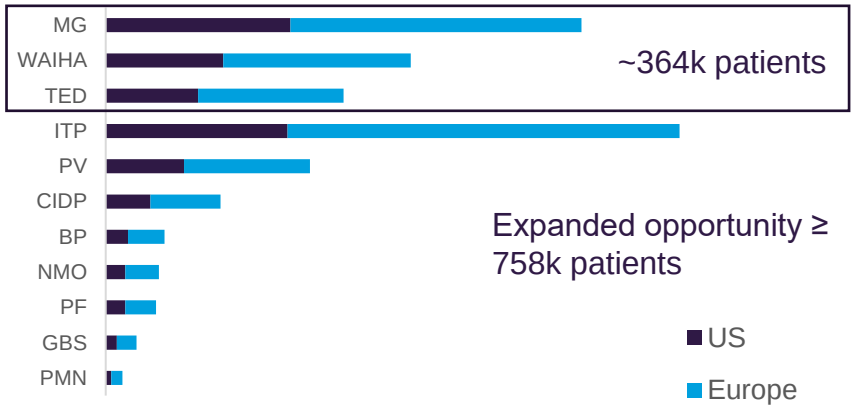
Note: All drugs in current pipeline are investigational and subject to health authority approval. All trademarks are property of their respective owners. VCN = vector copy number.
1. Approximate market capitalizations as of August 31, 2021. There is no guarantee that Aruvant will achieve a valuation in line with these companies.
2. ASH 2020.

IMMUNOVANT

Rapidly initiated multiple Phase 2 trials to develop anti-FcRn antibody IMVT-1401 as a best-in-class or first-in-class subcutaneous injection

Value Added by Roivant Platform

- Identified and licensed drug from HanAll Biopharma and expanded potential patient reach by selecting three initial indications with first- or best-in-class potential
- Funded and ran key Phase 1 pharmacodynamic trial, positioning for successful public listing via reverse merger
- Recruited key executive leadership, and board of directors led from inception by Roivant employee



Clinical Results to Date

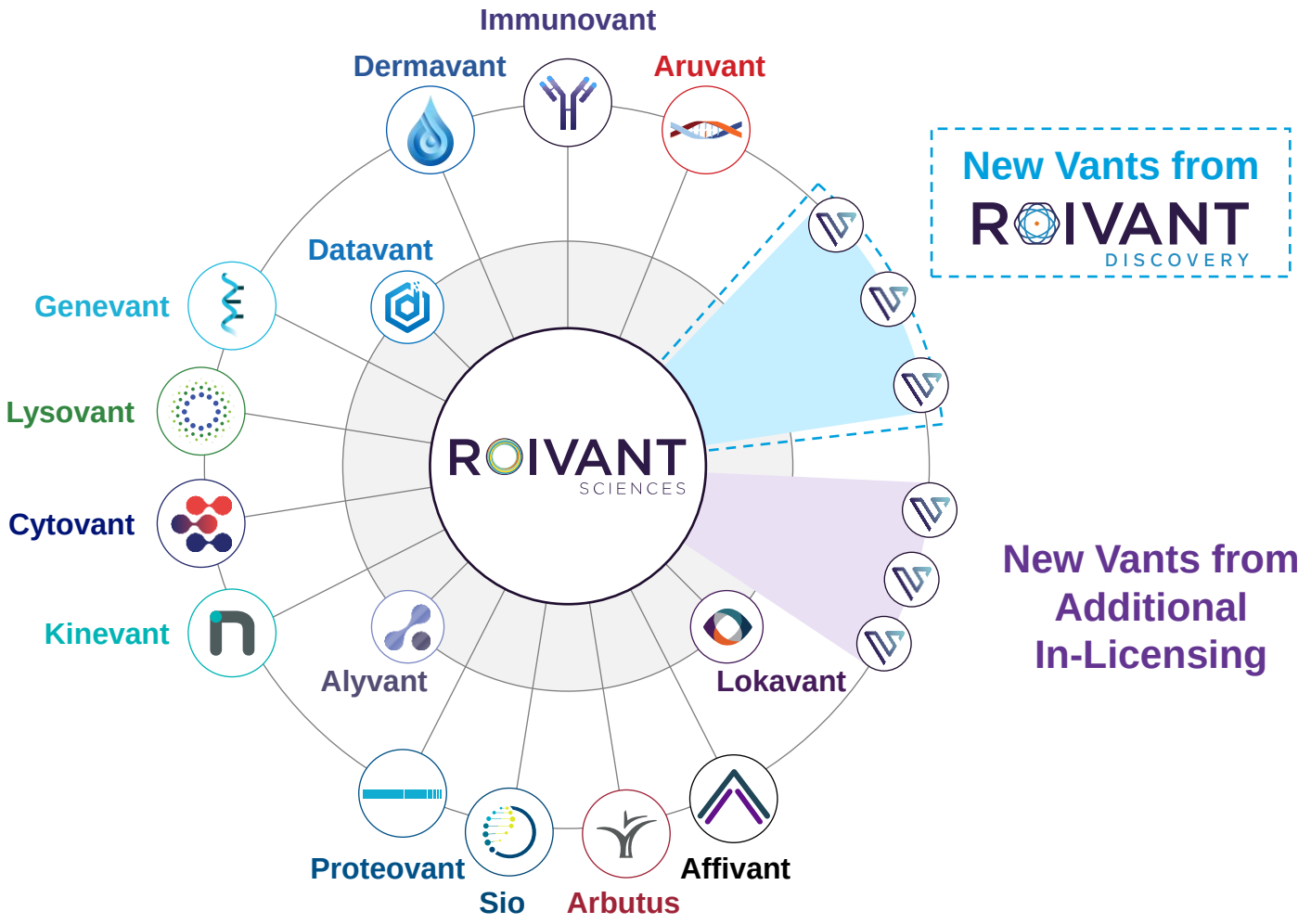
- Myasthenia Gravis[†]: 60% responder rate on the MG-ADL[‡‡] vs 20% for placebo, and 3.8-point mean improvement on myasthenia gravis activities of daily living (MG-ADL, p=0.039)
- Warm Autoimmune Hemolytic Anemia: 1 of 3 patients dosed ≥ 11 weeks achieved an increase in hemoglobin well over 2 g/dL from baseline, which was maintained during treatment
- Thyroid Eye Disease: In Phase 2a, 57% of patients improved by ≥ 2 points on clinical activity score (CAS), and 43% of patients were both proptosis responders* and CAS responders**; efficacy results in Phase 2b, which was terminated early, were inconclusive

Resuming Clinical Development Following Observed Increases in Cholesterol and LDL

- In February 2021, Immunovant voluntarily paused dosing in ongoing clinical studies to investigate observed elevated cholesterol levels
- Program-wide data review suggests that lipid elevations are predictable, manageable, and appear to be driven by reductions in albumin, with the 255 mg dose resulting in modest changes to LDL and albumin with potent knockdown in IgG
- The increases in LDL and reductions in albumin were reversible upon cessation of dosing, and no major adverse cardiovascular events have been reported to date

Note: All drugs in current pipeline are investigational and subject to health authority approval. All trademarks are property of their respective owners.
[†]Based on interim analysis of 15 trial participants. After the interim analysis, an additional two patients enrolled and were randomized. [‡‡]MG-ADL responders defined as patients showing ≥ 2-point improvement.
*Proptosis responders improved ≥ 2mm in study eye without significant deterioration in fellow eye. **CAS responders achieved a total CAS score of 0 or 1.
Source: Immunovant 10-K filed June 1, 2021. MG = Myasthenia Gravis. TED = Thyroid Eye Disease. WAIHA = Warm Autoimmune Hemolytic Anemia.

Vant Model Enables Rapid Scaling



The Roivant Model for Drug Discovery and Development

Identify drug targets and biological pathways

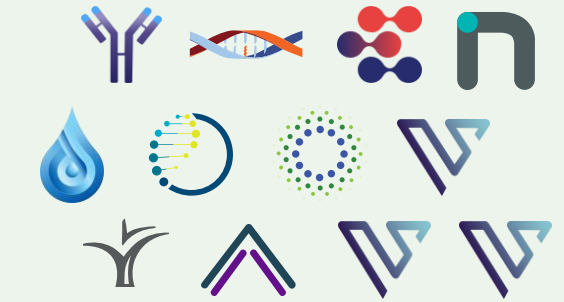
Find assets externally and in-license

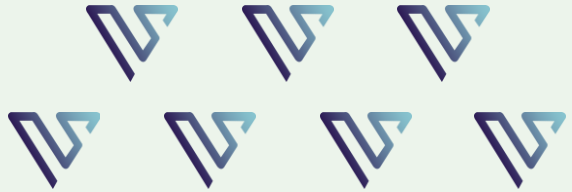
Plan to in-license multiple potentially category-leading drugs per year

Discover drugs internally and advance into the clinic

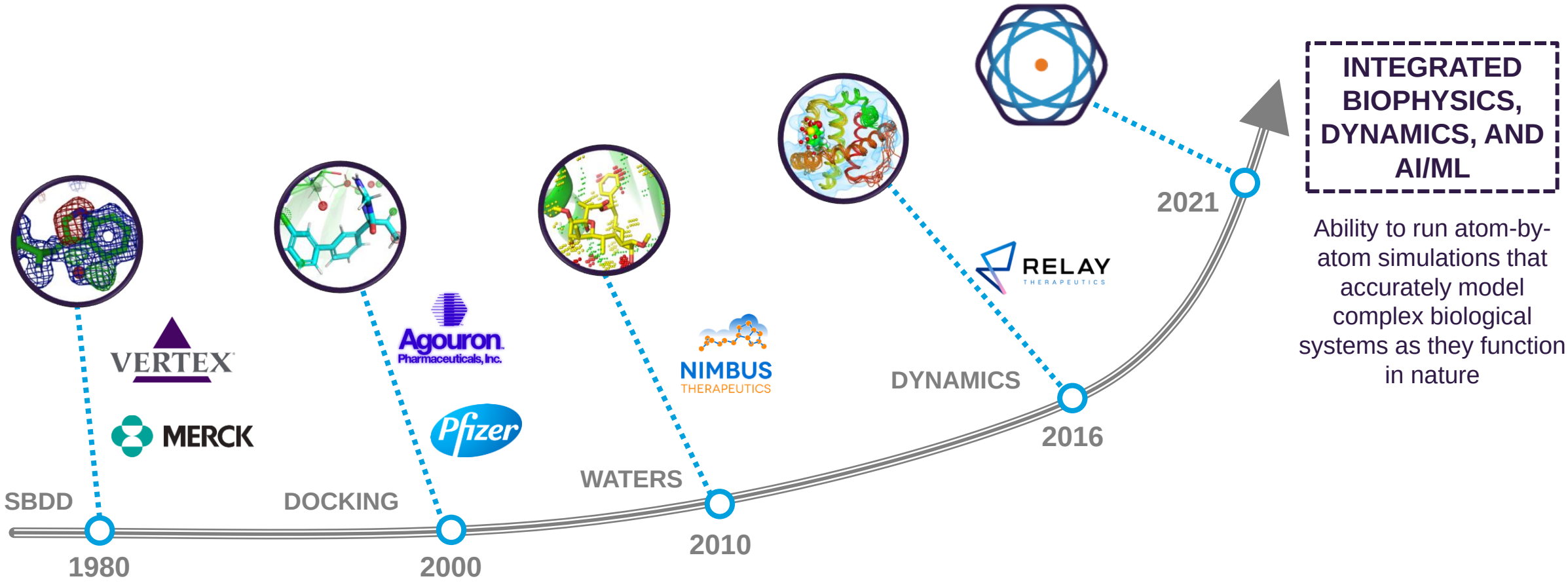
Plan to submit multiple INDs for novel drug candidates each year, starting with our first in 2022

Develop drugs at Vants





Entering the Era of Predictive, High-Precision Molecular Medicine

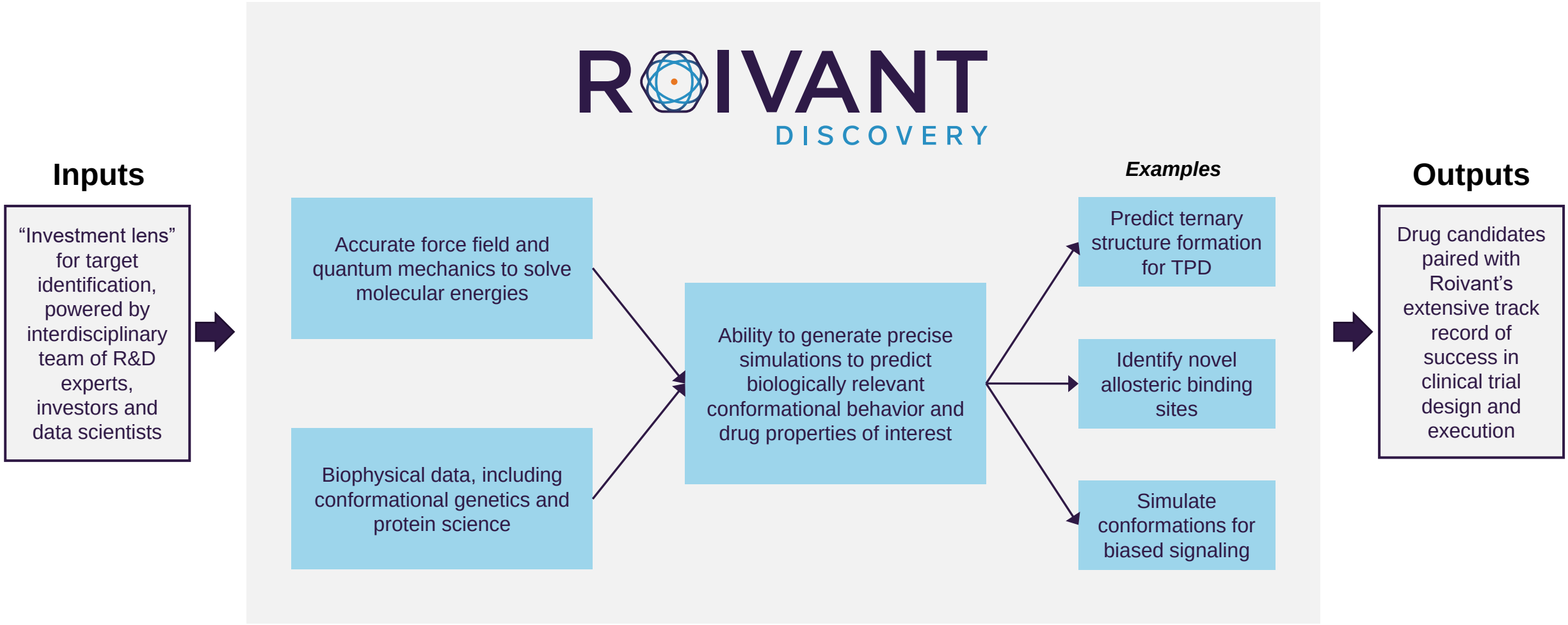


INTEGRATED BIOPHYSICS, DYNAMICS, AND AI/ML

Ability to run atom-by-atom simulations that accurately model complex biological systems as they function in nature

We are positioned to realize the promise of rational drug design by treating drug discovery as engineering

The Roivant Vision in Drug Discovery: Small Molecule Drug Design as *Engineering*



TPD: targeted protein degradation.

What's Really "Inside" Our Engine?

PROPRIETARY TOOLS

Conformational Genetics
Analyze genomic variants to define disease targets and map mutations to 3-D structures to predict novel MOA and conformational mechanism

Druggability Assessment
Predict high-energy water hotspots and druggable pockets using water thermodynamics and mixed-solvent molecular dynamics (MD)

Accurate Structures for Protein Complexes
Integrate molecular dynamics with biophysical data

Binding Energies
Ability to conduct >1,000 *in silico* binding affinity predictions/day

Beyond Binding (Dynamics and Kinetics)
Model complex biological motions, including agonism, allostery, biased signaling, and ternary structures

Atom-by-Atom Design
Visualize atom-by-atom free energy contributions of a ligand binding to a protein

Machine Learning and Generative Models
Predict ADMET properties, use of data-driven models to identify novel molecules

Our engine is powered by a supercomputing cluster with over 600 GPUs, allowing us to run thousands of molecular simulations in parallel

EXPERTISE

Expertise Across All Areas of Molecular Simulations
Software engineering, high-performance computing, methods development, applications, and experienced drug designers

Software Engineering and Methods Development
Own software stack, facilitating the most accurate, fast, and scalable target-specific simulations

Hardware Development
Maximize throughput, minimize bottlenecks, and tune hardware to optimize performance for bespoke predictive sciences methods

Experienced Drug Designers
Leverage medicinal chemistry, modeling, simulation, and biophysics to lead the new era of predictive, high-precision molecular medicines

Laboratory Facilities
Evaluate highest value candidates with in-house labs, enabling highest quality and rapid turnaround

Leaders in Computational Drug Discovery
Senior scientific leadership team with authorship of over 200 peer-reviewed articles and over 20,000 citations

In-house expertise across critical discovery capabilities can expand our engineering toolset as we pursue different types of hard biological problems

Roivant Builds Technologies to Transform Biopharma Development and Commercialization

DATAVANT

- Datavant seeks to power every exchange of health data, unlocking a massive ecosystem of companies using linked, longitudinal data to improve patient outcomes
- Continued growth across health data network, including >400 organizations and >100 subscription customers
- Powers the advanced use of real-world evidence, patient finding, outcomes research, and commercial analytics
- Customers and partners include Janssen/J&J and other top 20 pharmas, ZS, Medidata, Cigna, Parexel, Symphony Health, Komodo Health, and the NIH

Merged with Ciox Health, providing Roivant with $320MM in cash and minority equity stake in combined entity[1]

Lokavant

- Lokavant offers software that integrates real-time data from ongoing clinical trials and monitors risks related to time, cost, and quality
- Proprietary data model serves as a “common language” for trial operational data and enables real-time data integration
- AI trained on proprietary dataset of 1,300+ trials designed to identify the most important risks quickly, when there is still time to mitigate them
- Expanded international footprint through partnership with leading Japanese CRO CMIC

Deployed as Parexel’s next generation remote monitoring platform

1. The implied enterprise value of the combined company at the conversion price cap of the new preferred equity investment made concurrently with the merger was $7.0 billion. This enterprise value implies an equity value of $6.1 billion (after netting out approximately $900 million of debt and other adjustments). No assurance can be given that the implied enterprise or equity value is an accurate reflection of the value of the combined business at closing or in the future. At closing of the merger and assuming a $7.0 billion enterprise value, Roivant’s ongoing, fully diluted equity ownership in the combined entity was approximately 12% (without giving effect to certain liquidation preferences held by the preferred equity shareholders).

Key Near-Term Potential Catalysts

dermavant	Tapinarof NDA Filing in Psoriasis	Mid-2021 ✓
	Tapinarof Phase 3 Initiation in Atopic Dermatitis	2H 2021 ✓
	FDA Approval Decision on Tapinarof for Psoriasis	2Q 2022
	Topline Date from Tapinarof Phase 3 Trials in Atopic Dermatitis	1H 2023
IMMUNOVANT	IMVT-1401 Phase 3 Initiation in Myasthenia Gravis	Early 2022
	Two New Indications for IMVT-1401 to be Announced	By August 2022
	Initiate Pivotal Trial for IMVT-1401 in Second Indication	2022
ARUVANT	First Patient Dosed with Updated ARU-1801 Manufacturing Process	2H 2021 ✓
	Additional Clinical Data from ARU-1801 Phase 1/2	2H 2021 ✓
	ARU-1801 Phase 3 Initiation	1H 2023
kinevant	Namilumab Phase 2 Initiation in Sarcoidosis	1H 2022
lysovant	LSVT-1701 MAD Initiation	1H 2022
proteovant THERAPEUTICS	Phase 1 Initiation for First Degrader Candidate	2022
ROIVANT SCIENCES proteovant THERAPEUTICS	Multiple Additional Degrader Candidates Entering IND-Enabling Studies Each Year	Starting 2022

ROIVANT DISCOVERY

From Chip to Clinic

Integrating Advanced Simulation and AI Approaches to Design Novel Medicines for Challenging Disease Targets

Integrated Drug Discovery at Roivant – From Chip to Clinic

SUPERCOMPUTER

- >600 GPUs
- >6000 CPUs
- Cloud for bursts
- Custom FPGA research

SIMULATION PLATFORM

- Quantum mechanics for the most accuracy
- Molecular dynamics to simulate biological motions
- Advanced AI/ML capabilities

SCIENTIFIC EXPERTISE

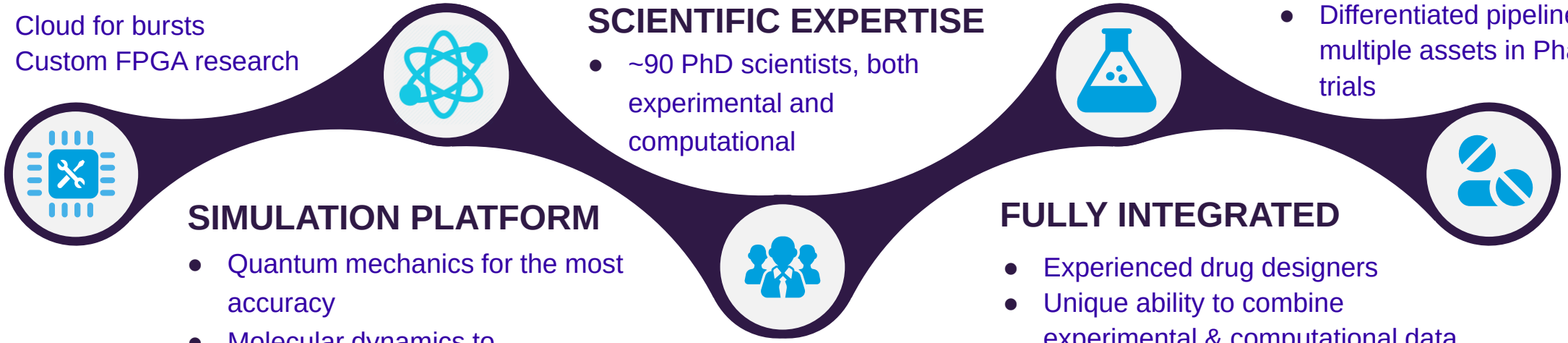
- ~90 PhD scientists, both experimental and computational

FULLY INTEGRATED

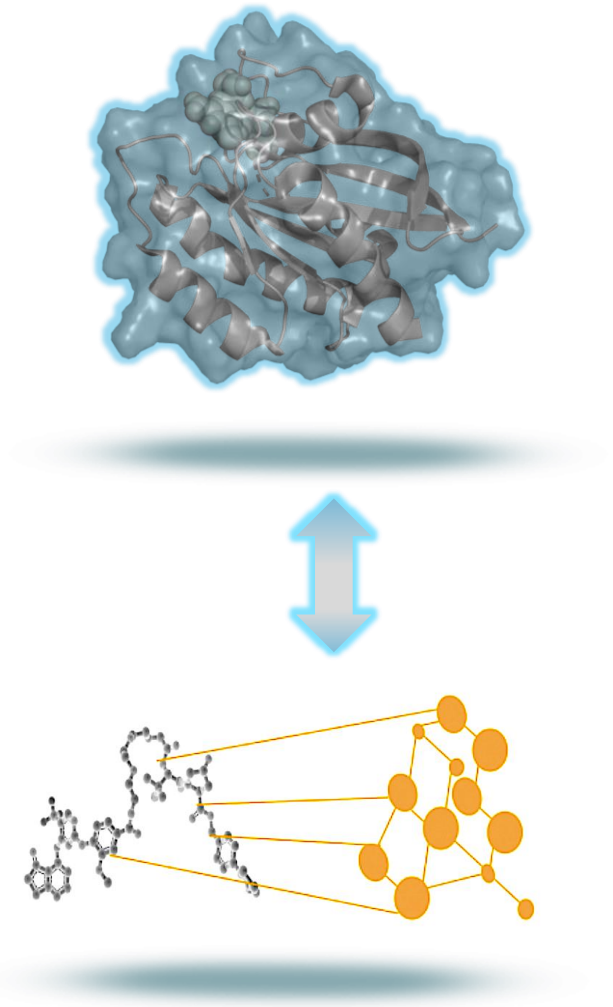
- Experienced drug designers
- Unique ability to combine experimental & computational data
- 10,000 sq. ft. in-house laboratory

PIPELINE INTEGRATION

- Roivant pipeline informs discovery process
- Differentiated pipeline with multiple assets in Phase I-III trials



Leading Computational Discovery Capabilities in Physics and AI/ML



Computational Physics

Sample *in silico* Assays

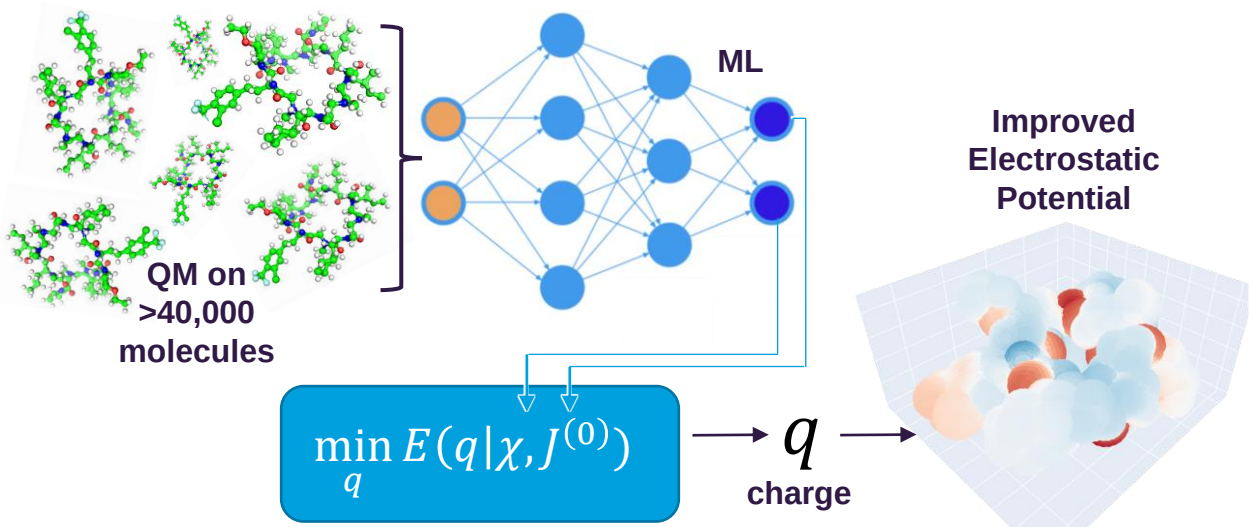
- Identify novel binding sites on a protein and assess druggability
- Predict binding affinity and selectivity of a ligand to a protein, including ternary complexes
- Simulate conformational dynamics of a protein as it shifts between active and inactive states

Machine Learning

- Machine learning using known protein-protein interactions to design new degraders that can effectively stabilize target-E3 interfaces
- Hit finding for induced proximity modulators (molecular glues and heterobifunctional molecules)
- Ubiquitin proteasome system map to identify degron motifs

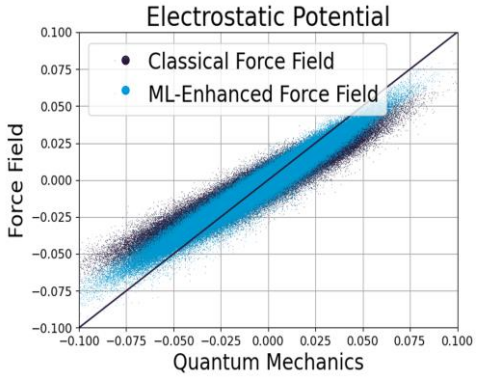
Improvements from Combining AI and Physics Approaches

ML-Enhanced Force Field

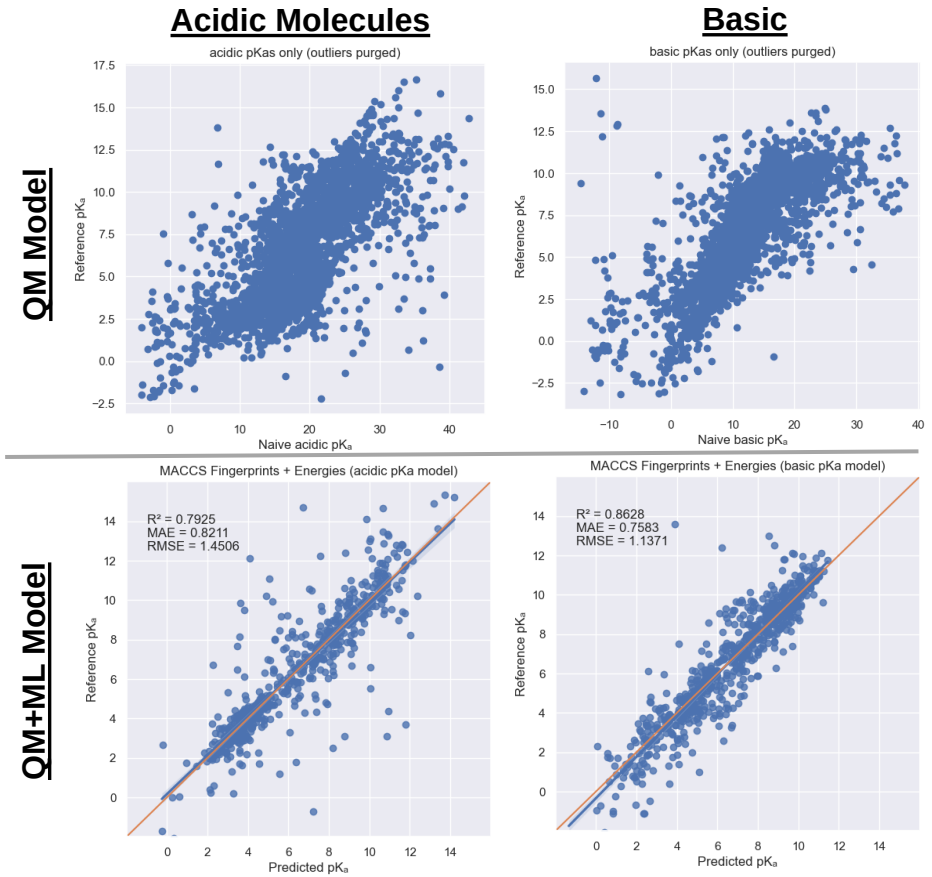


Physics – Captures the distribution of charge within the molecule and interactions with the environment

Machine Learning – Assigns atomic parameters so that electrostatic potential matches quantum mechanical calculations



Improved pK_a Predictions



χ: atomic electronegativity that characterizes how strongly an electron is associated with an atom
$J^{(0)}$: atomic hardness that characterizes how much the atomic charge varies under a external field
E: electrostatic potential energy
q: atomic charges

Roivant Biophysics and Structural Biology Advantage

Biophysics ⟷ **Structural Biology**

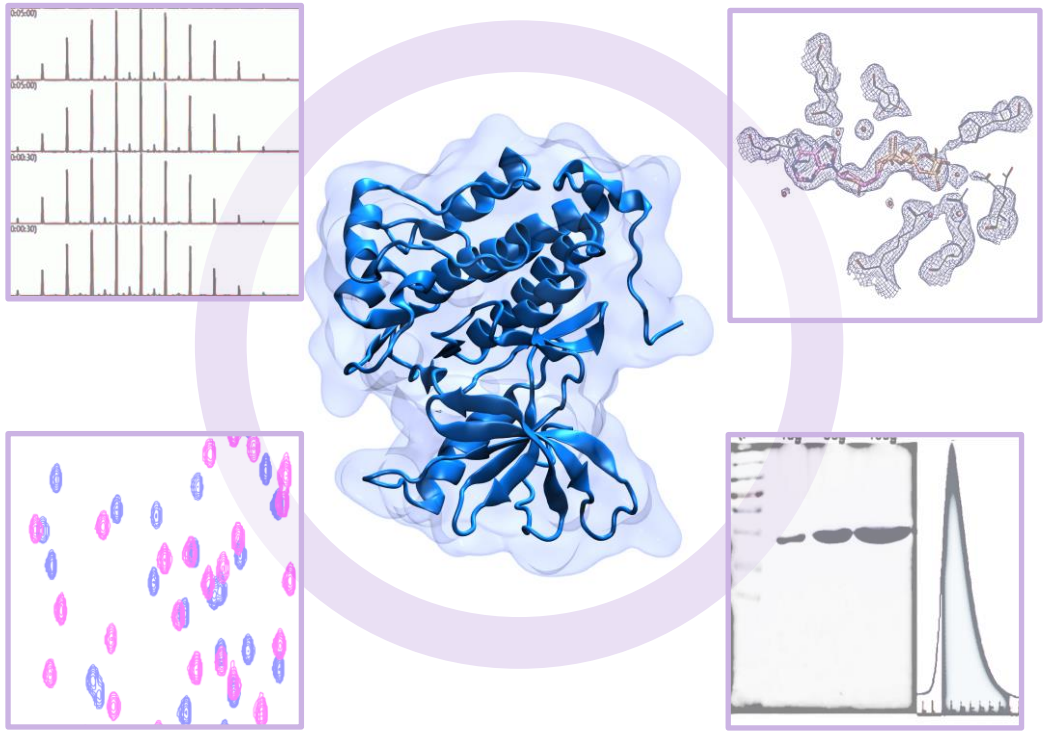
Enhance Simulations with Biologically Relevant Data

Hydrogen-Deuterium Exchange (HDX)

- Detect buried protein regions in binary and ternary complexes
- Augment simulations to generate atomic-resolution models in days (X-ray or CryoEM take months or longer)

Nuclear Magnetic Resonance (NMR)

- Fragment screening
- Binding affinity in solution without protein labels, tags, or attachments
- Ligand-observed techniques
- Protein-observed NMR to characterize interactions with specific pockets



X-ray Crystallography

- Solved high-resolution crystal structures for challenging targets
  - KRAS G12D
  - HIF-2a
  - SMARCA2/VHL
- Complementary to simulations
- Electron density can be used as a collective variable in MD simulations

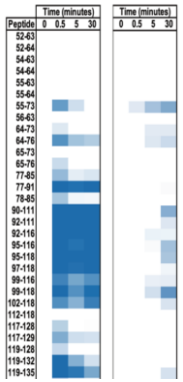
Protein Science

- Generated hundreds of protein samples using 3 expression systems (mammalian, insect, and bacterial)
- Protein labeling for NMR

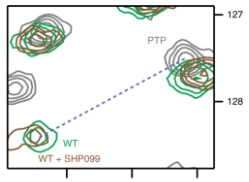
Conformational Modulation Assays with Integrated MD + Biophysics

Experimental Biophysical Data

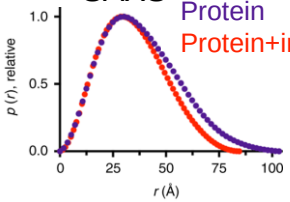
HDX-MS



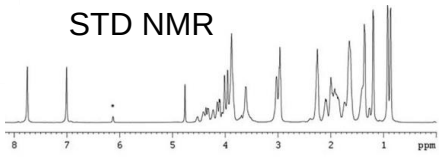
TROSY-HSQC NMR



SAXS



STD NMR

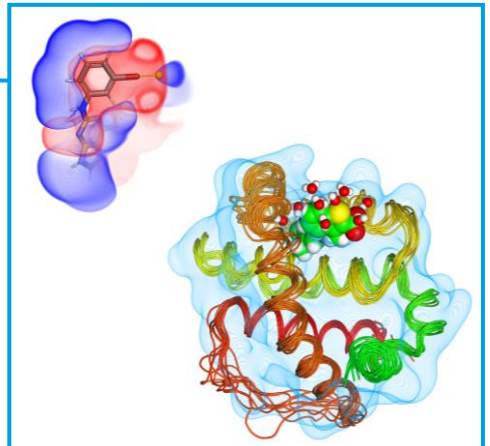


experimental data **simulation data**

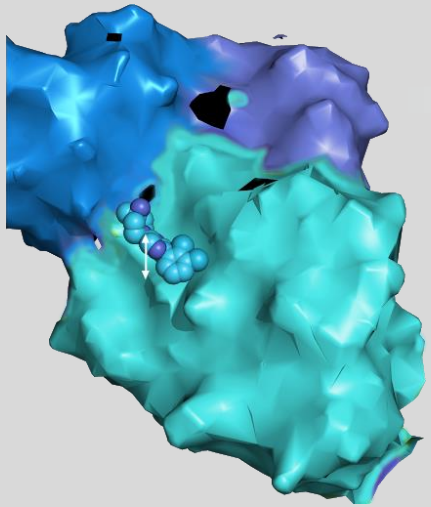
$$E_r(\boldsymbol{x}) = E_0(\boldsymbol{x}) + R(\boldsymbol{x}, D_e)$$

conformation **expt. bias**

Accurate Force Field



Coarse grained information from experimental measurements



The Journal of Chemical Physics

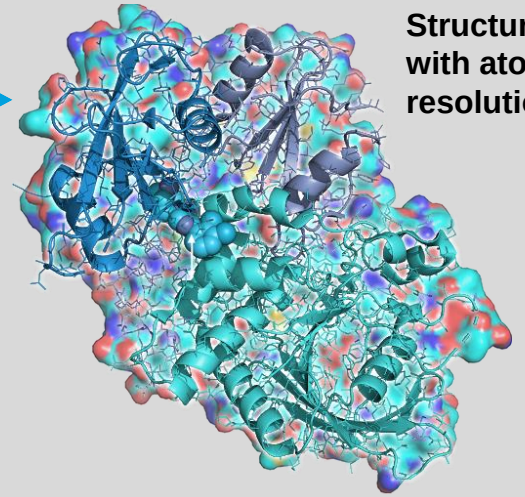
Molecular simulations minimally restrained by experimental data

Huafeng Xu

AFFILIATIONS

Silicon Therapeutics LLC, Boston, Massachusetts 02210, USA

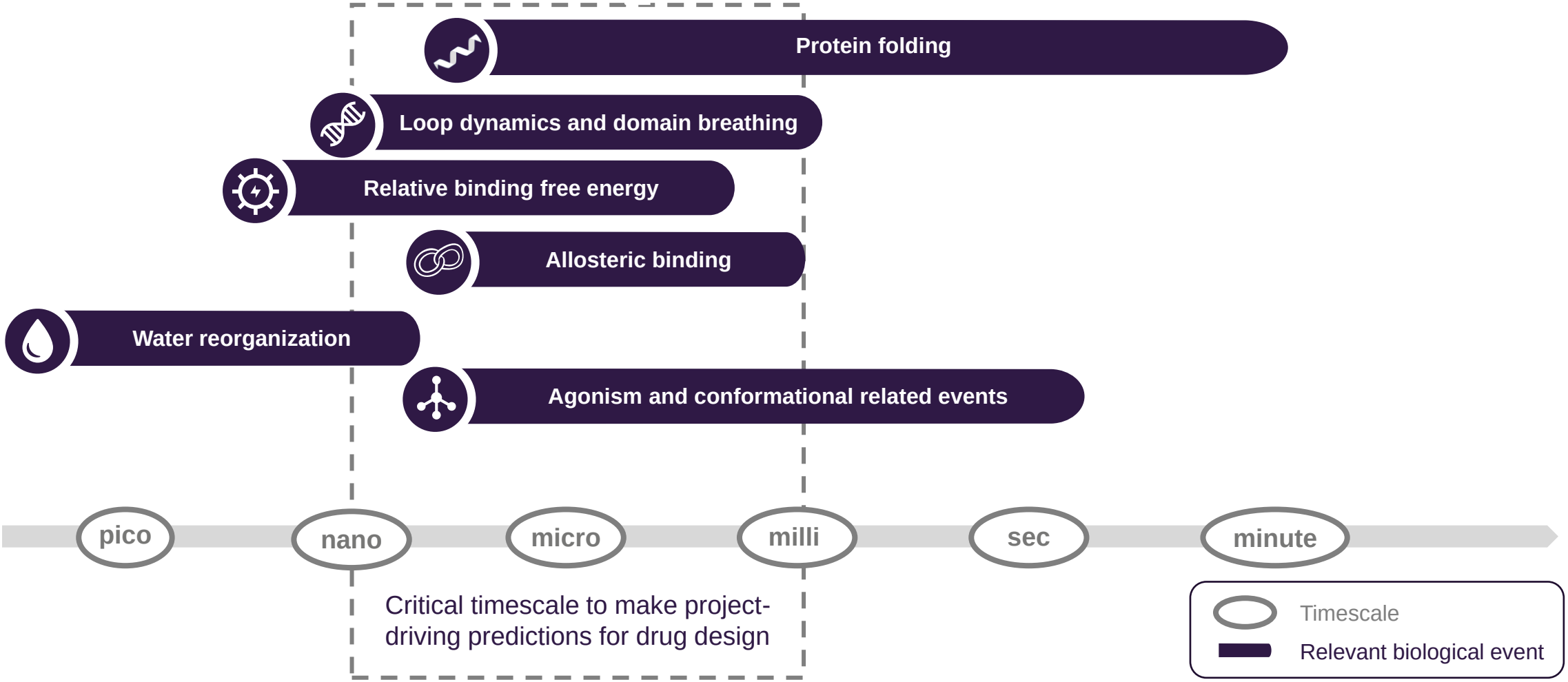
https://aip.scitation.org/doi/abs/10.1063/1.5089924



Structural model with atomistic resolution

x: atomic coordinates
E_r: restrained potential energy function
E_0: unbiased potential energy function
R: experimental restraining energy
D_e: experimental data

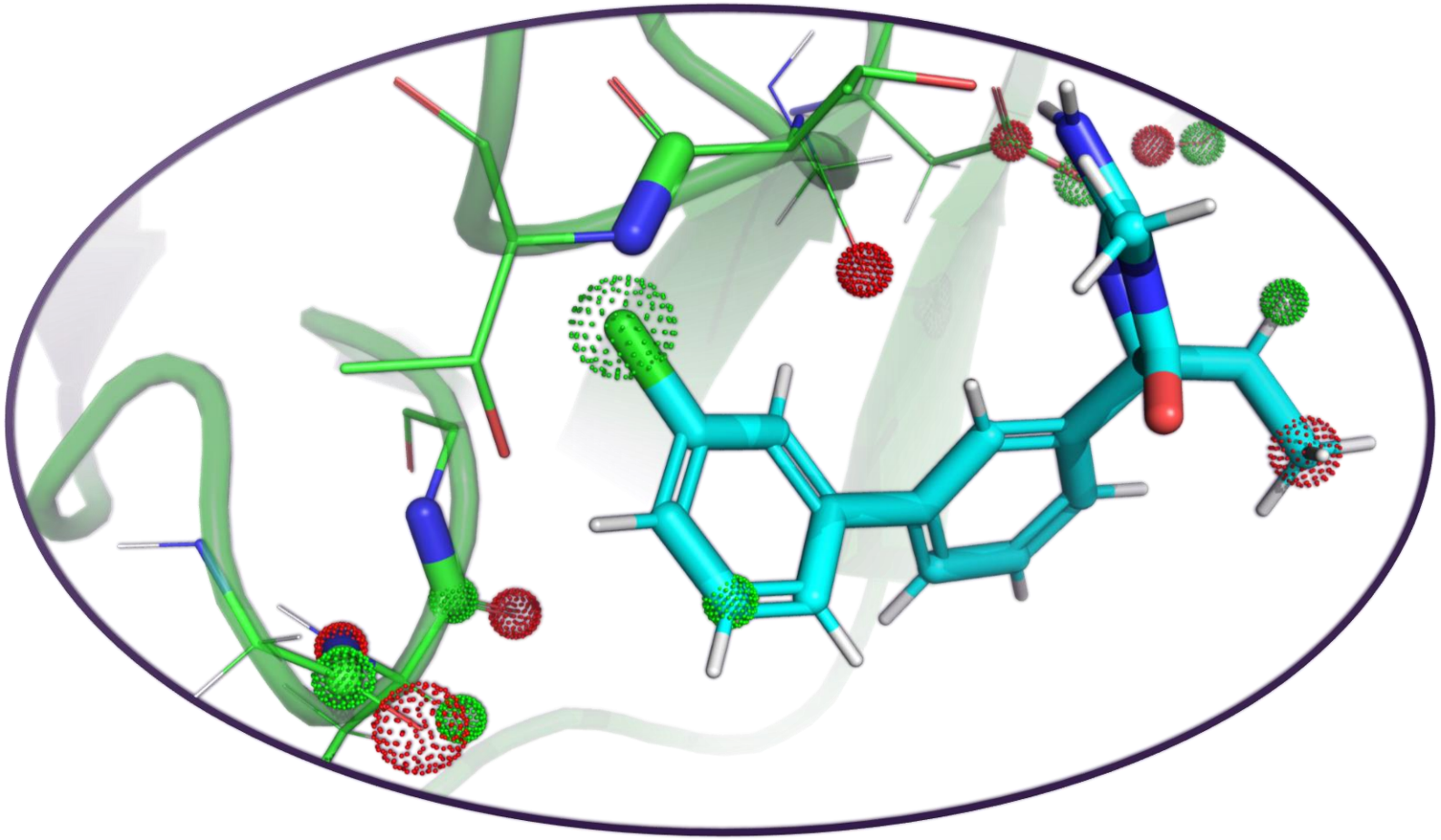
Witnessing Relevant Biological Timescales with Atomic Resolution

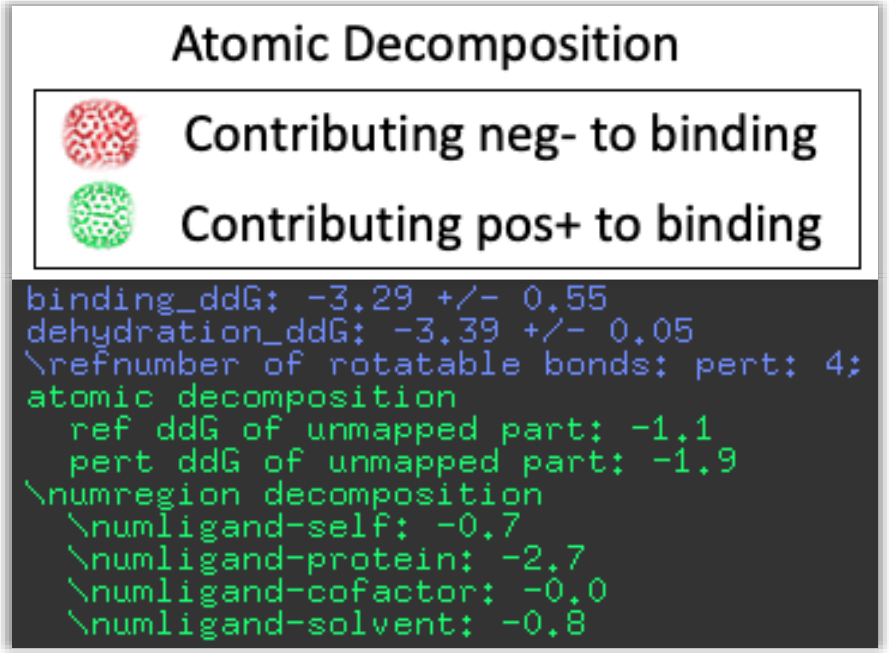


Free Energy Calculations and Atomic Decomposition for Better Designs

Peer to Schrödinger's FEP+ for speed and accuracy of binding free energy calculations.

Novel atomic decomposition of binding free energy lets our drug designers "see" areas for improvement.

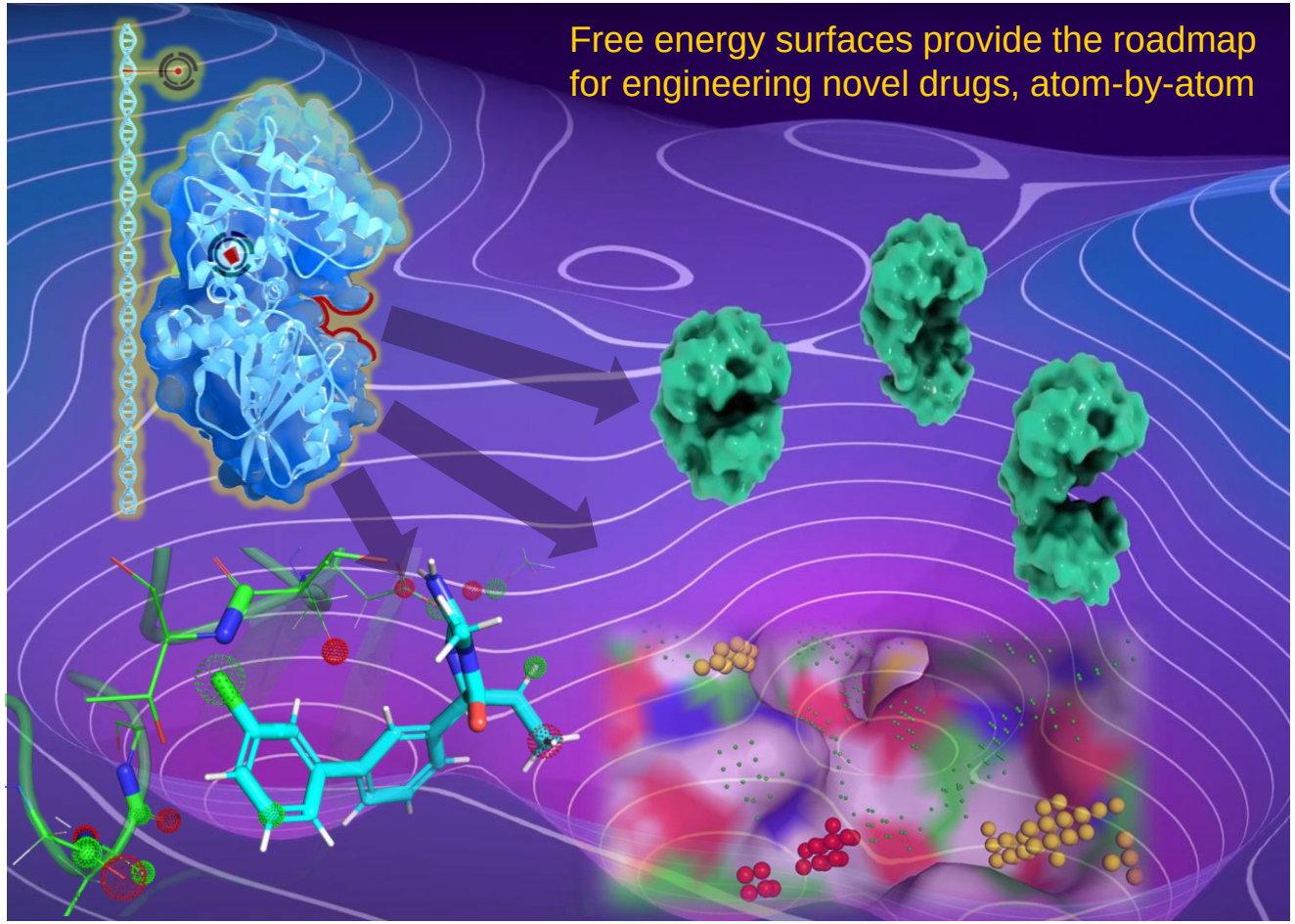




What Does The Predictive Sciences Platform Enable?

The era of predictive, high-precision molecular medicines across multiple modalities

- **Target ID**
  - Relating genetics to protein conformations
  - Identification of novel MOAs
- **Druggability and Novel Binding Sites**
  - Detection of cryptic/dynamic pockets
  - Fragment soaking crystallography
  - Computational mixed-solvent MD
- **Competitive Binders**
  - Agonists
  - Antagonists
- **Allosteric Modulators**
  - Distal dynamic modulation
  - Conformational stabilization
- **Induced Proximity Modulators**
  - Heterobifunctional degraders
  - Molecular glue degraders
  - Phosphorylation-inducing molecules



Design Cycle – Ideate, Design, Predict, Make, Test, Analyze, Iterate

IDEATE	DESIGN	PREDICT	MAKE/TEST

Medicinal Chemistry

Water Thermodynamics

Atomic Energy Decomposition

Conformational Modulation

Generative Models

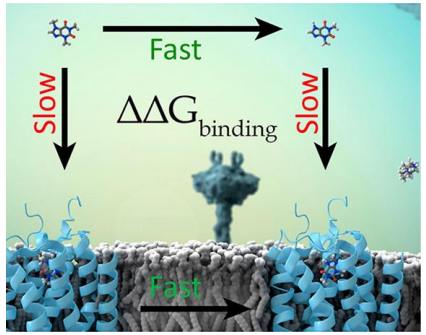
Explore billions of new molecule designs

Design Team
Med. Chem.
Modeling
Simulation
Biophysics
Predictive Sciences
Platform

Platform team develops bespoke methods to solve target-specific problems

ANALYZE & ITERATE

Predictive Simulations



Binding Free Energies
Conformational Energies
Off-target Selectivity
ADME/Tox Models
AI/ML Models

Experimental Data

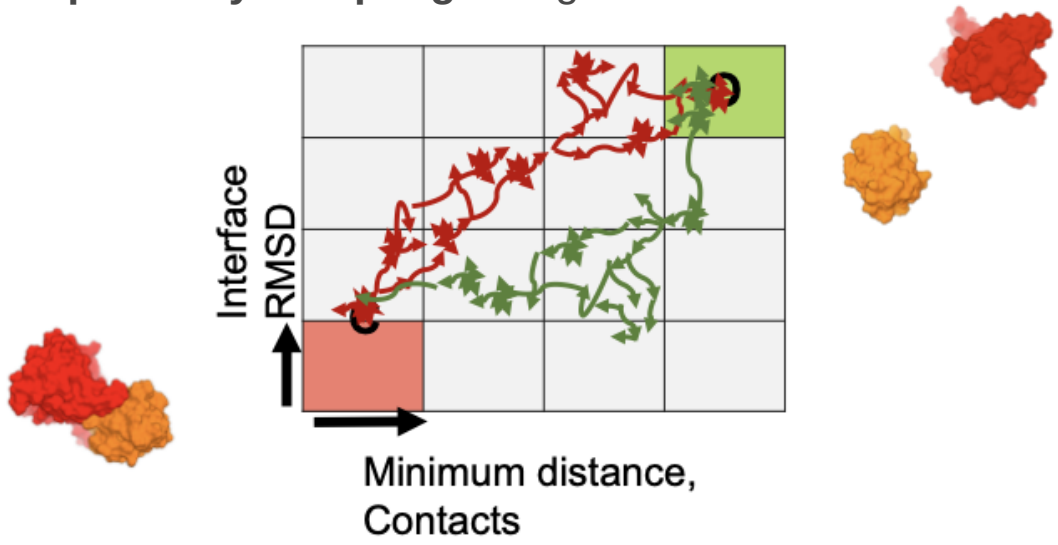
Drug Candidate

Beyond Binding: Conformational Modulation and Induced Proximity

Advanced Simulation Approach

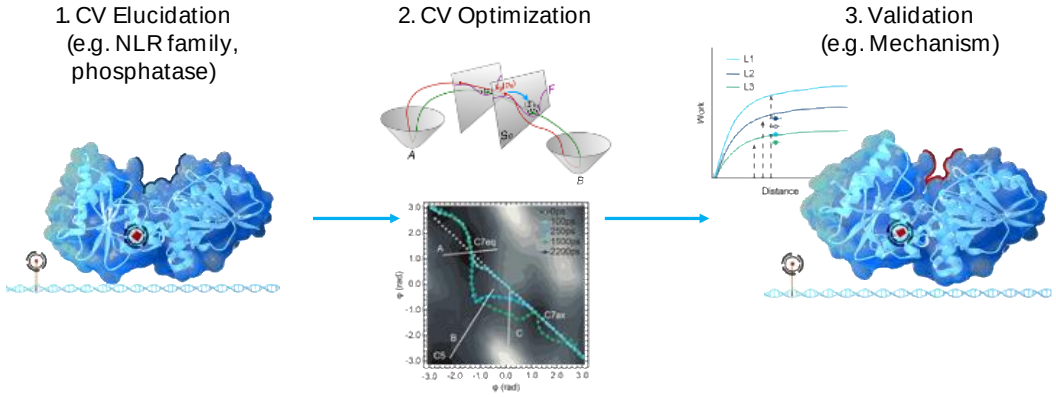
- **Bespoke Force Field**
  - All ligands are parameterized from scratch with QM
- **Advanced Simulations**
  - Long timescale
  - Biophysics constraints
  - Conformational free energies
- **Protein-Protein Interactions**
  - Docking
  - Refinement
  - Analysis
- **Binding Free Energies**
  - Relative
  - Absolute
  - Energy decomposition
- **HPC**
  - >600 GPUs
  - >6000 CPUs
  - Cloud for burst computing
  - Folding@Home
  - National Labs

Exploratory Sampling: Weighted Ensemble Simulations (WES)



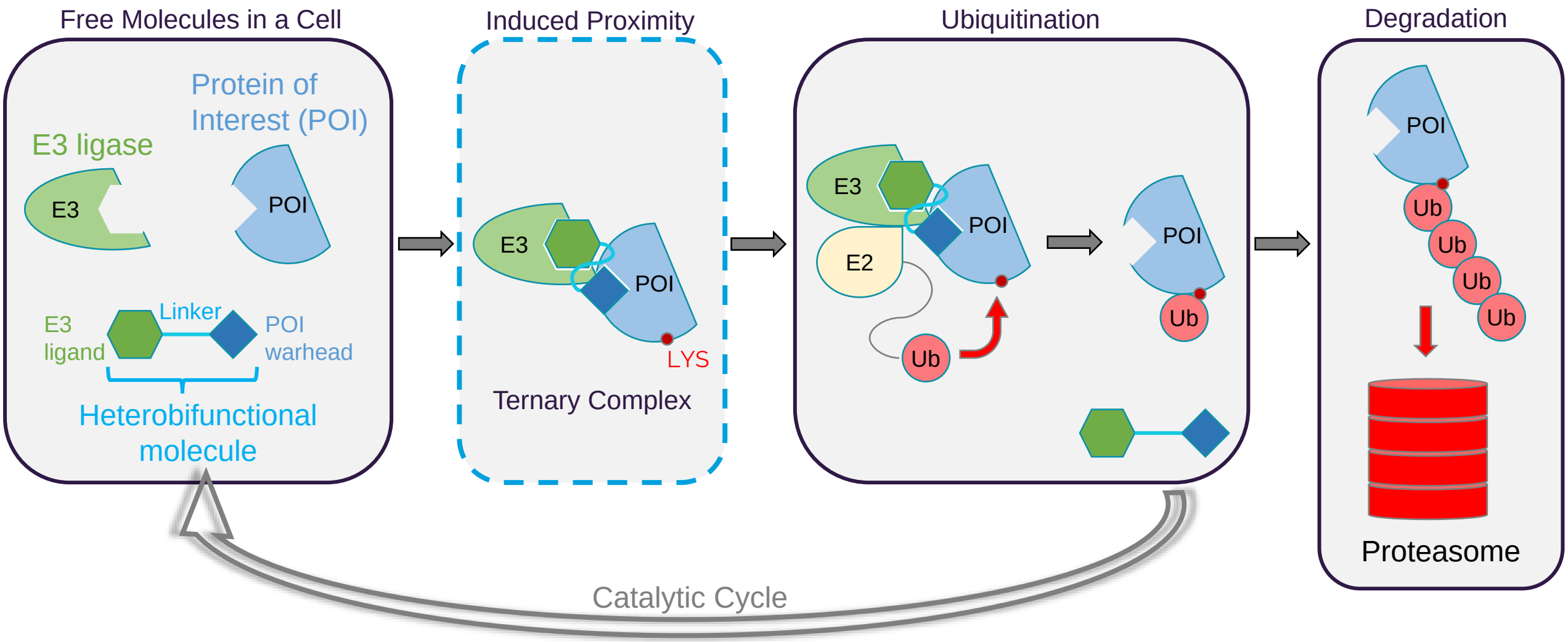
- Discretize conformational space according to Collective Variables (CVs) related to relevant biology
- Replicate trajectories that cross conformational “bins” and spend more time on reactive trajectories
- Elucidate free energy surfaces
- Discovery biologically relevant conformational states, pathways, rates, and free energies

Path Sampling: Metadynamics + Extended ABF (Meta-eABF)



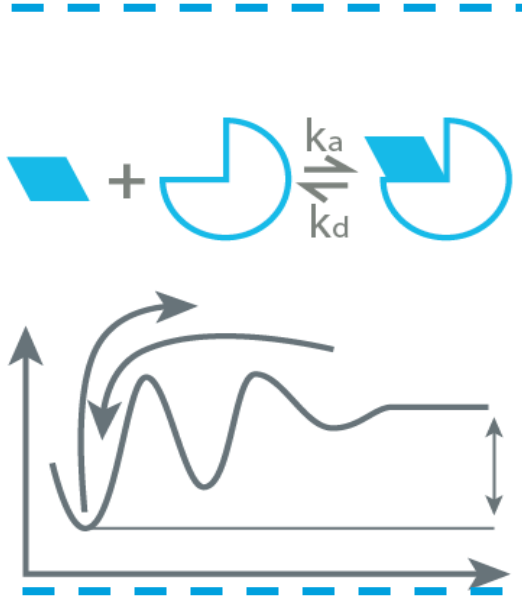
- Biological motions are captured with Collective Variables (CVs)
- CV elucidation is unique to each biological system, but once determined it can accelerate simulations on system of interest
- Adaptive path allows refinement of CV to specific target class for increased speed and accuracy

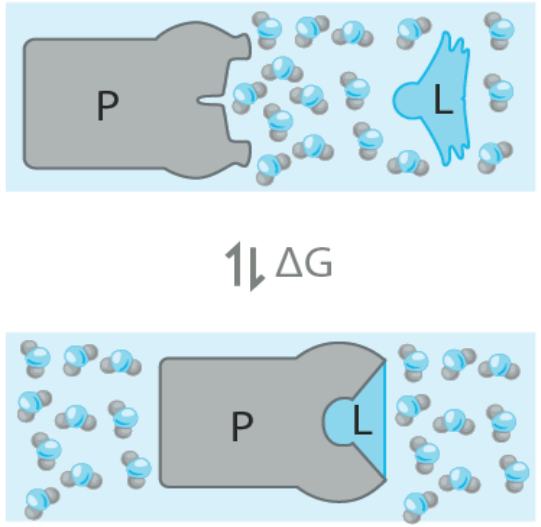
Example of How We Develop Methods to Overcome Critical Bottlenecks: Heterobifunctional Molecules for Protein Degradation

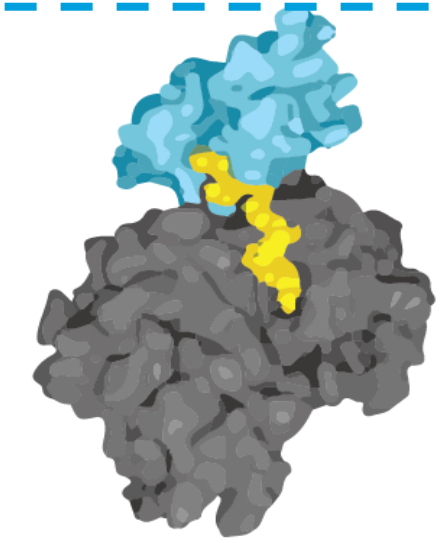


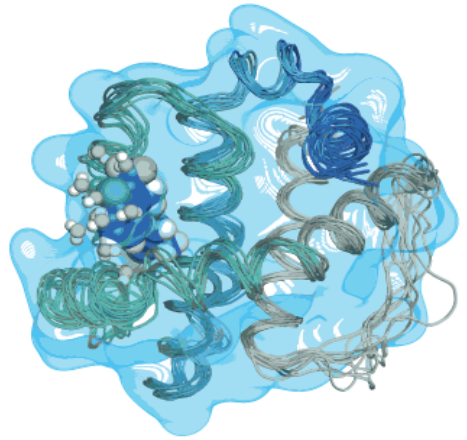
Modeling the Ternary Structure is Critical to a Predictive TPD Platform

Binding Kinetics	Binding Affinity	Structure	Dynamics









Off-the-shelf computational methods are not suited to accurately predict the dynamic solution-state ternary complex

Fully Integrated Binding Simulation with Hydrogen-Deuterium Exchange Data

Most Accurate Ternary Structure Prediction Known

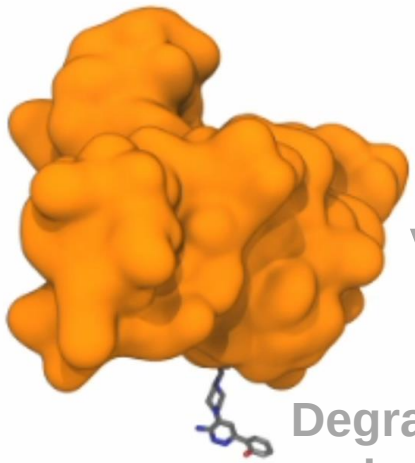
Integration of experimental hydrogen-deuterium exchange mass spectrometry (HDX-MS) data offers unique advantage

Final Statistics:

- Warhead-interface RMSD = 0.40 Å
- Ligand-interface RMSD = 0.65 Å
- Protein-protein interface RMSD = 1.3 Å
- Fraction of native contacts = 90%

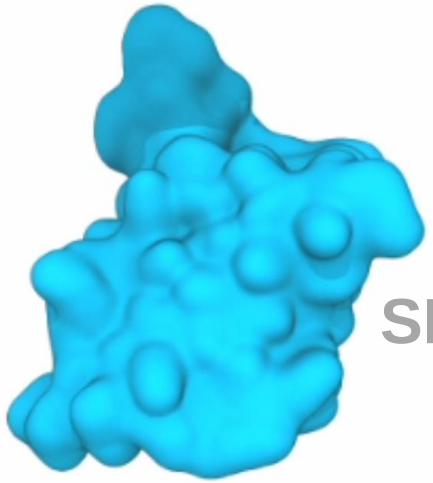
Computational Details:

- **Simulation times:**
  - 4 µs for formation of encounter complex
  - 4 µs for re-arrangement
- **GPUs and time to solution:**
  - 64 GPUs x 1 day
- **System size:**
  - 125K atoms
- **Weighted Ensemble Collective Variables (CVs):**
  - CV1: Minimum distance
  - CV2: Number of native contacts
  - CV3: HDX-MS protection



VHL

Degrader molecule



SMARCA2

Conclusions

- Roivant is a fully integrated drug discovery company – “From Chip to Clinic”
- We have built an industry-leading computational platform for molecular simulations and AI/ML to overcome critical bottlenecks in drug discovery
- The development of custom apps is key for drugging challenging targets
- Integration of experimental data enables more accurate and biologically relevant simulations
- Pipeline expansion into induced proximity and selective cooperativity opens new opportunities for predictive computational platform

Degrading Proteins, Defeating Disease

Degrading Proteins, Defeating Disease

The power of protein degradation is now being realized!

By harnessing the human body's innate cellular machinery to selectively 'delete' proteins, we aim to create new medicines to treat patients with debilitating diseases

We are pursuing this expansive field with the scientific knowledge, proprietary technologies, business acumen, and risk tolerance required to succeed

Why Targeted Protein Degradation?

Protein degradation offers distinct advantages over other drug modalities including inhibitors

Targeted Protein Degradation

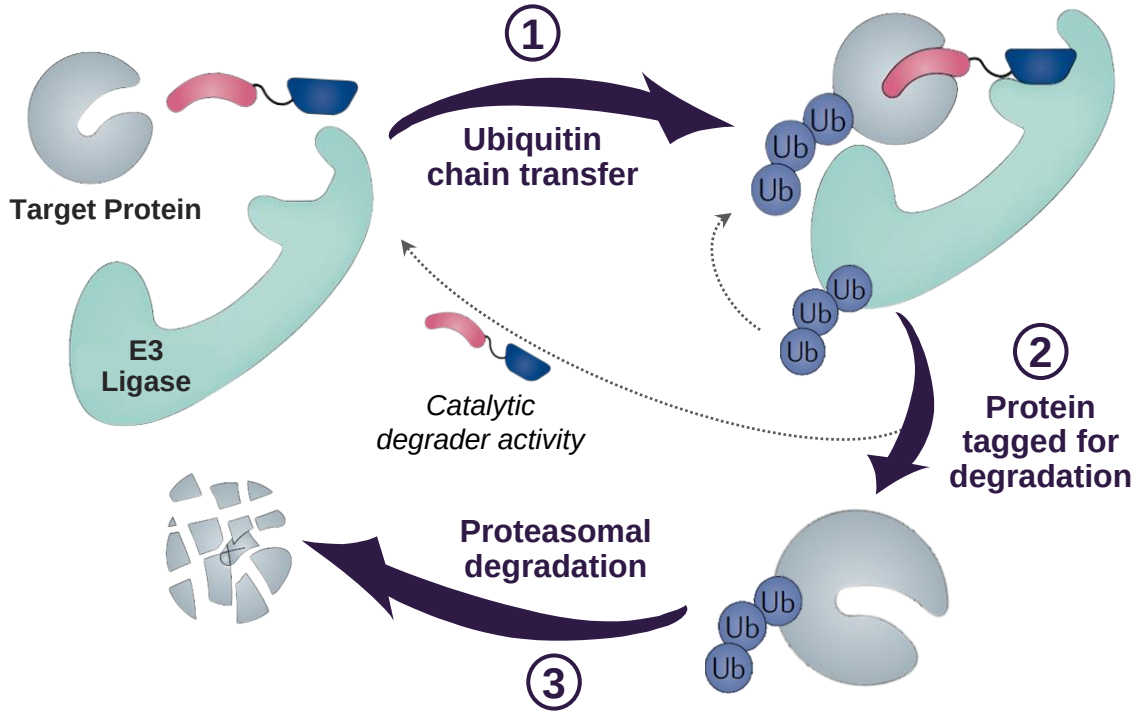
1. **Unconstrained by Active Site Requirements** — *Target historically "undruggable" proteins, including transcription factors and scaffolding proteins that lack a catalytic pocket*
2. **Selective Degradation of Target Proteins** — *Highly selective degradation of target protein vs. isozymes or paralog proteins with high homology*
3. **Demonstrated Efficacy in Drug Resistant Disease** — *Demonstrated efficacy, as a function of protein depletion, in tumors that are resistant to inhibitors/antagonists*
4. **Catalytic Action Enabling Activity at Lower Doses** — *Catalytic mechanism of degraders potentially enables therapeutic activity at lower doses*

2015 Crews et al. Nature Chemical Biology; 2017 Crews et al. Cell Chemical Biology; 2019 Chamberlain et al. Cell Chemical Biology; 2019 Sun et al. Signal Transduction and Targeted Therapy

Unlocking The Vast Opportunity To Expand The Druggable Proteome By Exploiting the Ubiquitin-Proteasome System (UPS)

Protein degradation via the UPS is a multiple step process:

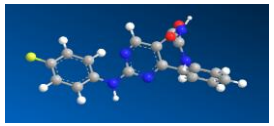
- **The degrader simultaneously engages the target protein and E3 ligase complex**
- **Optimal orientation of the new ternary complex ensures optimal proximity of the two proteins such that ubiquitin is transferred from the E3 ligase complex to the target protein**
- **Successful ubiquitination marks the target protein for destruction, resulting in degradation by the proteosome**



Proteovant Degrader Design Capabilities Span an Array of E3 Ligase Modulation Modalities

Heterobifunctional Degraders

Monovalent Degraders



Potential Future Modalities

Graphic: Adapted from Advances in targeting 'undruggable' transcription factors with small molecules. Henley M.J. Nature Reviews (2021).

Proteovant – Positioned As A Leading Pioneer In Protein Degrader Discovery and Development

- Formed new Vant focused on the discovery and development of novel targeted protein degraders
- Assembled a world-class team of discovery scientists, drug developers and business professionals
- Acquired Oncopia Therapeutics

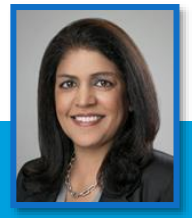
  - Cofounded by Dr. Wang, a world-renowned scientist focused on protein degradation at the University of Michigan. Over 15 years, Dr. Wang and his team have developed a deep degrader pipeline and generated a large global IP estate
  - Broad initial pipeline of degraders to more than 10 targets - oncology and immunology
  - Established long-term, exclusive discovery partnership with Dr. Wang and his lab for targeted protein degradation
- Closed initial $200 million equity investment with SK Holdings
- Leveraging Roivant's investments in computational sciences through close collaborations with VantAI (machine learning and focus on protein degrader discovery and development)

World-Class Executive Team Positioned to Execute on Our Vision

Drew Fromkin

Chief Executive Officer

30+ years leadership in healthcare co's, serves as Vant Portfolio Operating Partner. Previously CEO Tarveda Therapeutics; CEO of Clinical Data (CLDA – $1.5 Billion Sale); Head Corp Dev. Merck- Medco



Ruby Holder, MBA

Chief Strategy Officer

30+ years in healthcare, majority spent as a long-short healthcare portfolio manager. Previously VP of Roivant Governance, Managing Partner & Portfolio Manager at Greywall Asset Management

Tiago Girao, CPA

Chief Financial Officer

20+ years leading teams in accounting, finance, treasury, IR and other corporate operations functions. Previously CFO of Respivant, CFO of Cytori, and 10+ years of experience in public accounting

Zhihua Sui, PhD

Chief Scientific Officer

30+ years in drug discovery and advancement of >20 compounds to the clinic in multiple therapeutic areas. Previously VP of Chemistry and Strategic Outsourcing at Agios, and various leadership roles at Janssen

Helai Mohammad, PhD

VP, Cancer Biology

15+ years of experience in oncology research with emphasis on epigenetics. Previously Senior Scientific Director at GlaxoSmithKline

Scott Priestley, PhD

VP, Discovery Chemistry

23+ years leading drug hunting chemistry teams, delivering numerous compounds across various disease areas. Previously Director of Discovery Chemistry at BMS

Christine Stuhlmiller, MBA

VP, Program Management

17+ years of experience in healthcare, most recently as Executive Director, Global Product Development and Supply Program Management BMS/Celgene.

Winston Wu, PhD

VP, CMC

27+ years of experience in chemistry process development and manufacturing. Previously VP of Chemical Research, Development and Manufacturing at Lexicon Pharmaceuticals

Corey Strickland, PhD

VP, Molecular Technology

25+ years in building structural biology drug discovery platforms across multiple disease areas. Previously Senior Principal Scientist at Merck

John Athanasopoulos, MBA

VP, R&D Operations

20+ years in various research and operational roles in biotech, pharma, and academic settings. Previously held leadership roles at Jnana Therapeutics, C-4 Therapeutics and the Broad Institute

Proteovant's Leading Protein Degrader Discovery and Development Engine Is Fueled By Differentiated Capabilities

Target Selection and Validation

Driven by seasoned team of R&D, structural biology, and strategy experts

Degrader Expertise

Multi-year, exclusive partnership with the University of Michigan lab of Dr. Wang & internal R&D leadership

Wet Labs

In-house and academic facilities equipped for biology, chemistry, and biophysics

Machine Learning

Leading machine learning platform *for in silico* target ID, degrader design, ligase optimization

Machine Learning Infused Across The Continuum Of Proteovant Capabilities

proteovant THERAPEUTICS

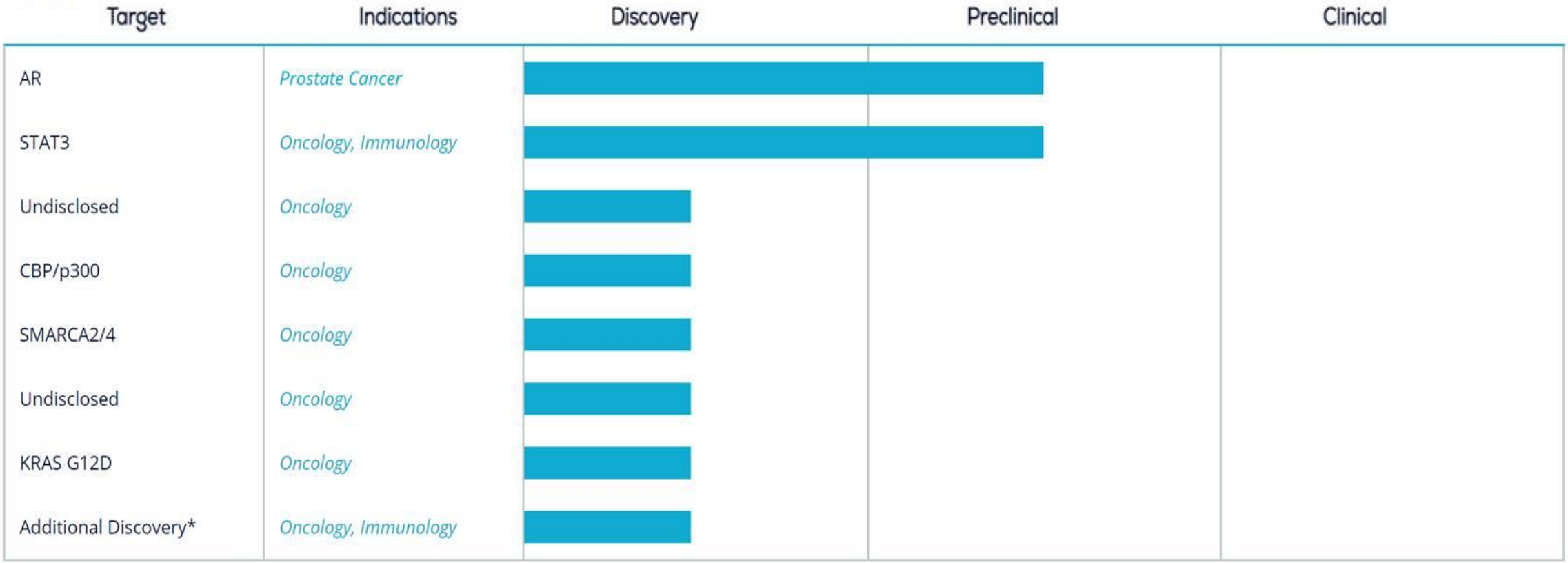
POWERED BY MICHIGAN TECHNOLOGY

ROIVANT SCIENCES

VANTAI

Selected Pipeline Programs

- **Balanced pipeline of protein degrader targets spanning Oncology and Immunology**
- **Advancing initial protein degrader programs from the Oncopia acquisition**
- **Enhancing pipeline with degraders to new targets and novel E3 ligase discovery work through our internal R&D capabilities as well as our collaborations with Dr. Wang and VantAI**



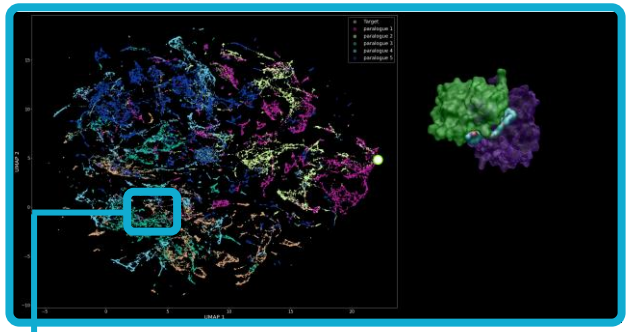
* Multiple programs

VantAI: A Novel Paradigm For Rational Degrader Discovery

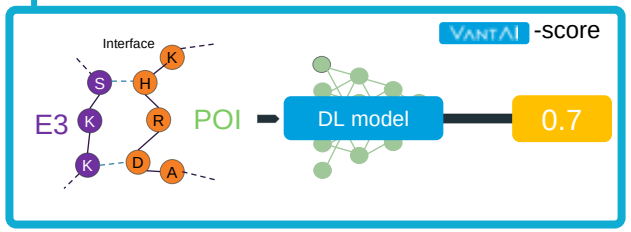
Classical small molecule machine learning starts chemistry first - VantAI flips this script

Protein-Contacts First, Learning From Evolution

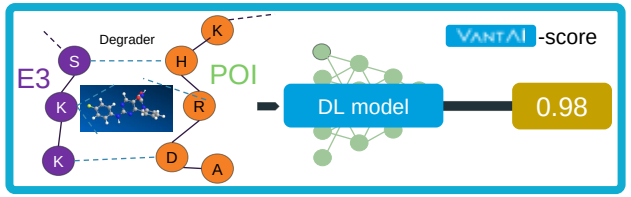
I) Look at every possible interface



II) Evolutionary scoring

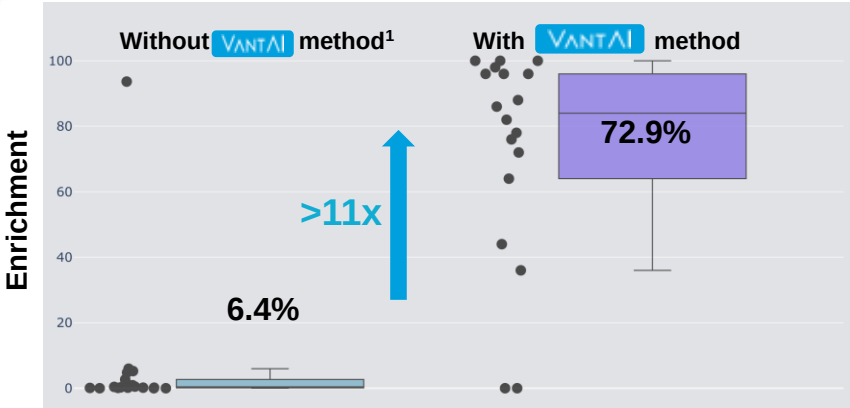


III) Chemistry to fill the gap



1. Protein-Contacts First: VantAI starts with protein-protein interfaces, independent of specific protein (E3 or POI)
2. Value of Evolution: possible protein interfaces are highly conserved, providing learnings from millions of examples in nature
3. Leveraging Deep Learning: training models on evolutionary information to learn differences in interfaces
   - Models produce VantAI score - scoring similarity of E3-POI interfaces to naturally occurring interfaces
4. Close The Gap: optimize towards small, drug-like chemistry de-novo designed to mimic most favorable natural interfaces

Validated In Extensive Benchmarking



- Enrichment: for each benchmark structure, percent of predicted ternary complexes alike[2] to real, crystalized glue system
- >11x accuracy increase, allowing rational molecule design to fill the gap

Real World Discovery Impact

- **Increase Hit Rate**: impact from example[3] project: 6/8 initial compound designs showed >50% degradation for target without previous recorded degradation
- **Faster Pipeline Progress**: 5 targets with PoC degradation[4] in <1 year

ROIVANT DISCOVERY

For Investor Audiences Only

1 Restrained Protein Docking using LightDock
2 Enrichment: % of predicted ternary complexes within 10A Ligand RMSD (based on CAPRI) of crystalized ground truth glue ternary complexes reported in PDB (Benchmark structures: 6HOF, 6HOG, 6UML, 5HXB, 5FQD, 6UE5, 6UD7, 6PAI, 6SJ7, 6QOR, 6QOV, 6QOW, 6TD3, 6M90, 6M91, 6M92, 6M93, 6IQN)
3 Prior VantAI project
4 >30% degradation vs control

Proteovant – Positioned To Lead In Protein Degrader Discovery and Development

- Well-financed to advance pipeline of protein degraders to the next level of value creation
- World-class team assembled to drive discovery and development of optimized protein degraders
- Advancing broad pipeline of protein degraders
  - Long-term, exclusive discovery research partnership in protein degradation established with Dr. Wang
  - Investing in internal discovery to expedite current programs and further expand the pipeline with novel degraders
- Exclusive partnership with VantAI to access unique and proprietary, degrader-optimized machine learning and systems biology

Business and Technology

For Investor Audiences Only

Genevant Overview

Industry-Leading Nucleic Acid Delivery Company

- World-class delivery platforms to enable delivery of mRNA, siRNA, gene editing constructs, and other nucleic acids
- Best-in-class proprietary lipid nanoparticle (LNP) platform and proprietary ligand conjugate platform
- Focused business of collaboration around delivery expertise and technology platforms
- Offers partners attractive potential to deliver payloads to traditionally hard-to-reach tissues/cell types, plus NA design capability
- More than 600 LNP-related issued patents and pending patent applications, directed to individual lipid structure, particle composition, particle morphology, manufacturing and mRNA-LNP formulations

Business Model Designed to be Profitable While Building Further Advances in Nucleic Acid Delivery Technology

- Genevant uses its expertise in the delivery of nucleic acid therapeutics to develop optimal delivery systems for its collaborators' identified payloads or target tissues
- Genevant provides collaborators access to validated technology to deliver nucleic acid therapeutics, eliminating the need to build internal delivery expertise or build IP estate from scratch in complex field
- Genevant typically retains ownership or certain rights to delivery-related IP developed in context of collaboration, which can be leveraged for other out-licenses and to build on developments for future deals

Business model exemplified by numerous recent collaborations and licensing deals

Decades of Experience in Nucleic Acid Delivery, Creative Corporate Partnering

Peter Lutwyche, PhD
Chief Executive Officer and President, GSC

- Former CTO, Arbutus Biopharma; Head of Pharmaceutical Development, QLT
- Developed and commercialized VISUDYNE® at QLT
- Over 20 years experience in nucleic acid-based products

Pete Zorn
President and Chief Legal Officer, GSI

- Former COO, Genevant, Chief Corporate Officer and General Counsel, Albireo Pharma; General Counsel and VP, Communications, Santaris Pharma; General Counsel and SVP, Targacept

James Heyes, PhD
Chief Scientific Officer

- Former VP, Drug Delivery, Arbutus Biopharma
- Over 17 years experience in lipid chemistry and nucleic acid drug delivery
- Over 20 issued and published US patents in lipid nanoparticle and ligand conjugate technology

Tracy Meffen
VP Quality & Regulatory

- Former Head Quality, Arbutus Biopharma
- Over 25 years experience in QA and RA management roles at various organizations including Lungpacer, INEX, Lilly and Genzyme

Ed Yaworski
VP Pharmaceutical Development

- Head of CMC, Arbutus Biopharma
- Over 30 years experience in pharma including 18 years nucleic acid drug delivery
- Inventor of leading nucleic acid delivery technology used in more than a dozen clinical trials

santaris pharma a/s
RNA Medicines for the 21st Century

TARGACEPT

Albireo

QLT Inc.

Arbutus BIOPHARMA

genzyme

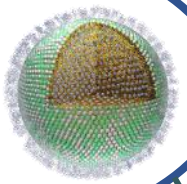
Lilly

Industry-Leading Delivery Capabilities Enable Diverse NA Therapeutics

mRNA vaccines
Infectious Disease
Personalized Oncology

mRNA/DNA
(Hepatocyte/other cell types)
Therapeutic Proteins/mAbs

LNP



- •Proven, best-in-class LNP technology
- •First and only FDA-approved systemically administered RNA-LNP (Alnylams's ONPATTRO®)
- •Clinically validated for **hepatocyte** and **vaccine** applications; ongoing development for **lung, eye, stellate and immune cells**
- •600+ issued patents and pending applications

siRNA/ASO
hepatocyte delivery

Gene Editing
hepatocyte/
other cell types

siRNA/ASO
other cell types

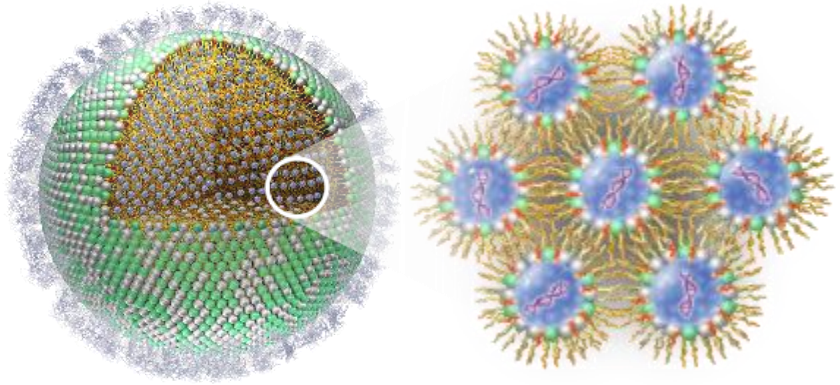
Ligand Conjugates

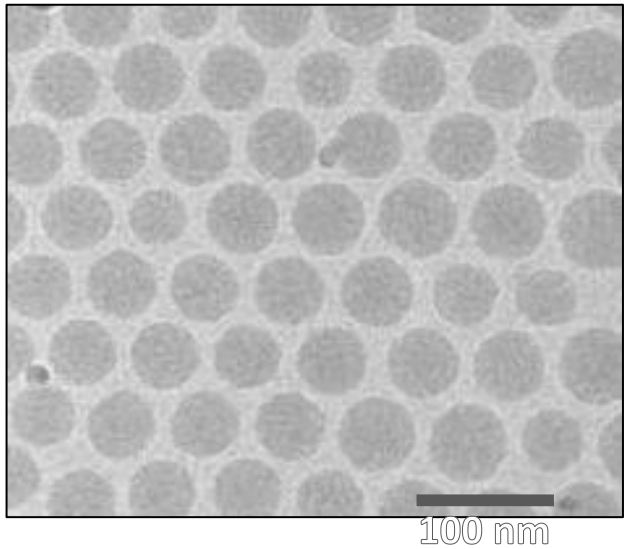
- •Novel GalNAc ligands for **hepatocyte** delivery administered subcutaneously
- •Equal or better potency/ safety to industry benchmark in preclinical models
- •Next gen in development with best-in-class potential
- •Ongoing research for **novel extrahepatic ligands**

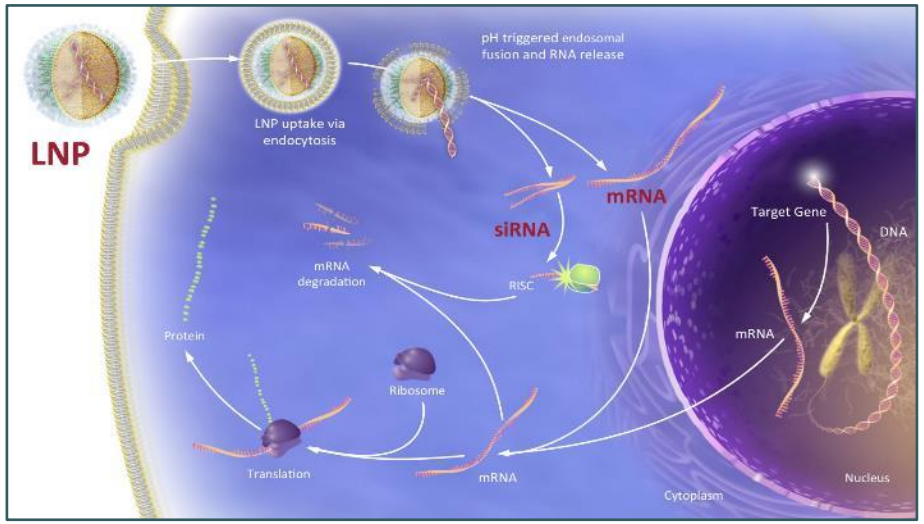
LNP Platform

Genevant's Lipid Nanoparticle (LNP) Delivery Platform

- Multi-component lipid formulations encapsulating nucleic acid payload(s) within a lipid core
- Limited constraints on NA payload composition, structure or size
- Stable uniform dispersion of colloidal nanoparticles
- Efficient intracellular delivery to cytoplasm via receptor-mediated endocytosis







PEG Lipid

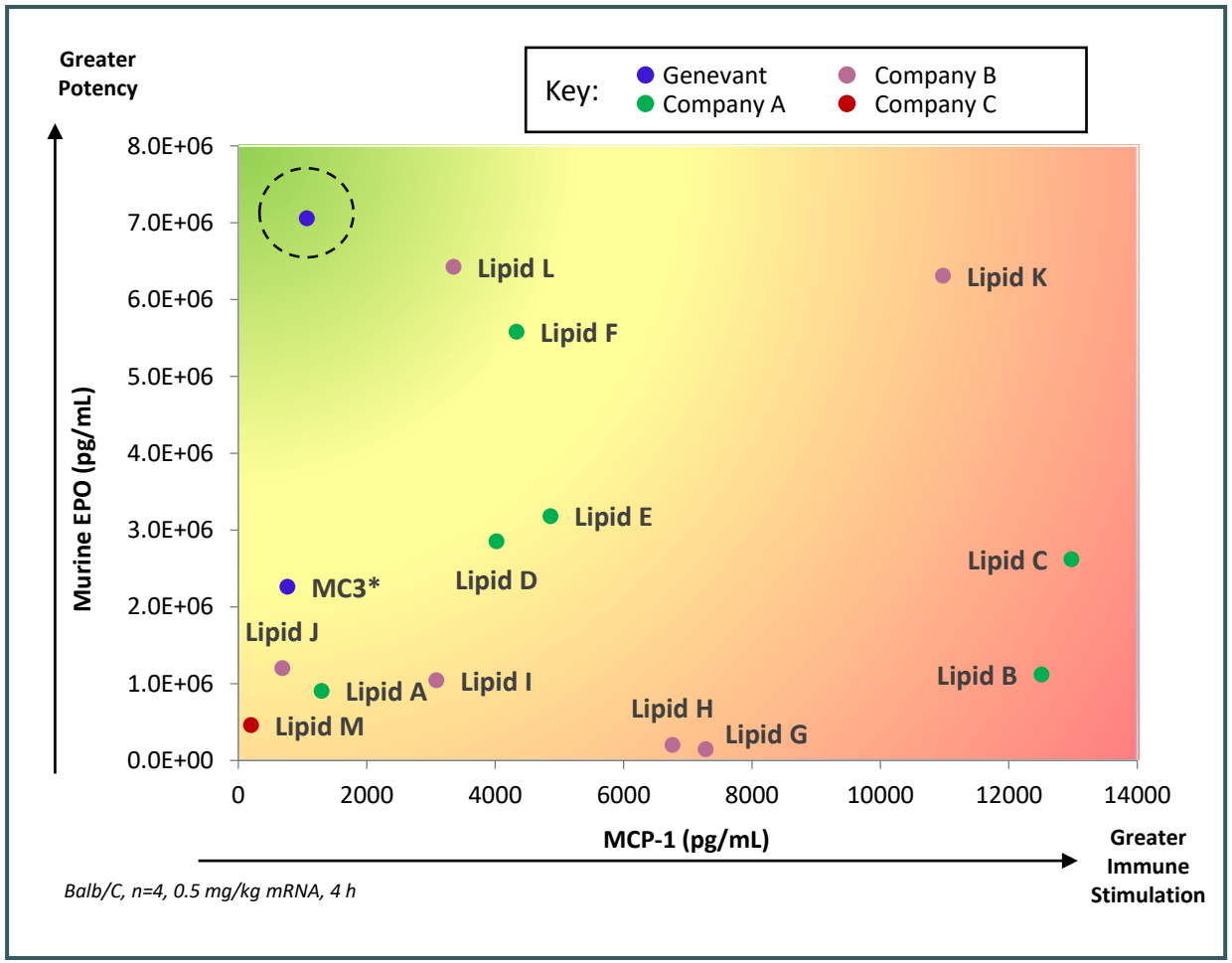
Ionizable Lipid

Structural Lipid

Cholesterol

Nucleic Acid

Genevant has Unparalleled Experience Designing Ionizable Lipids



- In a head-to-head study comparing multiple LNP formulations varying only the ionizable lipid, a newer Genevant formulation outperformed third party formulations
- Superior potency and avoidance of immune stimulation relative to others, including the formulation used in Alnylam's Onpattro®

Genevant LNP Technology has Entered the Clinic in More than a Dozen Product Candidates Representing Hundreds of Subjects

Clinical Highlights (non-exhaustive)

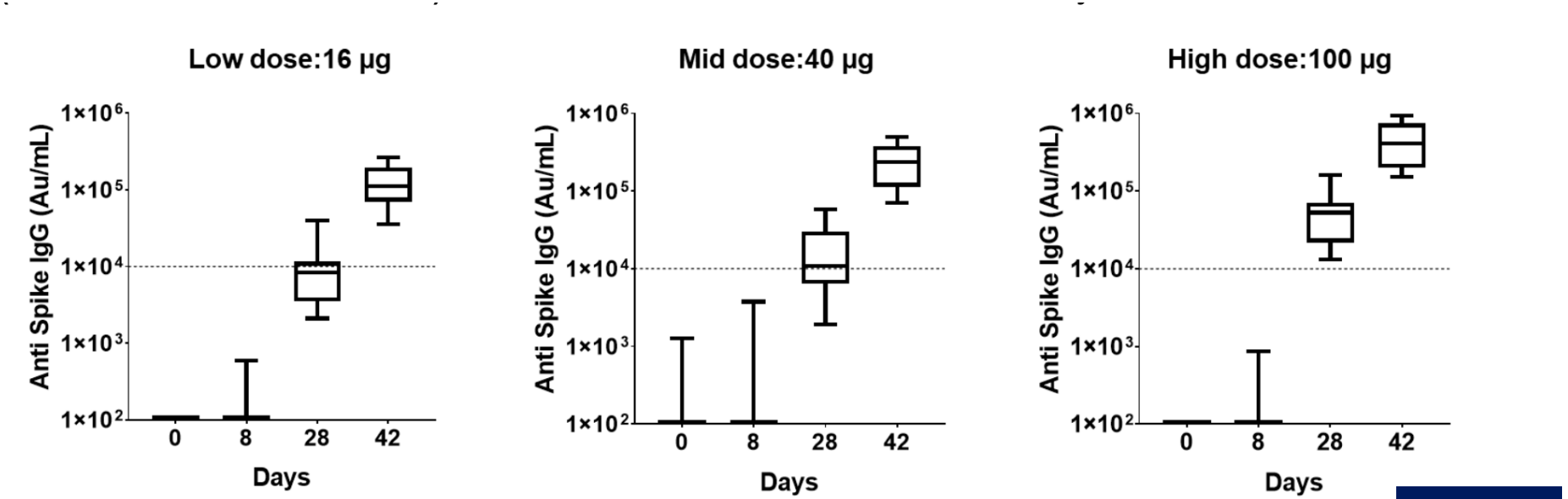
Company	Product	Indication	Activity	Latest Phase
Alnylam Pharmaceuticals	ONPATTRO (patisiran)	ATTR Amyloidosis	• Safely dosed for up to 25 months in some patients • Efficacy of up to 94% TTR knockdown with physiological effect • Approved by the FDA August 2018	Approved
Arbutus Biopharma	ARB-1467 (TKM-HBV)	Hepatitis B	• Completed Phase 2b trial in HBV patients • Clear PD effect (knock down of surface antigen)	Phase 2
	TKM-PLK1	Oncology	• Safely dosed for up to 18 months • Evidence of anti-tumor activity based on a decrease in tumor size and a decrease in tumor density consistent with necrosis	Phase 2
	TKM-Ebola (three LNP products)	Ebola Infection	• 100% protection in lethal primate model of EVD • Compassionate use in 2014 Ebola outbreak	Phase 2
moderna	Four Prophylactic mRNA Vaccines	Various infectious diseases	• Successful completion of first in human mRNA vaccine trial • Met primary endpoint of neutralizing Ab titers in healthy subjects	Phase I
gritstone oncology	GRANITE-001	Oncology	• Personalized oncology vaccine; self replicating RNA payload encoding tumor neoantigens • Promising immunogenicity activity and safety data released	Phase 2
Providence Therapeutics	PTX-COVID19-B	SARS-CoV-2	• Promising immunogenicity data released	Phase 1

Favorable safety data in a variety of repeat-dosing schedules

Collaborator Providence Therapeutics Reported Favorable Interim Phase 1 Antibody Data for mRNA-LNP COVID-19 Vaccine*

- Data from 60 subjects; two doses, 28 days apart
- Compelling safety data also reported

Robust Anti-spike Ab Titers



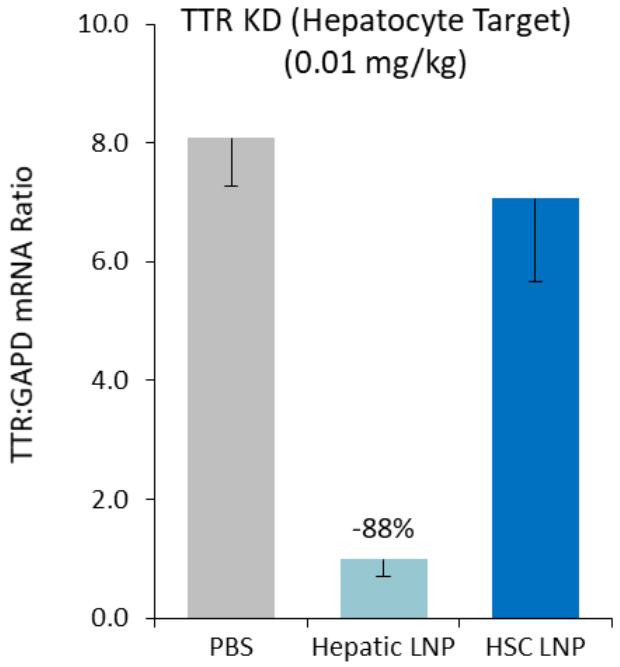
Dotted line represents convalescent sera average

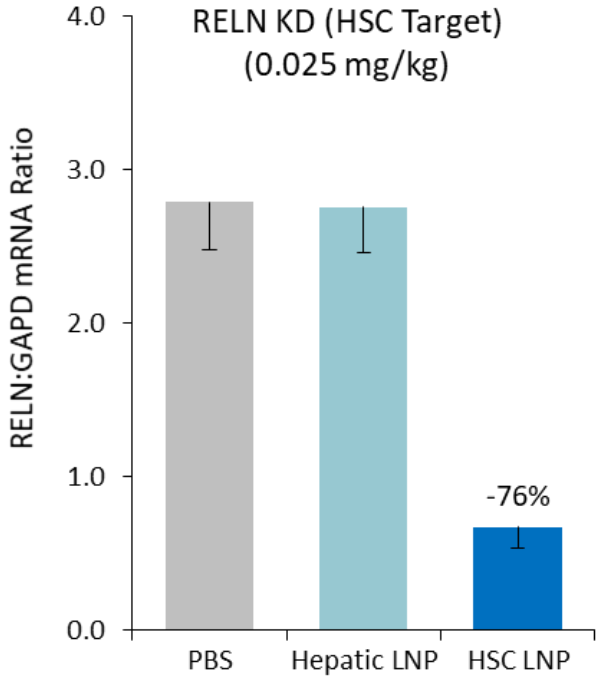
*https://providencetherapeutics.com/article-details/providence-therapeutics-announces-very-favorable-interim-phase-1-trial-data-for-ptx-covid19-b-its-mrna-vaccine-against-covid-19.html

Both expts: (2 IM doses, 3-week interval). Measurements 14 days post boost.

Hepatic Stellate Cell (HSC)-Directed LNP: Strong Target-Specific Knockdown

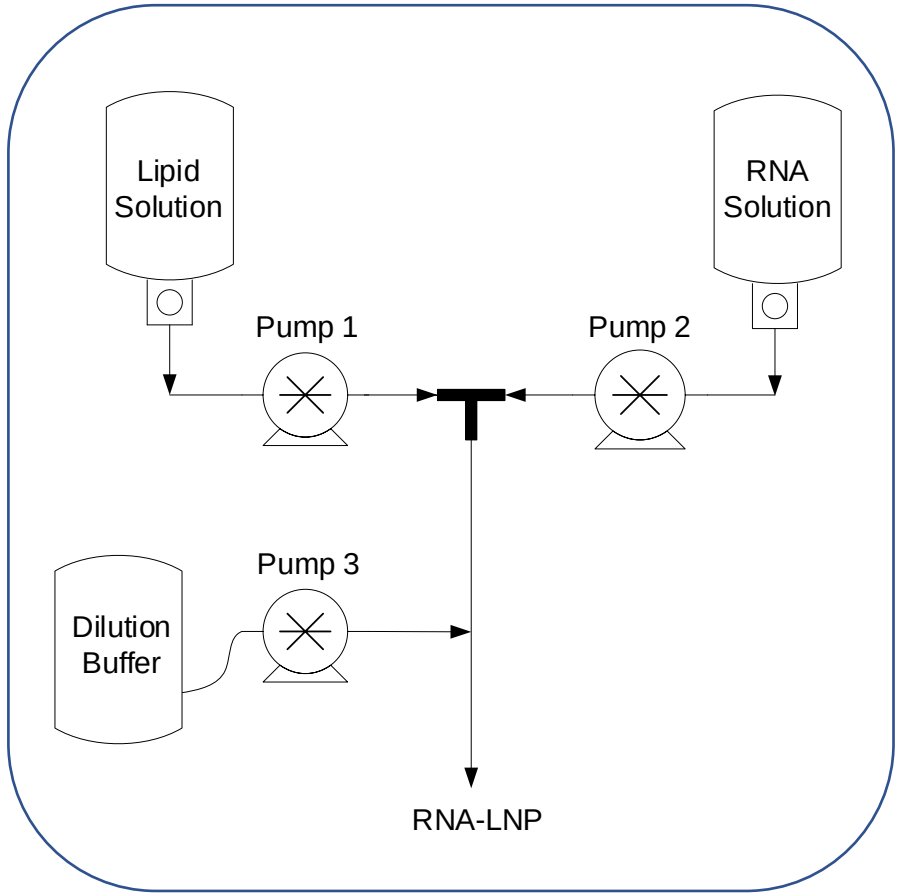
- Building on track record of success, focusing on access to historically challenging tissues and cell types
- Hepatic stellate cells well established as central driver of fibrosis
- In preclinical studies, delivery of siRNA to HSCs via Genevant's LNP demonstrated selective knockdown of mRNA in mice with minimal activity in hepatocytes
- Additional research in lung, muscle, CNS, eye





Genevant LNP Manufacturing Technology

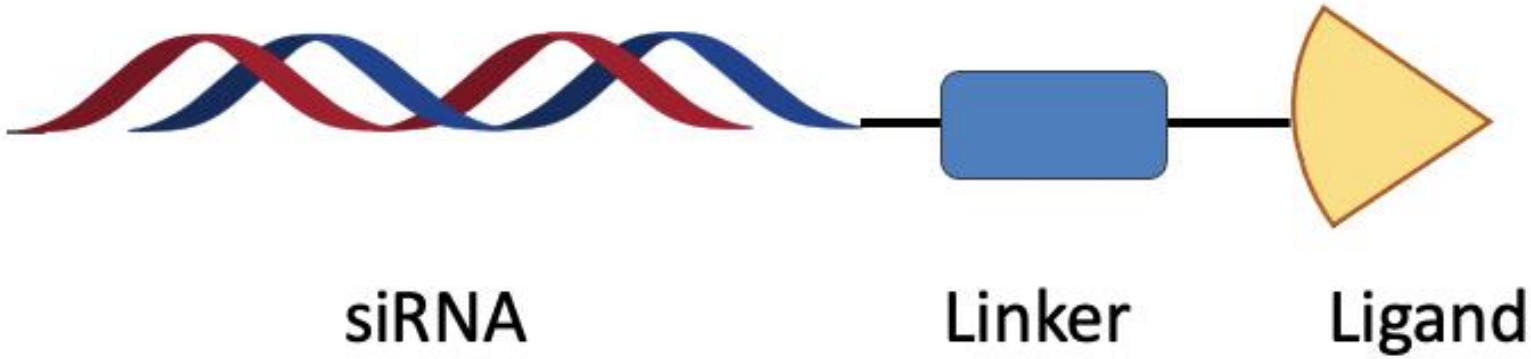
- Controlled mixing process (not microfluidic or extrusion based)
- Broadly applicable to nucleic acids including plasmid DNA, siRNA, and mRNA
- High encapsulation efficiency
- Rapid, reproducible and robust
- Easily scalable
- Modular design is transferable
- GMP compliant



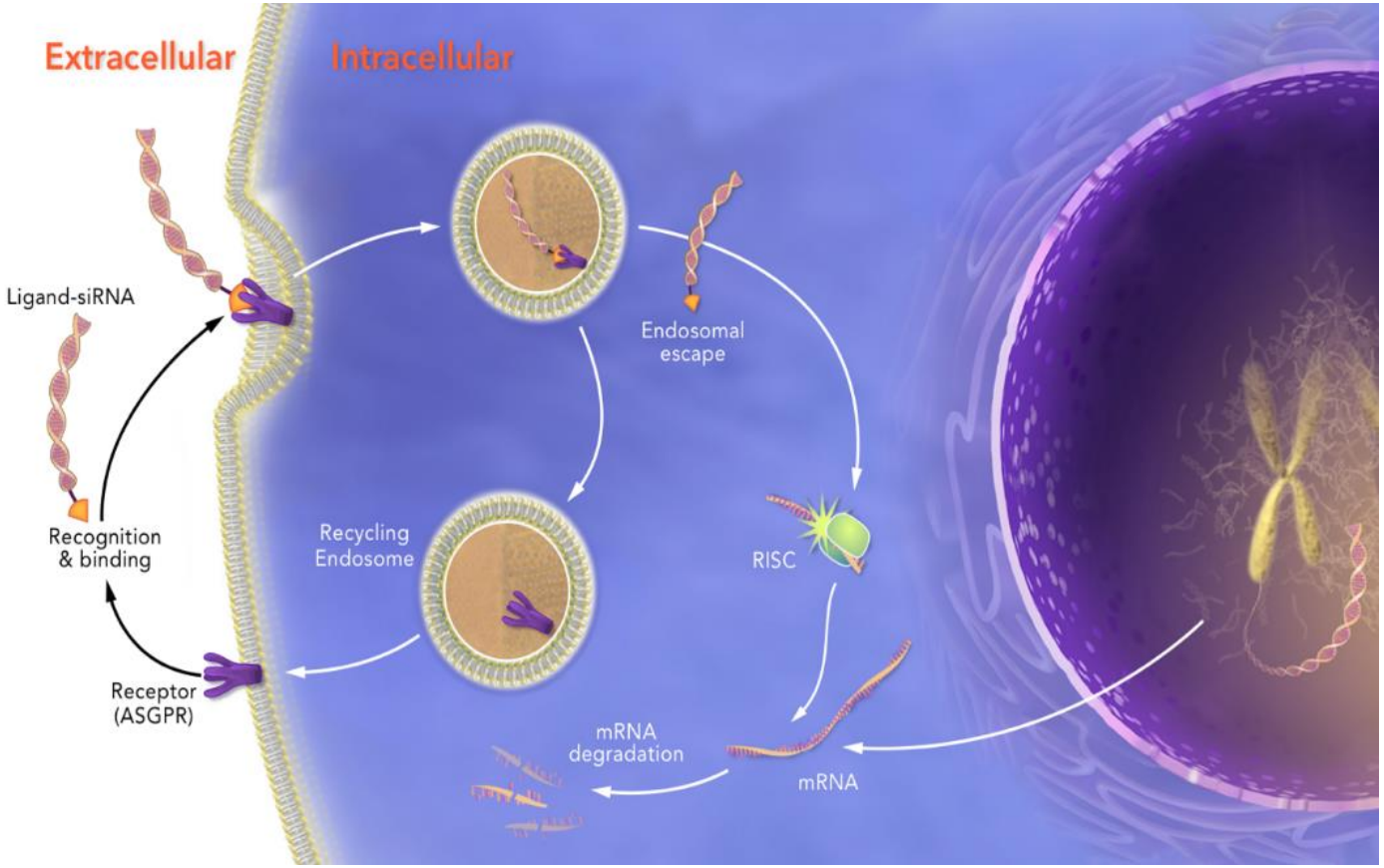
Ligand Conjugate Platform

Genevant's siRNA-Ligand Conjugate Delivery Platform

siRNA design stabilizes the conjugate and enhances cellular delivery	Linker chemistry increases the Stability, potency, and duration of activity	Ligand-targeting moiety mediates binding and internalization of conjugate: 5' or 3' coupled



siRNA-GalNAc Conjugates Mechanism of Action

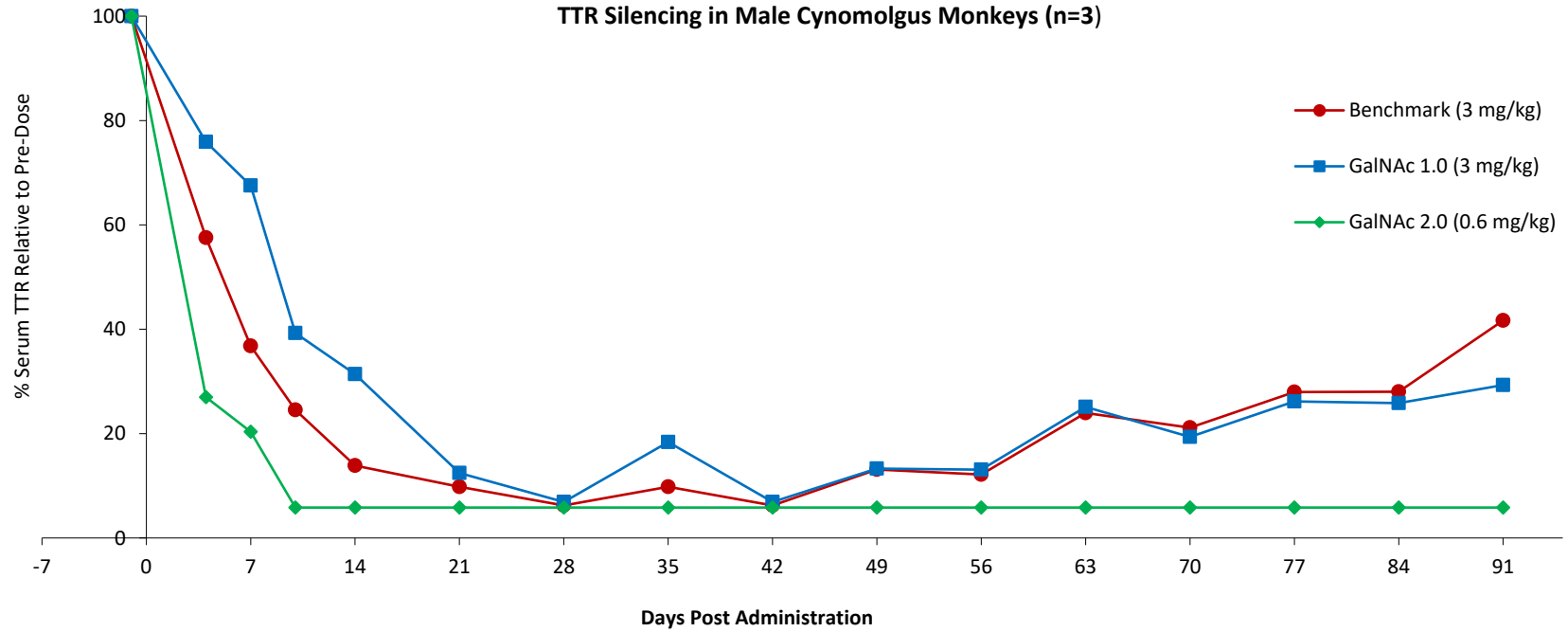


GalNAc-conjugated ligand mediates siRNA delivery

- GalNAc binds & internalized by ASGPR (Asialoglycoprotein Receptor);
  - Clears serum glycoproteins via clathrin-mediated endocytosis
  - High capacity uptake system
  - Highly expressed and conserved across species
- siRNA passively released from endosome and engages RISC
- Results in mRNA cleavage and inhibition of translation

First Generation Compared Favorably to Benchmark, RNAi 2.0 Provided Enhanced Potency and Duration of Effect in NHP

- RNAi 2.0 contains intrinsic endosomolytic properties
- Single subcutaneous dose NHP study; all groups used same TTR sequence to allow direct comparison
- Marked enhancement in potency
- Compatible with GalNAc or other ligand types



Representative Corporate Partnering

BIONTECH	• Co-develop + co-commercialize specified mRNA-LNP rare disease programs; 50-50 profit/cost share; additional LNP licenses for specified oncology target
gritstone ONCOLOGY	• License to LNP for SAM RNA vaccine products for COVID-19 • License to LNP for SAM RNA vaccine products for specified undisclosed indication
SAREPTA THERAPEUTICS	• Collaboration for LNP-based gene editing therapeutics for specified rare diseases
Takeda	• Collaboration for LNP access to specified targets in hep. stellate cells for liver fibrosis • Collaboration for LNP delivery for nonviral gene therapy for specified rare liver diseases
PROVIDENCE therapeutics	• License to LNP for vaccine containing mRNA encoding for antigen for SARS-CoV-2
ST PHARM	• License to LNP for vaccine containing mRNA encoding for antigen for SARS-CoV-2
Other Recent Transactions (undisclosed)	• Collaboration for LNP-based gene editing therapeutics for specified rare disease • Licenses to LNP for mRNA COVID-19 vaccines or therapeutics to universities in the U.S. and abroad


Dermavant Sciences
WE WILL
TRANSFORM
DERMATOLOGY
dermavant™

Investment Summary

Poised to *TRANSFORM* Immuno-Dermatology

Transformational 2 in 1 Lead Product Candidate

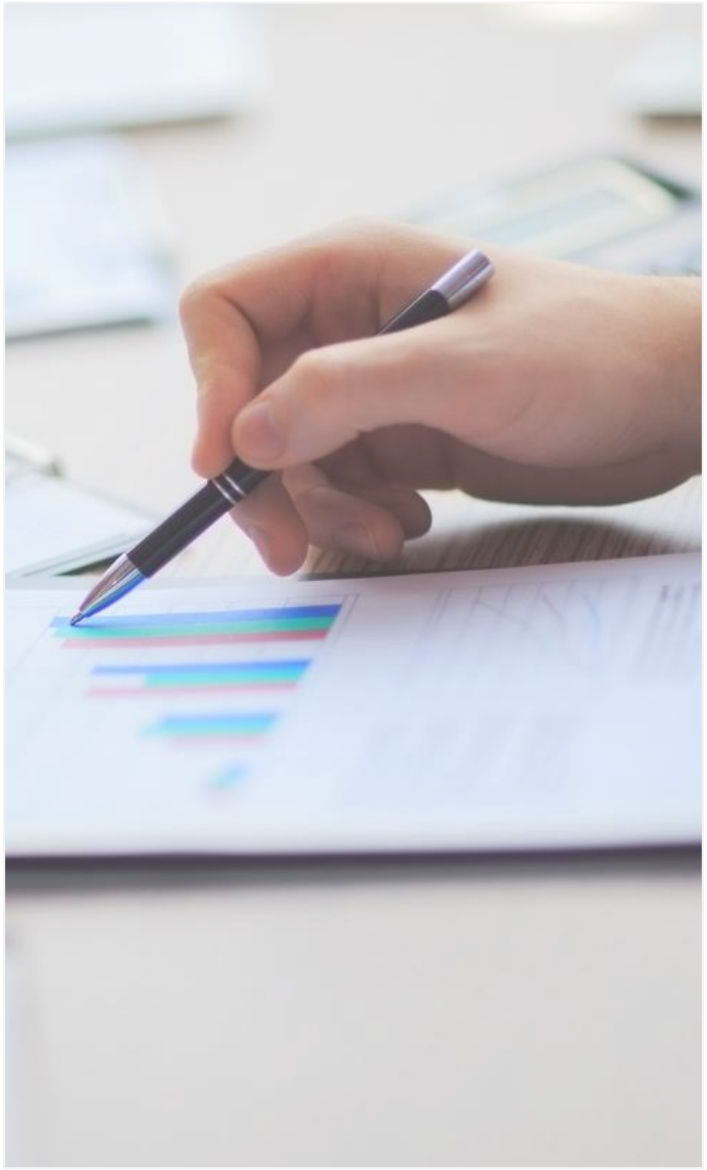
- Tapinarof, a novel chemical entity, was shown to have rapid onset and efficacy with clinically meaningful and statistically significant differences observed for all primary and secondary endpoints in pivotal studies.
- ~40% of tapinarof treated patients achieved complete disease clearance (PGA=0) in the long-term extension trial with treatment effect consistent regardless of baseline disease characteristics, severity, and patient demographics.
- Uniquely positioned to potentially transform the two largest global immuno-dermatology markets: psoriasis ($16.5B in 2019) and atopic dermatitis ($2.3B in 2019)
- NDA filed; FDA PDUFA action expected in 2Q 2022
- Comprehensive commercial planning underway for 2H 2022

Tapinarof: Phase 3 Program Points to Five Key Attributes

- **Treatment Effect –** Primary efficacy endpoints met in PSOARING 1 and PSOARING 2 (p-values <0.0001); all secondary endpoints achieved including PASI75
- **Durability (On Therapy) –** No evidence of tachyphylaxis observed, suggesting treatment durability during the trials
- **Remittive Effect (Off Therapy) –** PSOARING 3 interim analysis showed median remittive effect of ~4 months (defined as off-therapy maintenance of PGA score of 0 or 1) for some patients during the trials
- **Safety –** No Tapinarof SAEs reported in Phase 3 program; majority of AEs localized, mild to moderate in nature
- **Tolerability –** Well tolerated by patients; discontinuation rates due to AEs of 5.6-5.8% across studies; potential to be used across mild, moderate, & severe plaque psoriasis, including sensitive areas

Growing Development Pipeline

- Tapinarof in atopic dermatitis – Phase 3 Program initiated 3Q 2021; topline results anticipated 1H 2023
- Development pipeline addressing additional disease states & indications



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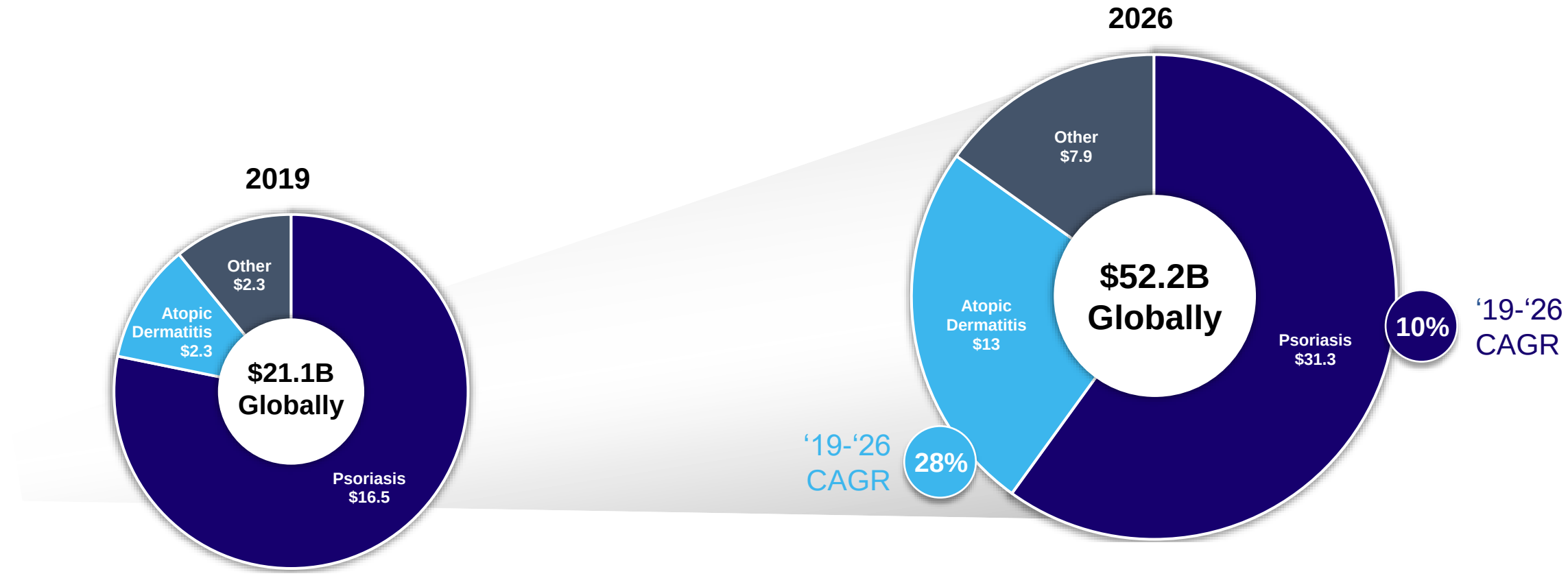
Tapinarof Targets the Two Largest Markets in Immuno-Dermatology

Psoriasis & atopic dermatitis markets projected to reach ~$31B in the US and ~$44B globally by 2026



U.S. Sales

Psoriasis: **$12.0B** (~73% of Global Sales)

Atopic Dermatitis: **$1.9B** (~82% of Global Sales)

U.S. Sales

Psoriasis: **$21.6B** (~69% of Global Sales)

Atopic Dermatitis: **$9.0B** (~70% of Global Sales)

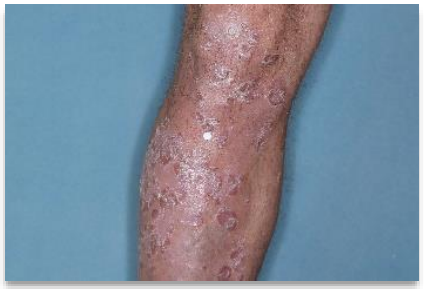
Evaluate Pharma Data: Global Psoriasis and Atopic Dermatitis Prescription Drugs Market and Forecast 2019 – 2026 (excluding aesthetic indications); Psoriasis Indication Profile, USA Market Analysis; Atopic Dermatitis Indication Profile, USA Market Analysis (extracted September 2021).

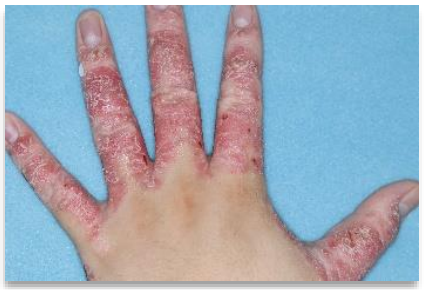
Tapinarof Offers a Transformational 2-in-1 Lead Product Candidate

Novel MOA delivering a unique & differentiated target product profile

Psoriasis Overview

Chronic, inflammatory disease characterized by red patches & plaques with silvery scales on skin

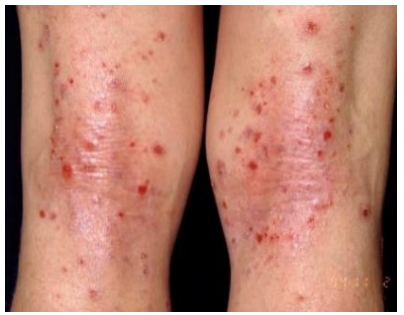




1. Large, mostly adult population (~8M people in U.S.)[1]
2. Limited topical options for long-term use prior to orals and biologics[2,3]
3. Long-term steroid use carries risk of significant side effects (e.g., skin atrophy)[4,5,6]

Atopic Dermatitis Overview

Chronic, itchy, inflammatory skin disease



1. Large, mostly pediatric population (~26M in United States)[7,8]
2. Safety concerns limit TCS long-term use, particularly for children[4,5]
3. Recent launches have not addressed unmet needs either due to tolerability issues or biologics that are not appropriate for patients with mild disease[9,10]

Sources: 1. Armstrong, AW., et al., JAMA Dermatol. 2021;157(8):940-946. doi:10.1001/jamadermatol.2021.2007. 2. Lebwohl, M. A clinician's paradigm in the treatment of psoriasis. Journal of the American Academy of Dermatology, 53, S59-69, 2005. 3. Kerdel, F., & Zaiac, M. An evolution in switching therapy for psoriasis patients who fail to meet treatment goals. Dermatologic Therapy 28, 390-403, 2015. 4. Draelos, ZD (2008) Current Medical Research and Opinion 24(4): 985-994. 5. Coondoo, A. et al. Side-effects of topical steroids: A long overdue revisit. Indian Dermatology Online Journal. V.5(4); 2014. 6. Alexander T. et al. (2018) Prescriptions for atopic dermatitis: oral corticosteroids remain commonplace. Journal of Dermatological Treatment, 29:3, 238-240. 7. National Eczema Association. (November 2020). Retrieved from https://nationaleczema.org/research/eczema-facts/. 8. Bieber T. Atopic dermatitis. New England Journal of Medicine. 2008;358(14):1483-1494. 9. Lin CP-L, Gordon S, Her MJ, Rosmarin D, A Retrospective Study: Application Site Pain with the Use of Crisaborole, a Topical PDE4 Inhibitor, Journal of the American Academy of Dermatology (2018), doi:https://doi.org/10.1016/j.jaad.2018.10.054. 10. DUPIXENT Package Insert.

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Track Record of Success in Developing & Commercializing Innovative Dermatology Products at Multiple Companies

Todd Zavodnick

Chief Executive Officer

Phil Brown MD, JD

Chief Medical Officer

Chris Chapman

Chief Commercial Officer

David Rubenstein MD, PhD

Chief Scientific Officer

Michael Swartzburg

Chief Financial Officer

Chris Van Tuyl Esq

General Counsel

Elaine Clark

VP, Global Regulatory Affairs, QA & PV

Paul Seaback

SVP, Technical Operations

Anna Tallman

VP, Medical Affairs

Diana Villalobos

VP, Clinical

Peter Nicholson

SVP, Business Development

Innovative Immuno-Dermatology Pipeline with Global Rights[1]

PRODUCT CANDIDATE	INDICATION	STAGE OF DEVELOPMENT				KEY MILESTONE
		Preclinical	Phase 1	Phase 2	Phase 3	
CLINICAL STAGE DEVELOPMENT PROGRAMS						
TAPINAROF (DMVT-505) A topical therapeutic AhR modulating agent inhibiting several proinflammatory factors	**Psoriasis**				→	**NDA submitted; FDA PDUFA action expected in 2Q 2022**
	Atopic Dermatitis				→	Phase 3 Program initiated 3Q 2021; topline results anticipated 1H 2023
CERDULATINIB (DMVT-502) A topical dual JAK/Syk inhibitor	**Vitiligo**			→		Phase 2a completed 1H 2021
	Atopic Dermatitis		→			Phase 2a protocol in development
OXYBUTYNIN/PILOCARPINE (DMVT-504) Oral combination of immediate-release muscarinic antagonist and delayed-release muscarinic agonist	**Hyperhidrosis**		→			Phase 2b protocol in development
EARLY-STAGE DEVELOPMENT PROGRAMS						
DMVT-503 A novel mechanism of action for the topical treatment of acne vulgaris	**Acne Vulgaris**	→				Preclinical studies ongoing

1. Excludes certain Asian territories.

TAPINAROF CREAM PSORIASIS PROGRAM

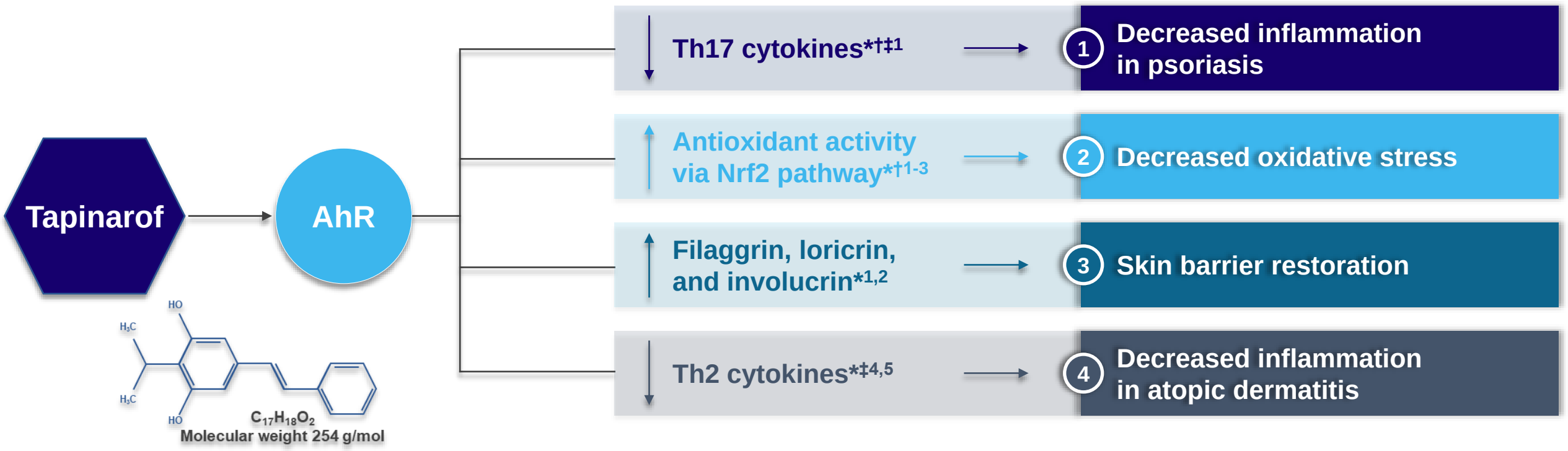
Phil Brown MD, JD, Chief Medical Officer

dermavant™

Tapinarof: Novel Multi-Modal Mechanism of Action

Inhibits inflammatory cytokines, promotes epidermal barrier restoration & decreases oxidative stress

TAMA is designed to inhibit two pro-inflammatory pathways implicated in psoriasis & atopic dermatitis. AhR modulation by tapinarof also increases antioxidant activity & promotes skin barrier restoration.[1-5]



*Demonstrated in vitro. †Demonstrated ex vivo. ‡Demonstrated in mice models. AhR, aryl hydrocarbon receptor; Nrf2, nuclear factor erythroid 2-related factor 2; TAMA, therapeutic AhR modulating agent; Th, T helper cell. 1. Smith SH et al. J Inv Dermatol 2017;137:2110–2119. 2. Furue M et al. J Dermatological Sci. 2015;80:83–88. 3. Tsuji G et al. J Invest Dermatol. 2012;132:59–68. 4. Dermavant DOF [DMVT-505 Th2 Polarization; Apr 2015]. 5. Dermavant DOF [DMVT-505 AD Mouse Model; Oct 2016].

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PSOARING Program – Executive Summary

Novel & differentiated attributes observed – NDA filed; PDUFA action expected in 2Q 2022

Treatment Effect

- PSOARING 1 and PSOARING 2 PGA primary endpoints met (P<0.0001) and PASI75 secondary endpoint met
- In interim analysis (IA) of PSOARING 3 LTE data, 57.3% of patients achieved PGA = 0 / 1 and 39.2% achieved PGA = 0

Durability (On-Therapy)

- Improvement in treatment effect observed with continued use beyond 12 weeks
- No evidence of tachyphylaxis, suggesting durability with continued use during the trial

Remittive Effect (Off-Therapy)

- Approximately 4-month median remittive effect observed among patients entering PSOARING 3 with PGA = 0 (n=78)
- Other anti-inflammatory compounds demonstrate rapid loss of clinical benefit after drug withdrawal

Safety

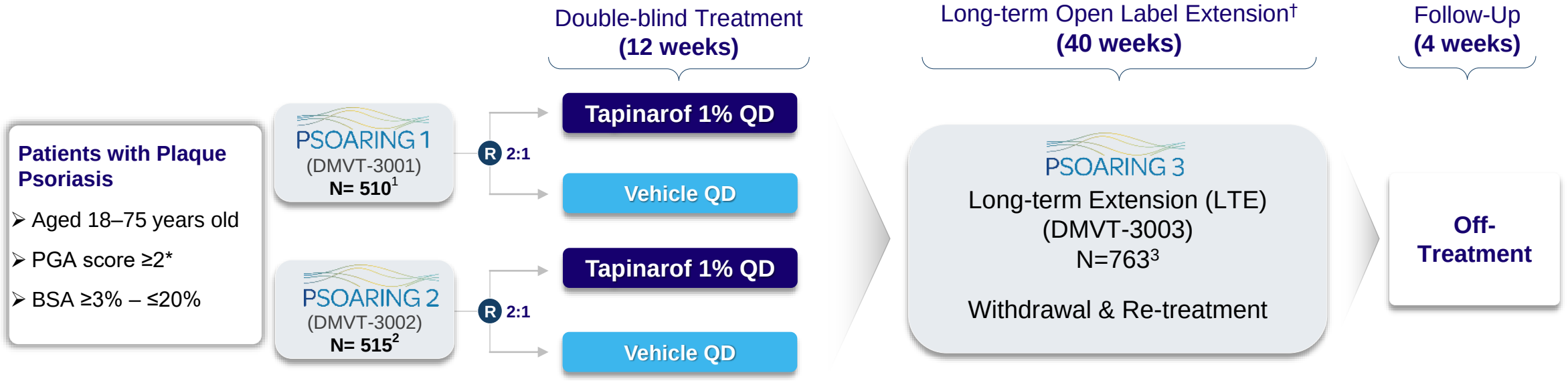
- AEs consistent with previous studies, no new safety signals identified
- No treatment-related serious adverse events reported in PSOARING 1, 2 or PSOARING 3 IA
- Over 2,200 patients have enrolled in 18 clinical trials (phase III trials included all disease severities)

Tolerability

- Consistent safety and tolerability observed for all skin locations and durations of treatment studied
- Discontinuation rate due to AEs was 5.6% - 5.8% across studies
- Greater than 90% of eligible patients from PSOARING 1 and PSOARING 2 enrolled in PSOARING 3

Phase 3 PSOARING Program – Study Design

Over 1,000 patients enrolled in two identically-designed pivotal trials followed by long-term open-label extension study



Primary endpoint:

› PGA score of 0 (clear) or 1 (almost clear) & ≥2-grade improvement from baseline at Week 12

Secondary endpoints:

› Proportion of patients achieving PASI75 from baseline at Week 12
› Proportion of patients achieving PASI90 from baseline at Week 12
› PGA score 0 or 1 at Week 12
› Mean % change in total BSA from baseline at Week 12

Open Label Extension:

› Patients entering open label extension remain on treatment with tapinarof 1% QD until a PGA score of 0 is achieved

Re-treatment criteria:

› Patients with psoriasis disease worsening, defined as PGA score ≥2, enter re-treatment with tapinarof 1% QD until a PGA of 0 is achieved

*Patients with PGA of 2 (mild) and PGA of 4 (severe) limited to ~10% each of the total randomized population; ~80% of the total randomized population with PGA of 3 (moderate); †Patients electing not to participate in LTE had follow-up visit 4 weeks after completion of treatment period. BSA, body surface area; LTE, long-term extension; PASI75, ≥75% improvement in Psoriasis Area and Severity Index; PASI90, ≥90% improvement in Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily.

1. Clinicaltrials.gov; NCT03956355. 2. Clinicaltrials.gov; NCT03983980. 3. Clinicaltrials.gov; NCT04053387.

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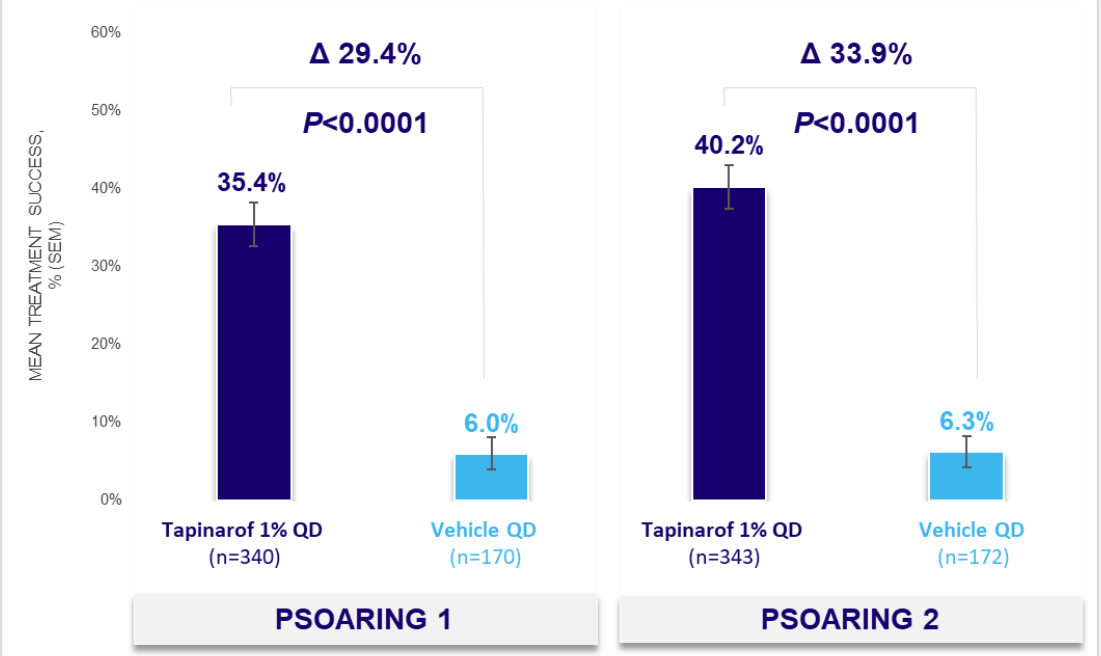
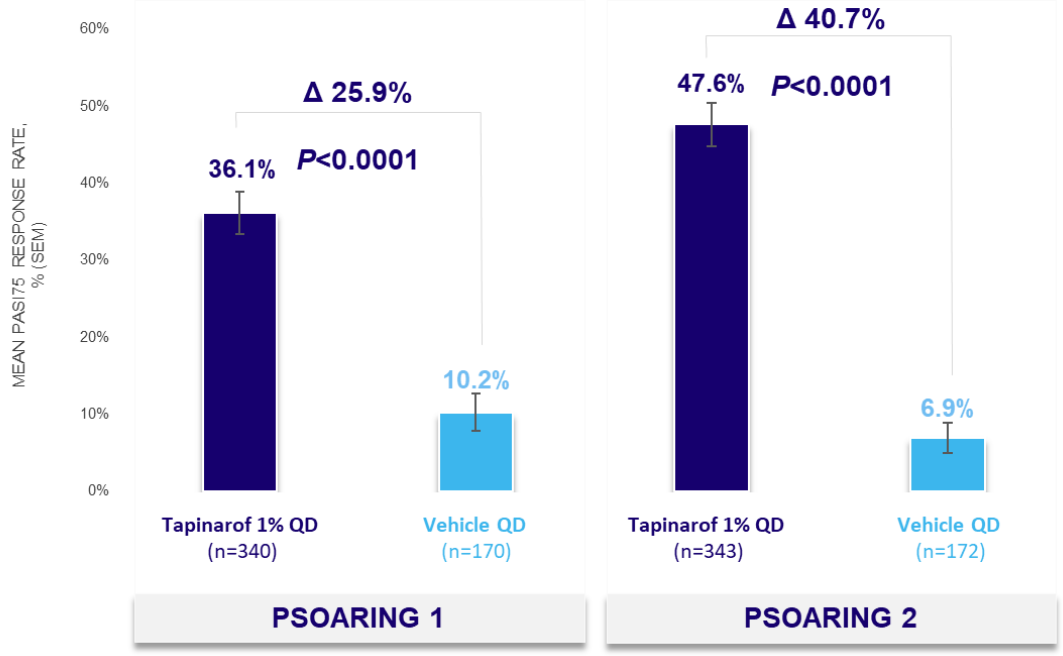
PSOARING 1 & 2 Pivotal Program – Primary & Secondary Efficacy Results

Primary efficacy endpoint met, as demonstrated by magnitude of PGA treatment success* & †PASI75

PGA Score of 0 or 1 & ≥2-grade Improvement from Baseline at Week 12 *(ITT, MI)*



PASI75 from Baseline at Week 12 *(ITT, MI)*



Key Safety Highlights

- AEs consistent with previous studies, no new safety signals identified, highlights predictability of drug safety profile
- Folliculitis, nasopharyngitis, contact dermatitis, headache, pruritis and dermatitis most common TEAEs
- Low study discontinuation rate due to folliculitis (1.8% in PSOARING 1 and 0.9% in PSOARING 2)
- Favorable tolerability on sensitive sites including face, neck, axillae, inframammary, skin folds, genitalia, and anal crux

*PGA score of 0 (clear) or 1 (almost clear) and ≥2-grade improvement from baseline. †PASI75 response: ≥75% improvement in PASI from baseline. ITT, intention-to-treat; MI, multiple imputation; NDA, new drug application; PGA, Physician Global Assessment; PASI, Psoriasis Area and Severity Index; QD, once daily; SEM, standard error of mean. P-value based upon Cochran-Mantel-Haenszel analysis stratified by baseline PGA score.

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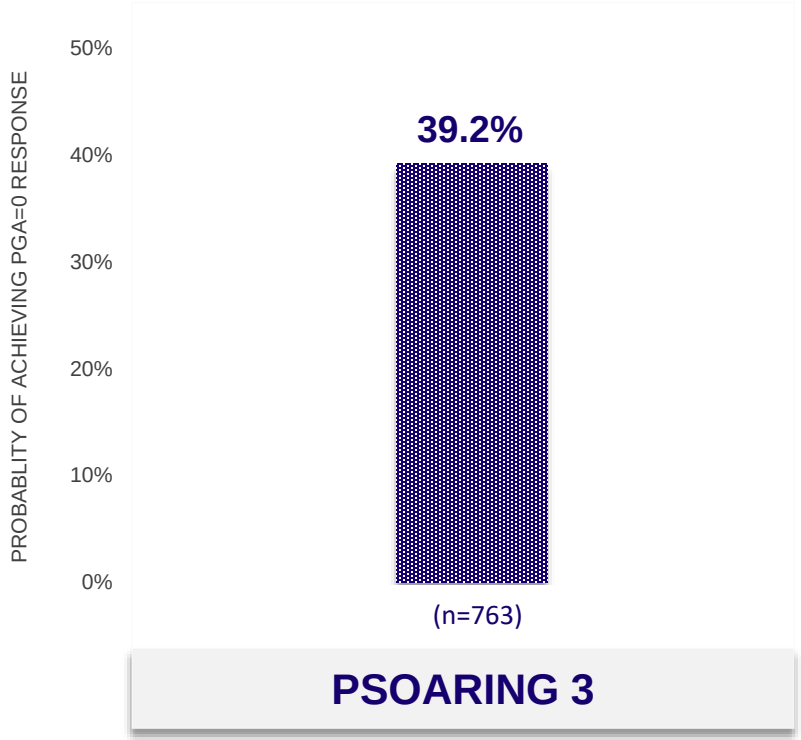
PSOARING 3 LTE Study – ~40% of Tapinarof Treated Patients Achieved PGA 0

PGA of 0 corresponds to complete disease clearance

Data from Interim Analysis, 11/25/20

PGA Score of 0 from Baseline

(ITT, OC)



% Patients Achieving PGA of 0 *(ITT, OC)*

	Overall (n=763)	Patients who Entered LTE Trial on Tapinarof 1% QD & **Continued** on Tapinarof 1% QD **(n=508)**	Patients who Entered LTE Trial on Vehicle QD & **Started** on Tapinarof 1% QD **(n=255)**
Number of Patients Who Entered the Study with PGA ≥ 1	221	139	82
Number of Patients Who Entered the Study with PGA=0	78	73	5
Overall achievement of a PGA=0 during the study, n (%)	**299/763 (39.2%)**	**212/508 (41.7%)**	**87/255 (34.1%)**

ITT, intention-to-treat, OC, observed cases; PGA, Physician Global Assessment; QD, once daily.

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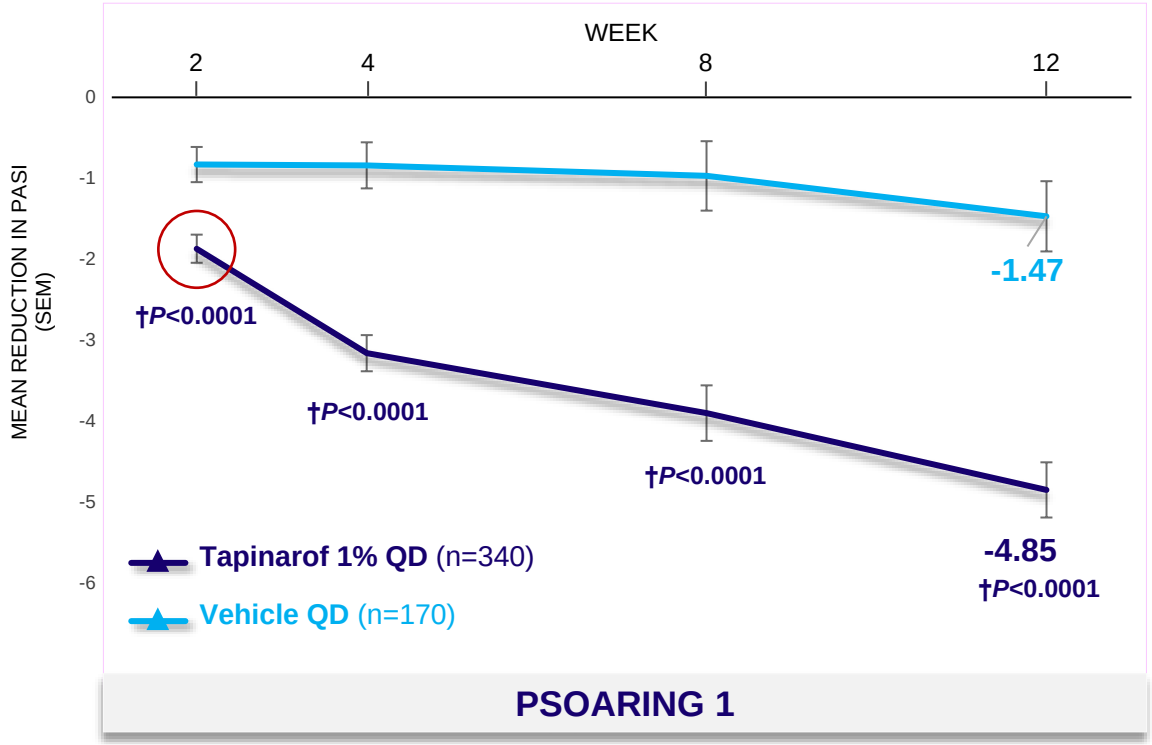
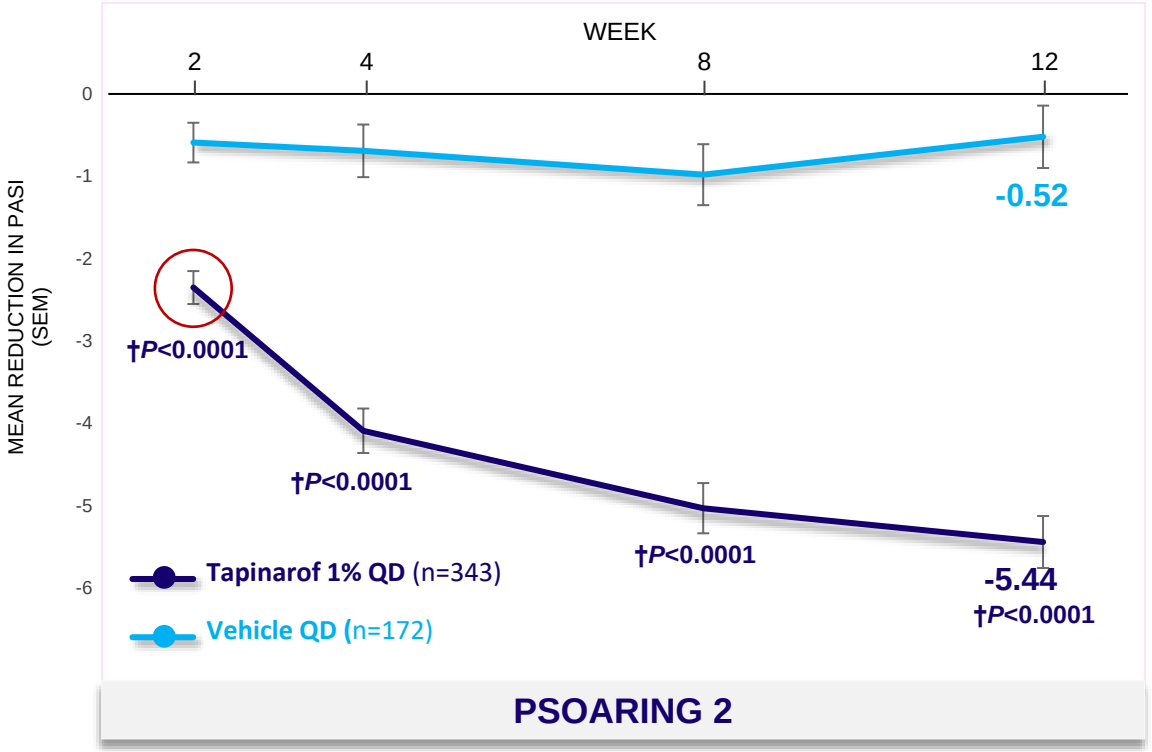
Phase 3 PSOARING Program – Rapid Onset of Action

Statistically significant PASI improvement as early as Week 2

Mean Change in PASI from Baseline to Week 12 (ITT, MI)*



PSOARING 1



PSOARING 2

Exploratory Endpoint Achieved

- Rapid onset of activity with 20% reduction in disease activity by Week 2 and difference versus vehicle continues to increase over time
- PASI, a quantitative measure, showed earlier separation than PGA global measures demonstrating reduction in disease activity

*Least squares mean. †Denotes statistical significance.
ITT, intention-to-treat; MI, multiple imputation; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily; SEM, standard error of mean.

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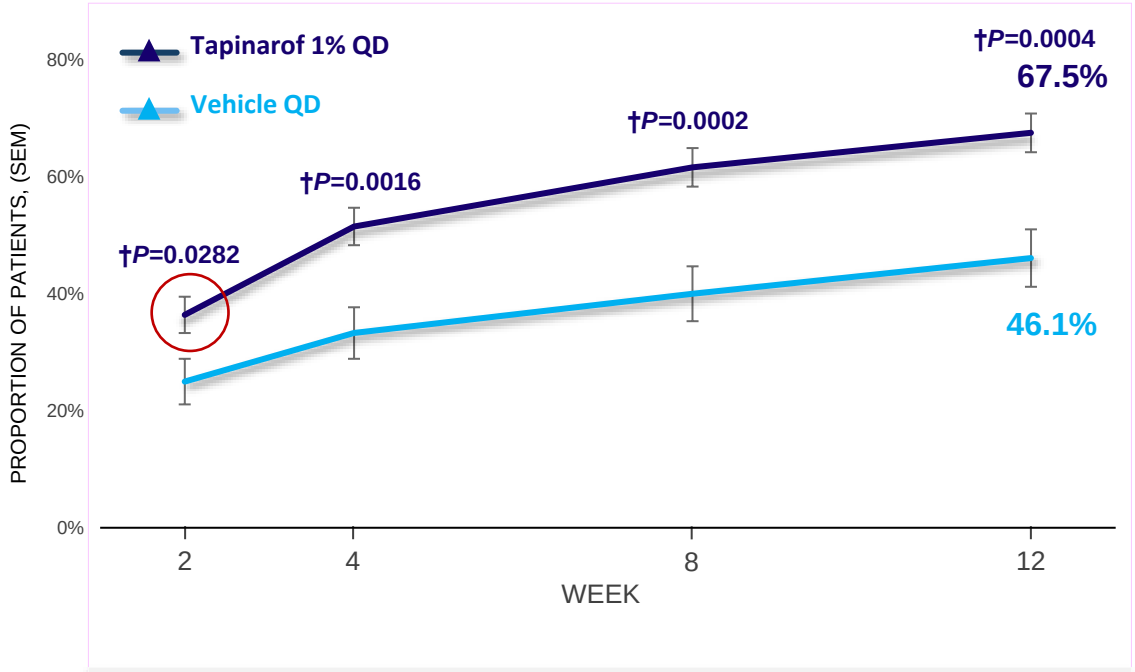
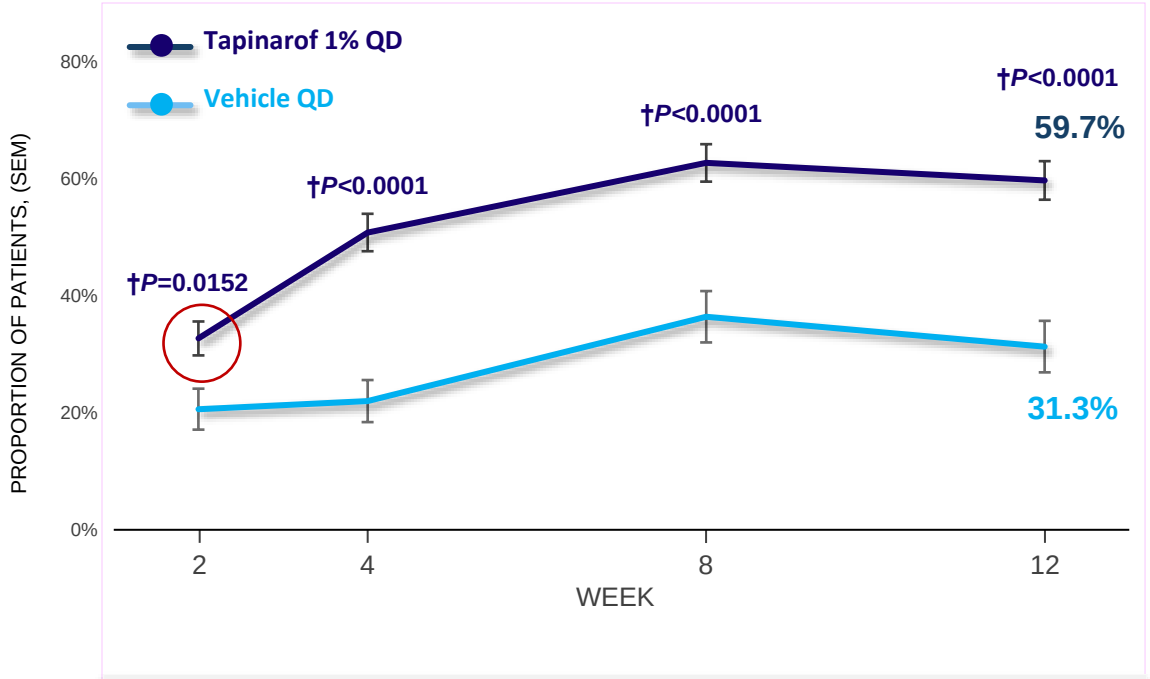
Phase 3 PSOARING Program – Rapid Peak Pruritis Improvement

NRS of at least a 4-point reduction achieved as early as Week 2

Minimum 4-point Improvement in Peak Pruritus NRS from Baseline to Week 12 (ITT, OC)*



PSOARING 1



PSOARING 2

Exploratory Endpoint Achieved

- Mean baseline peak NRS was 5.7 for tapinarof and 6.1 for vehicle in PSOARING 1 and 5.9 and 6.1, respectively in PSOARING 2
- Clinically meaningful improvement in itch for tapinarof using the gold standard of a minimum 4-point improvement on the NRS scale[1,2]

*Least squares mean. Peak Pruritus NRS 11-point scale from 'no itch' (0) to 'worst itch possible' (10) over 24-hour period. In those patients with at least a 4-point peak pruritus NRS at baseline. †Denotes statistical significance.
ITT, intention-to-treat; NRS, numeric rating scale; OC, observed cases; QD, once daily; SEM, standard error of mean.

1. Lebwohl M et al. Am J Clin Dermatol. 2016;17:87–97; 2. Kimball AB et al. Br J Dermatol. 2016;175:157–162.

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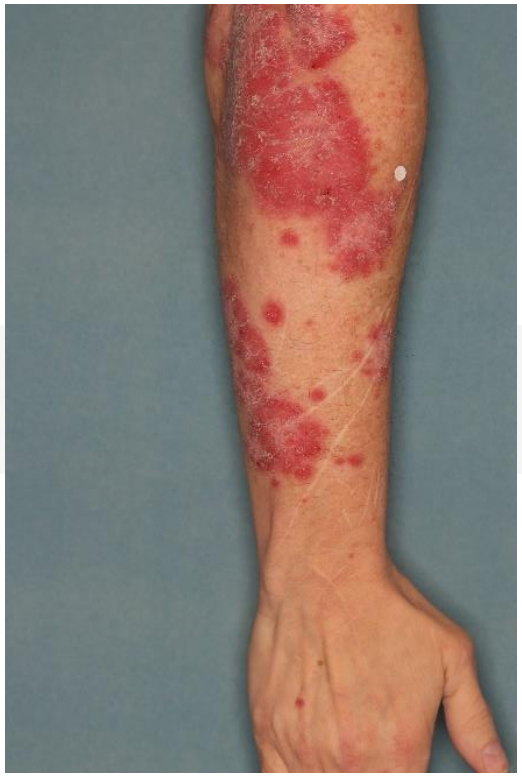
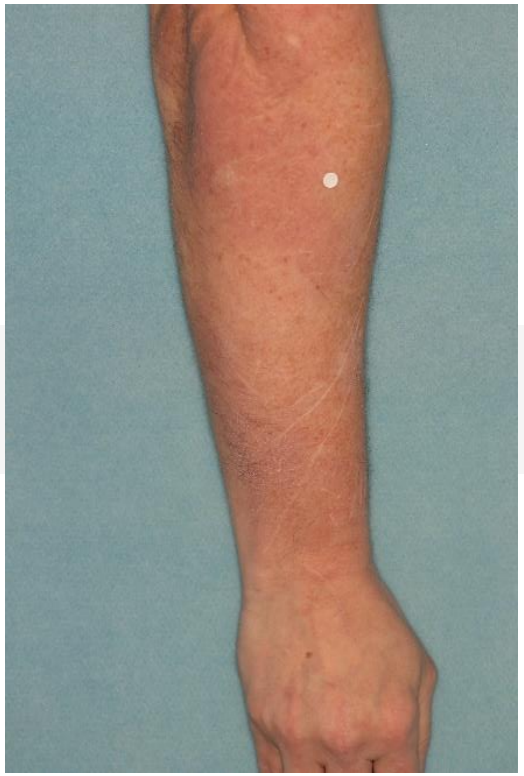
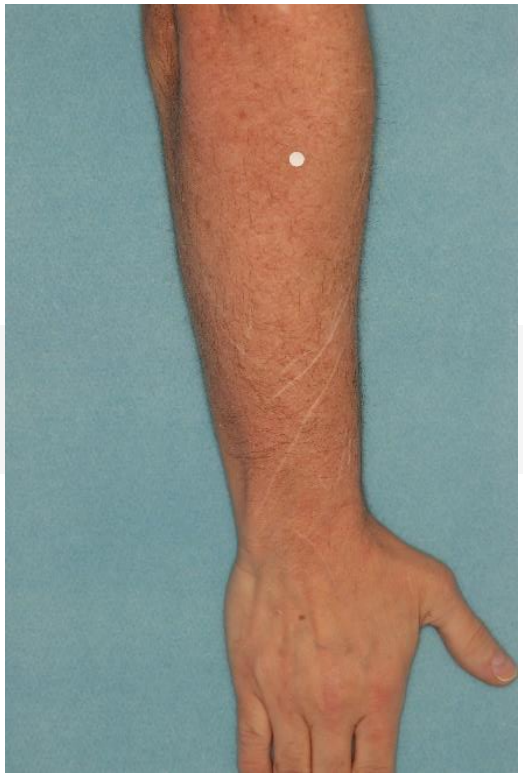
Phase 3 PSOARING Program – Tapinarof Achieves Primary Endpoint

Rapid & complete clearance of psoriasis in patient achieving primary endpoint

BASELINE	WEEK 4	WEEK 12
		
› PGA = 3 › PASI = 17.6	› PGA = 2 › PASI = 4	› PGA = 0 › PASI = 0

Results shown for one patient are not necessarily indicative of results for other patients, additional trials or other uses

PGA and PASI are global efficacy assessments. Example of one representative target lesion of one tapinarof treated patient from the PSOARING 1 clinical trial. PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.

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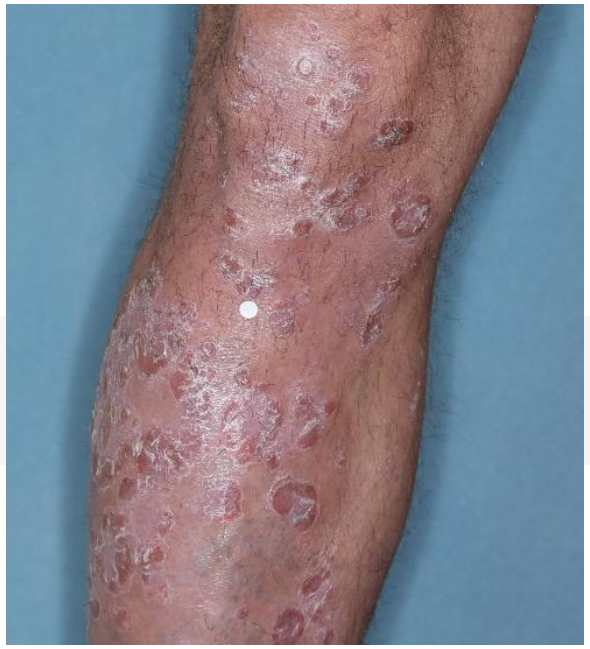
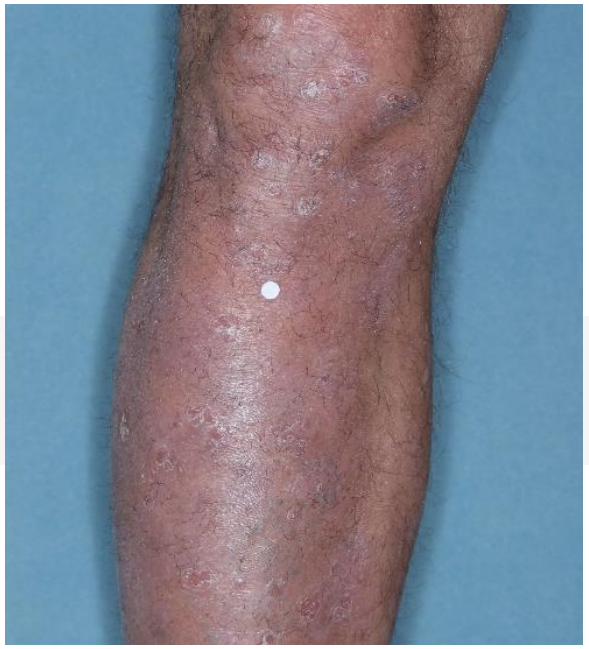
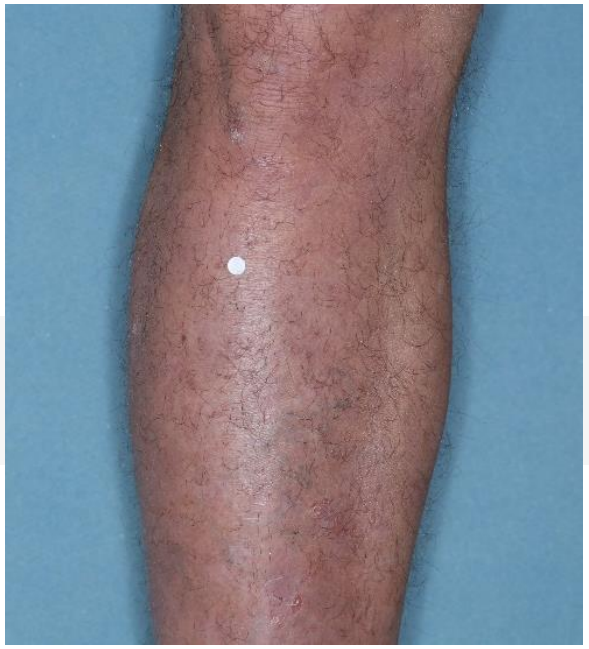
Phase 3 PSOARING Program – Tapinarof Achieves Primary Endpoint

Lower extremity disease: rapid response in patient achieving primary endpoint

BASELINE	WEEK 4	WEEK 12
		
› PGA = 3 › PASI = 16.0	› PGA = 2 › PASI = 5.5	› PGA = 1 › PASI = 2.4

Results shown for one patient are not necessarily indicative of results for other patients, additional trials or other uses

PGA and PASI are global efficacy assessments. Example of one representative target lesion of one tapinarof treated patient from the PSOARING 1 clinical trial. PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.

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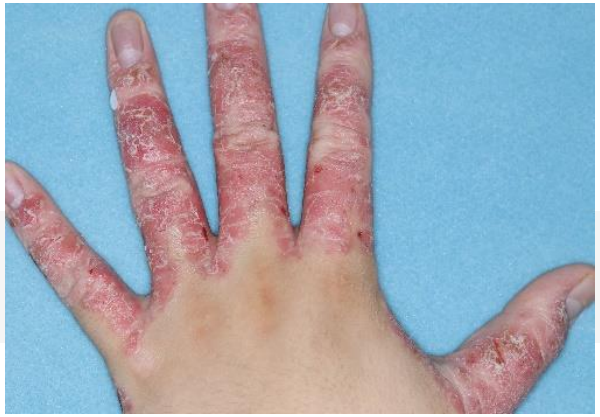
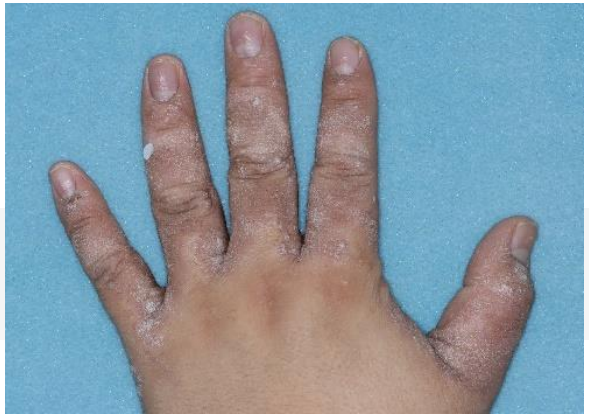
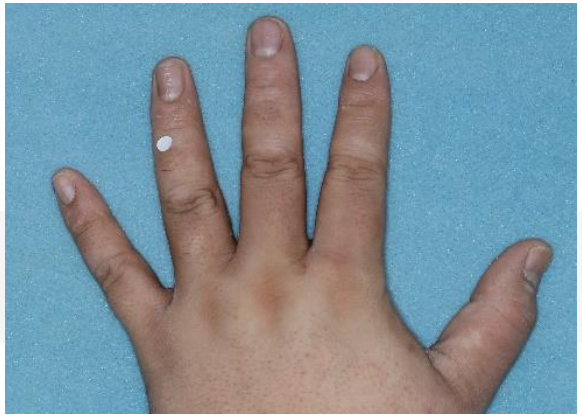
Phase 3 PSOARING Program – Tapinarof Clinical Improvement

Clinical improvement in a patient not achieving regulatory endpoint

BASELINE	WEEK 4	WEEK 12
		
› PGA = 3 › PASI = 12.0	› PGA = 3 › PASI = 12.0	› PGA = 2 › PASI = 8.4

Results shown for one patient are not necessarily indicative of results for other patients, additional trials or other uses

PGA and PASI are global efficacy assessments. Example of one representative target lesion of one tapinarof treated patient from the PSOARING 1 clinical trial. PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.

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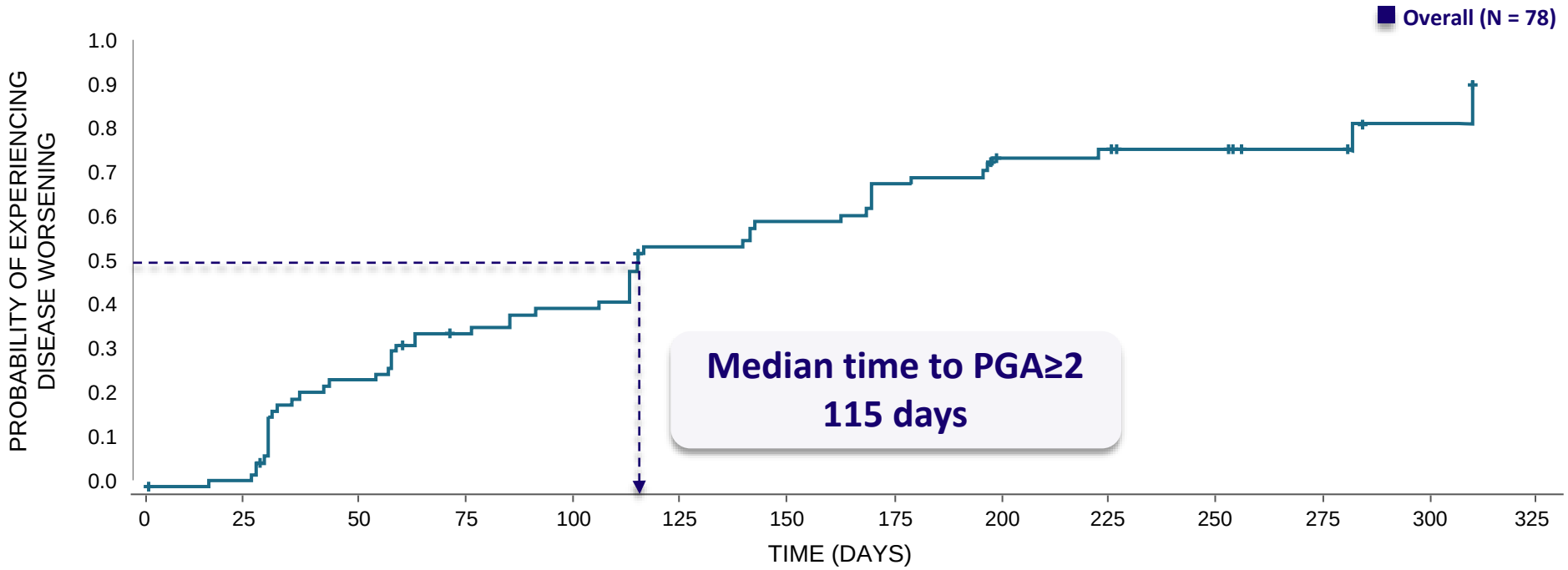
PSOARING 3 – Clear or Almost Clear for ~4 months Off Treatment

Remittive (off-therapy) effect observed among patients entering with PGA=0

Data from Interim Analysis

Time to First PGA ≥2 *(ITT, OC)*



Key Points

- Overall, median time to PGA ≥ 2 was 115 days (95% CI = 85 to 162 days, approximately 3 to 5 months)

CI, confidence interval; ITT, intention-to-treat, LTFU, lost to follow-up; OC, observed cases; PGA, Physician Global Assessment.

Phase 3 PSOARING Studies: Most Common Treatment-Related TEAEs ≥ 1%

Consistent & predictable safety profile observed

	PSOARING 1		PSOARING 2	
Patients, n (%)	**Tapinarof 1% QD (n=340)**	Vehicle QD (n=170)	**Tapinarof 1% QD (n=343)**	Vehicle QD (n=172)
Folliculitis	**70 (20.6%)**	2 (1.2%)	**54 (15.7%)**	1 (0.6%)
Contact dermatitis	**13 (3.8%)**	1 (0.6%)	**16 (4.7%)**	0 (0%)
Headache	**5 (1.5%)**	1 (0.6%)	**1 (0.3%)**	0 (0%)
Pruritus	**4 (1.2%)**	0 (0%)	**2 (0.6%)**	0 (0%)
Dermatitis	**1 (0.3%)**	0 (0%)	**4 (1.2%)**	0 (0%)

Key Points

- Favorable safety profile observed over 52 weeks, AEs consistent with previous studies[1,2], no tapinarof-related SAEs
- Most treatment-related events are localized to site of application & mild to moderate in nature
- Low overall AE discontinuation rate for patients on tapinarof: <5.8%
  - Discontinuation due to folliculitis: 1.8% / 0.9% (PSOARING 1 / PSOARING 2); 1.2% (PSOARING 3)
- Consistent & predictable safety profile - over 2,200 patients have enrolled in 18 clinical trials[3]

Count reflects numbers of patients reporting one or more AEs that map to grouped MedDRA preferred term. A patient is counted once only for each type of AE but could experience ≥1 event of the AE. QD, once daily; TEAE, treatment-emergent adverse event. 1. Robbins K, et al. J Am Acad Dermatol. 2019;80:714–721; 2. Stein Gold L, et al. J Am Acad Dermatol. 2020; doi: 10.1016/j.jaad.2020.04.181. 3. Dermavant Data on File, Dec 2020.

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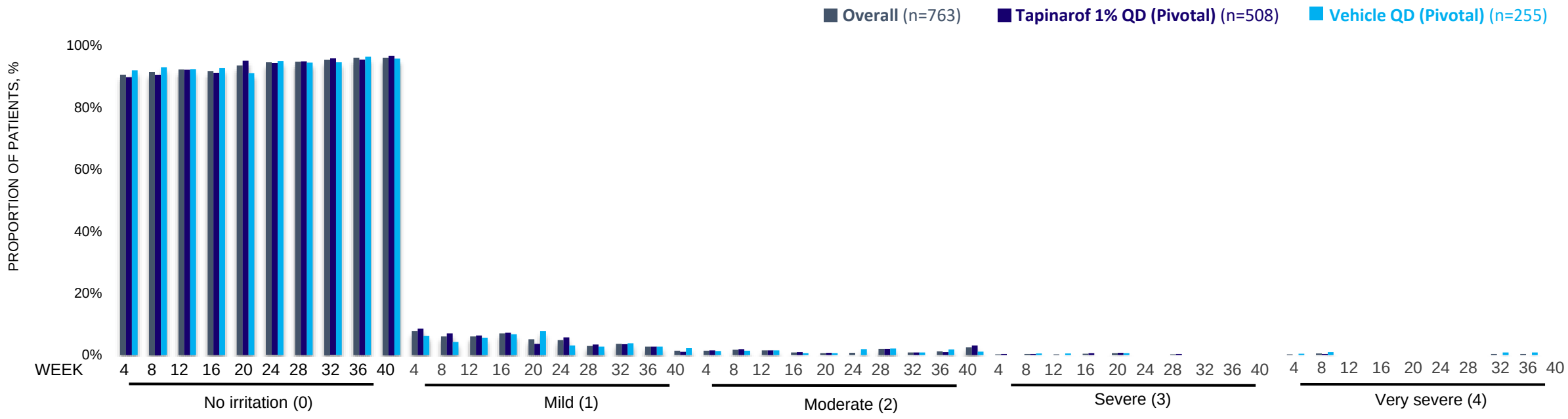
PSOARING 3 LTE Study – Investigator-Assessed Irritation

Favorable tolerability without regard to site of application or duration of use

Data from Interim Analysis

Investigator Assessed Irritation Scores* Across All Application Sites *(Safety population)*



Key Points

- Investigators assessed that ≥ 90% of patients had no irritation (score of 0) over 40 weeks of treatment
- Favorable tolerability on sensitive sites including face, neck, axillae, inframammary, skin folds, genitalia, & anal crux

*Investigator assessed irritation scores (0–4) assess the presence and overall degree of irritation at the application sites according to the Local Tolerability Scale (dryness, erythema, and peeling) – no irritation (0), mild (1), moderate (2), severe (3), very severe (4). The score ideally represents an 'average' across all application sites. QD, once daily.

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TAPINAROF CREAM
ATOPIC DERMATITIS PROGRAM
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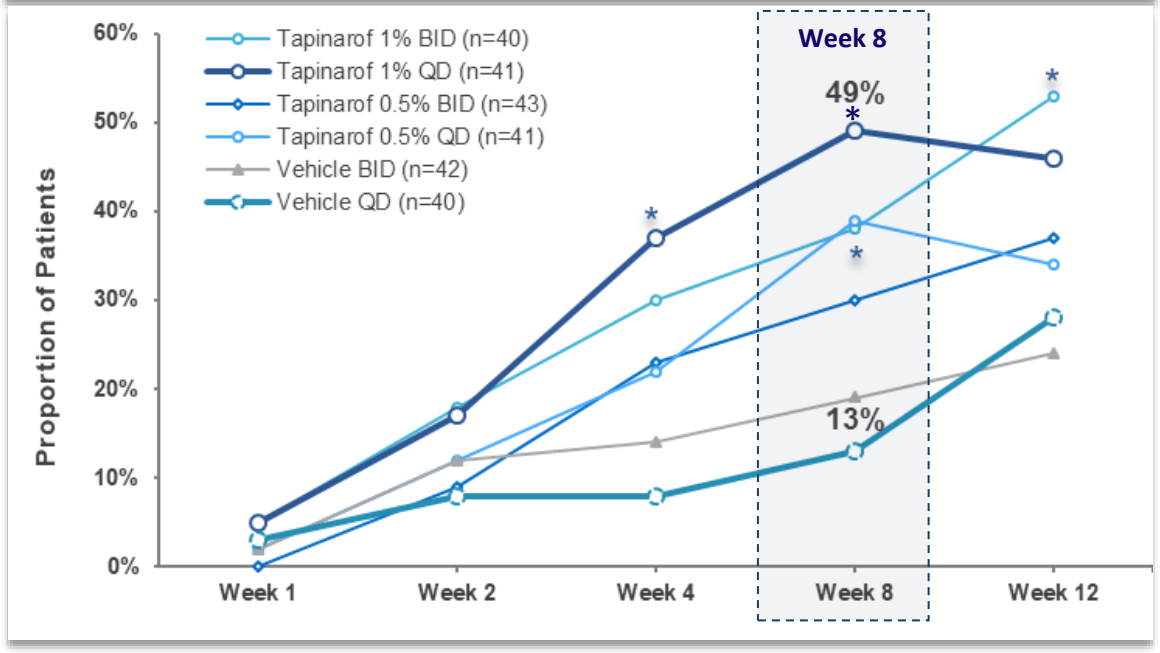
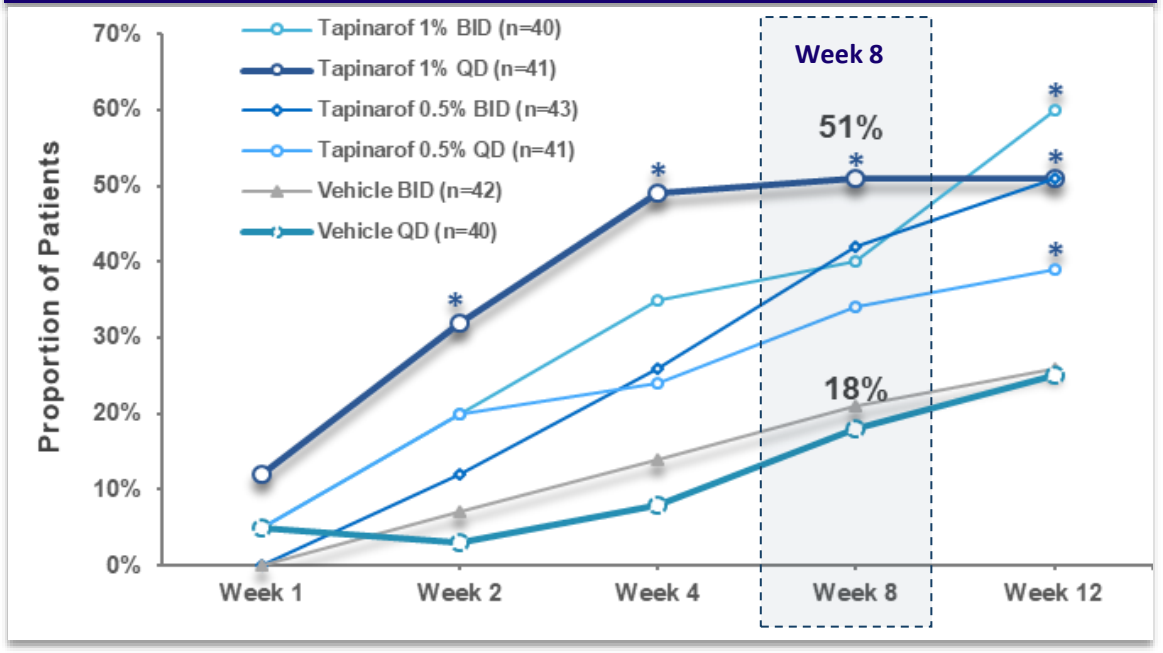
Tapinarof Atopic Dermatitis Phase 2b Trial – Efficacy Results

Response rates: 49% of patients achieved IGA clear or almost clear and ≥2-grade improvement and 51% of patients achieved EASI75 after 8 weeks of treatment with tapinarof 1% QD

IGA score 0 or 1 and ≥2-grade improvement at week 8 Primary Endpoint was at 12 Weeks: Assessed in ITT Population (NRI Analysis)



EASI75 at Week 8 Secondary Endpoint was at 12 Weeks: Assessed in ITT Population (NRI Analysis)



*Difference vs vehicle is statistically significant at p-value of 0.05 or lower. NRI analysis to account for higher dropout rates in vehicle group. BID, twice daily; IGA, Investigator Global Assessment; EASI, Eczema Area and Severity Index; ITT, intention to treat; NRI, non-responder imputation; QD, once daily. 1. Peppers J, et al. J Am Acad Dermatol. 2019;80:89-98 and Dermavant DOF [CSR 203121; 16Jun2017]. 2. Paller AS, et al. SKIN The Journal of Cutaneous Medicine. 2018;2:S60.

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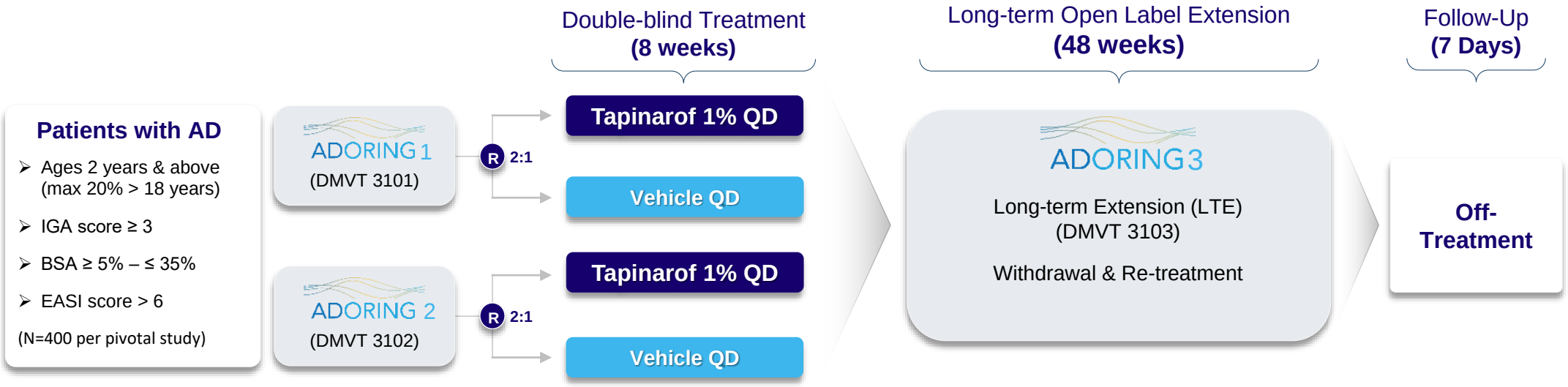
Phase 3 ADORING Program – Study Design

Two identically-designed pivotal trials followed by long-term, open-label extension

Study Objective: To demonstrate statistically significant treatment effect of tapinarof as compared with vehicle and an acceptable safety profile in moderate to severe atopic dermatitis patients



Primary endpoint:

› Proportion of subjects who have a vIGA-AD™ 0 or 1 Baseline at Week 8

Secondary endpoints:

› Proportion of subjects with EASI 75 @ week 8
› Mean change in %BSA from Baseline at Week 8
› Proportion of subjects with EASI 90 @ Week 8
› Proportion of subjects with > 4-pt reduction in PP-NRS @ Week 8

PROs:

› LTE
› DLQI/CLDQI/IDQOL
› EQ-5D-5L/EQ-5D-Y
› POEM
› DFI
› PP-NRS

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COMMERCIAL OVERVIEW

Chris Chapman, Chief Commercial Officer

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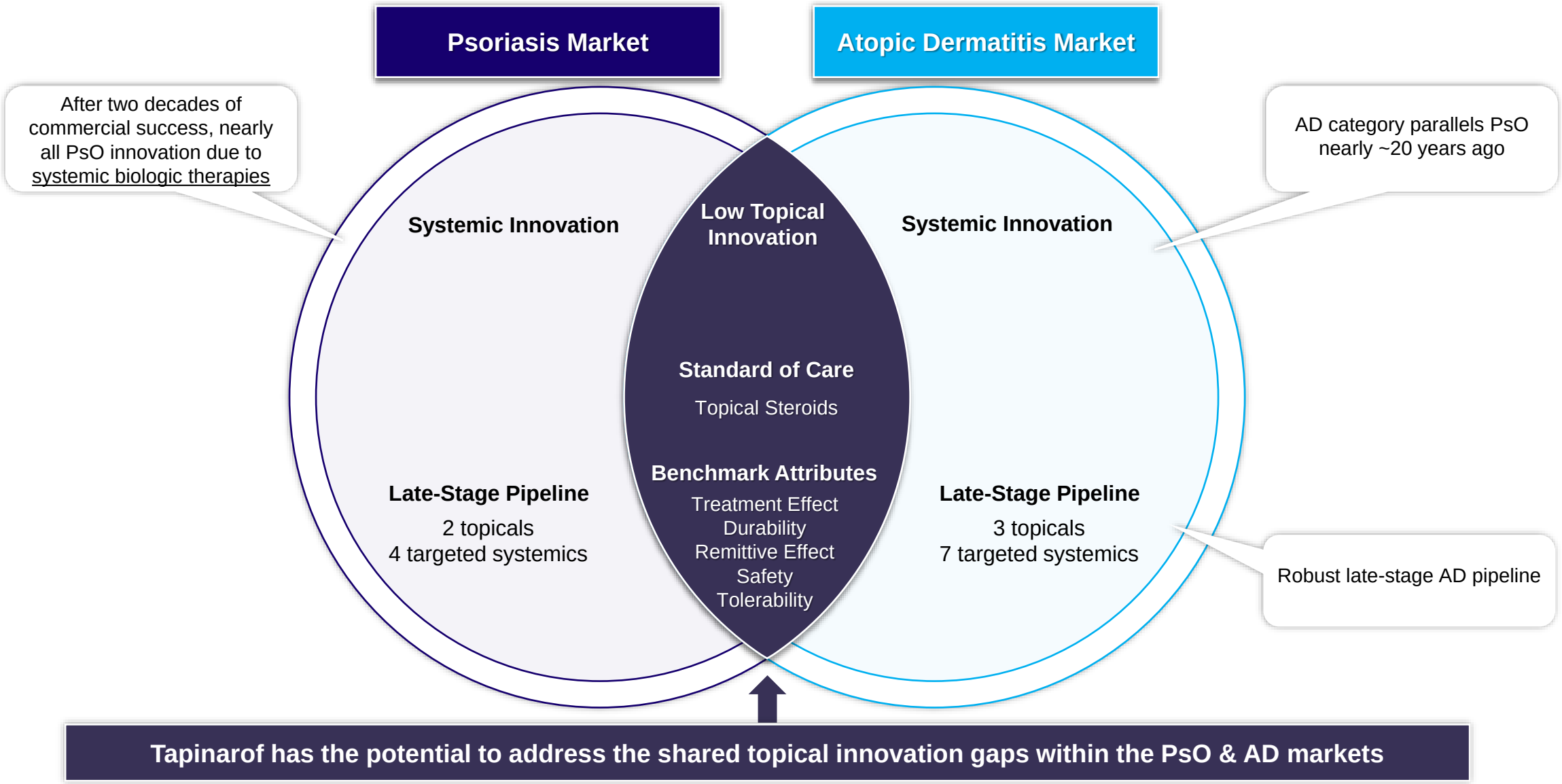
Lack of Topical Innovation Offers Tapinarof Unprecedented Opportunity

Establishing a potential new topical benchmark in psoriasis & atopic dermatitis

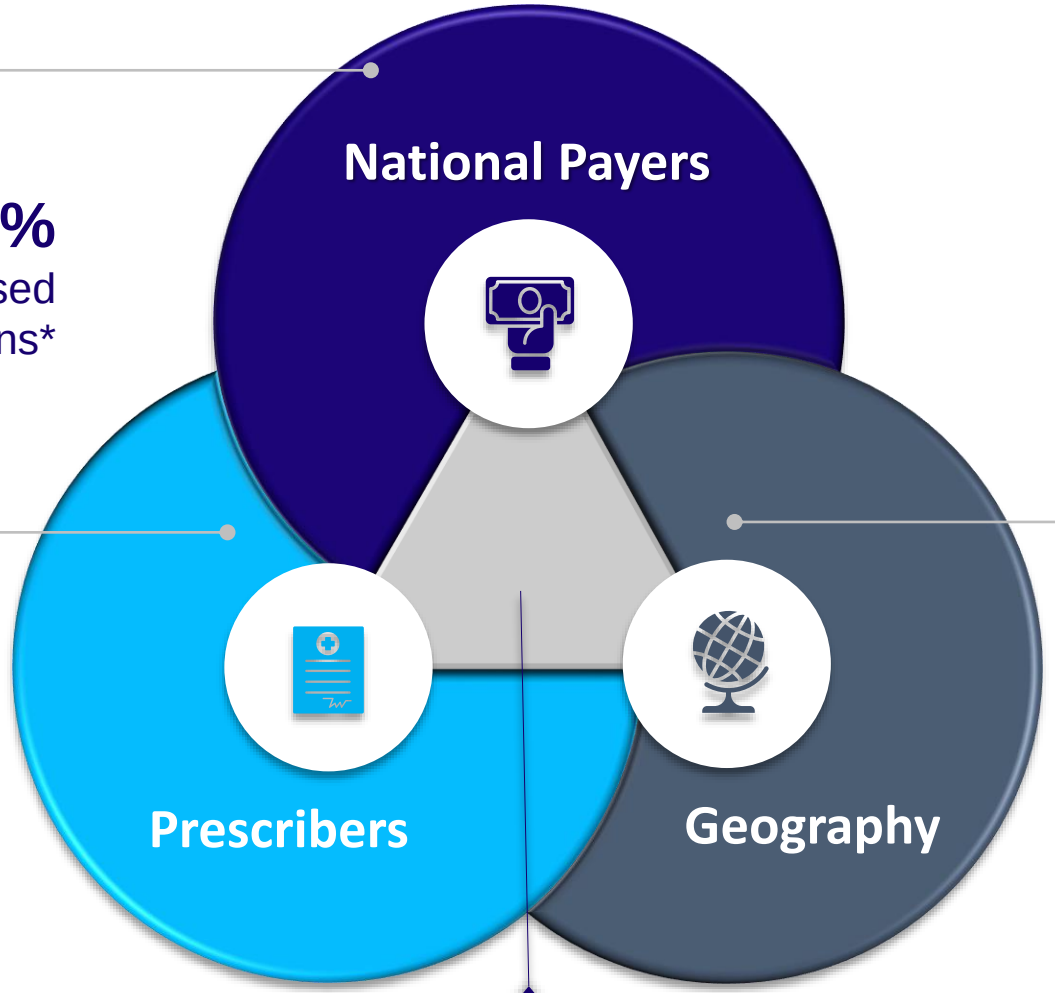


Sources: 1. PsO Market - Clinicaltrials.gov. (NCT03556202, NCT03598790, NCT03624127, NCT03611751, NCT03895372, NCT03431974, NCT02969018, NCT02776033, NCT02888236, NCT03308799, NCT03956355, NCT03983980, NCT04211389, NCT04211363). 2. AD Market - Clinicaltrials.gov. (NCT03308799, NCT03956355, NCT03983980, NCT04211389, NCT04211363, NCT03334396, NCT03334422, NCT03349060, NCT03575871, NCT03569293, NCT03568318, NCT03607422, NCT03568331, NCT03531957, NCT03911401, NCT03745638, NCT03745651, NCT02564055, NCT03916081, NCT03903822). Accessed August 28, 2021.

U.S. Psoriasis Market Highly Concentrated & Readily Accessible

80% of market value concentrated in tight payer, prescriber & geographic clusters

80%
of TRx claims are processed by 4 national PBMS/Plans*



80%
of Derm Commercial TRx volume made up by 5,649 HCPs

80%
of Derm Commercial TRx volume made up by 20 states

*Top 4 PBMS/Plans represent 85% of processed claims:
- CVS Health (Caremark): 32%
- Cigna (ESI & Ascent Health): 24%
- UnitedHealth (Optum): 21%
- Humana Pharmacy Solution: 8%

Sources: 1. Symphony Prescriber Source (November 2019 – October 2020). 2. Drug Store Channels: The Top PBMs of 2020: Vertical Integration drives Consolidation. April 6, 2021.

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Extensive Market Research Supports Early Access & Adoption

More than 500 HCPs, >300 patients, & 65 payer interviews (~200M+ covered lives)

STAKEHOLDER

Specialty/ Role	Cohort Size
Dermatology HCPs KOLs, High Decile Dermatologists & NPs/PAs	(n=195) 60-min Video Interviews (n=346) 60-min web survey
Payers National & Regional PBMs & MCOs**: Express Scripts, CVS caremark, OPTUM, Magellan Rx Management, Anthem, aetna, United Healthcare, Kaiser Permanente, Empire BlueCross BlueShield, Blue Cross Blue Shield of Michigan	(n=50) Incl. 8-hour Focus Group (n=15) 60-min web survey
Patients Psoriasis sufferers currently on prescription treatment	(n=76) 60-min Video Interviews (n=265) 30-min web survey

Qualitative ■ Quantitative

HCP Research respondents averaged ~260 psoriasis patients on average with ~66% of patients covered under commercial insurance

*Due to the anonymity of participants across payer organizations, there is likely overlap of participants and plans (i.e., these are not all "unique" payers/ plans)

**Example plans included in prior research, not exhaustive

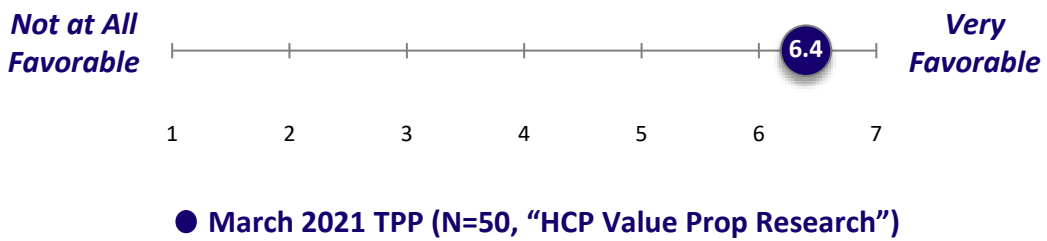
Sources: Phase 2b Qualitative research conducted by Triangle Insights, November 2018. Phase 3 Price Sensitivity Quantitative research conducted by Triangle Insights, July 2020. Qualitative research conducted by Triangle Insights, June 2020. Phase 3 HCP Value Prop Qualitative research conducted by Triangle Insights, November/December 2020 & January 2021.

94% of HCPs Believe Tapinarof Can Address an Unmet Need in Psoriasis

Prescribers have a ***CLEAR & PRESENT*** understanding of the limitations of the current standard of care, TCS

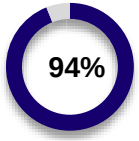
Phase 3 HCP Qualitative Value Prop Research Rating

How would you rate a product with the profile of tapinarof overall?



● **March 2021 TPP (N=50, "HCP Value Prop Research")**

Addressing the Unmet Need



of HCPs believe tapinarof has the potential to address the psoriasis unmet need as a novel topical treatment option that is safe for chronic use

HCP Value Prop Research Key Insights

01 TCS/Combination Steroid Products

~75% physicians are optimistic that tapinarof could replace TCS or *combination products* ***for first line use in mild-to-moderate patients***

02 Biologics / Otezla

Many physicians are optimistic that ***tapinarof can be a step before Otezla & delay the use of biologics***

"Tapinarof has the potential to replace steroids for first line use"

-Dermatologist

Tapinarof has not been studied in combination with other drugs
No head-to-head trials of tapinarof have been conducted against other psoriasis treatments

Source: Interviews conducted by Triangle Insights, November/December 2020 & January 2021 with dermatologists (n = 50)
1. What aspect of this product do you find most attractive?

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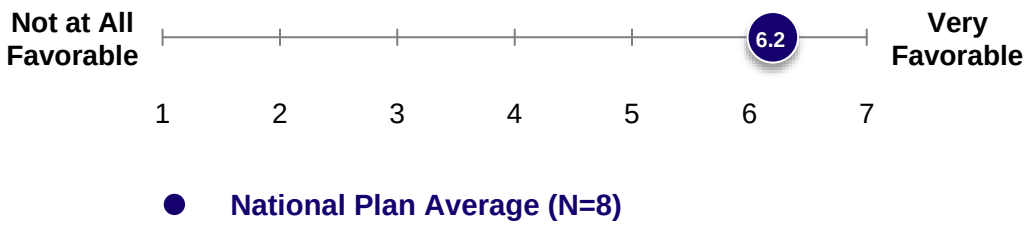
Payer & Prescriber Interests Aligned in the Need for Topical Innovation

Tapinarof could offer payers the opportunity to manage spend with ***INNOVATION*** vs. ***RESTRICTION***

Phase 3 Payer Qualitative Value Prop Research: National Plan Ratings

"How would you rate Product X overall?
(1-7 scale where 1 is not at all favorable and 7 is very favorable)"



Payer Key Insights

- **Delay Progression to Expensive Systemics**
  - Payers acknowledge the potential for tapinarof to delay the progression to expensive biologics that are driving spend in the psoriasis category
- **Innovative Contracting**
  - Several large national organizations indicated an interest in innovative risk-based contracting due to the potential treatment and remittive effect seen with tapinarof

Quotes from Payers

"The value is that it has a ***durable effect*** on a significant portion of the treated population."

-Regional MCO

"If you can show ***clearance for 3 months***, you may see a significant cost saving."

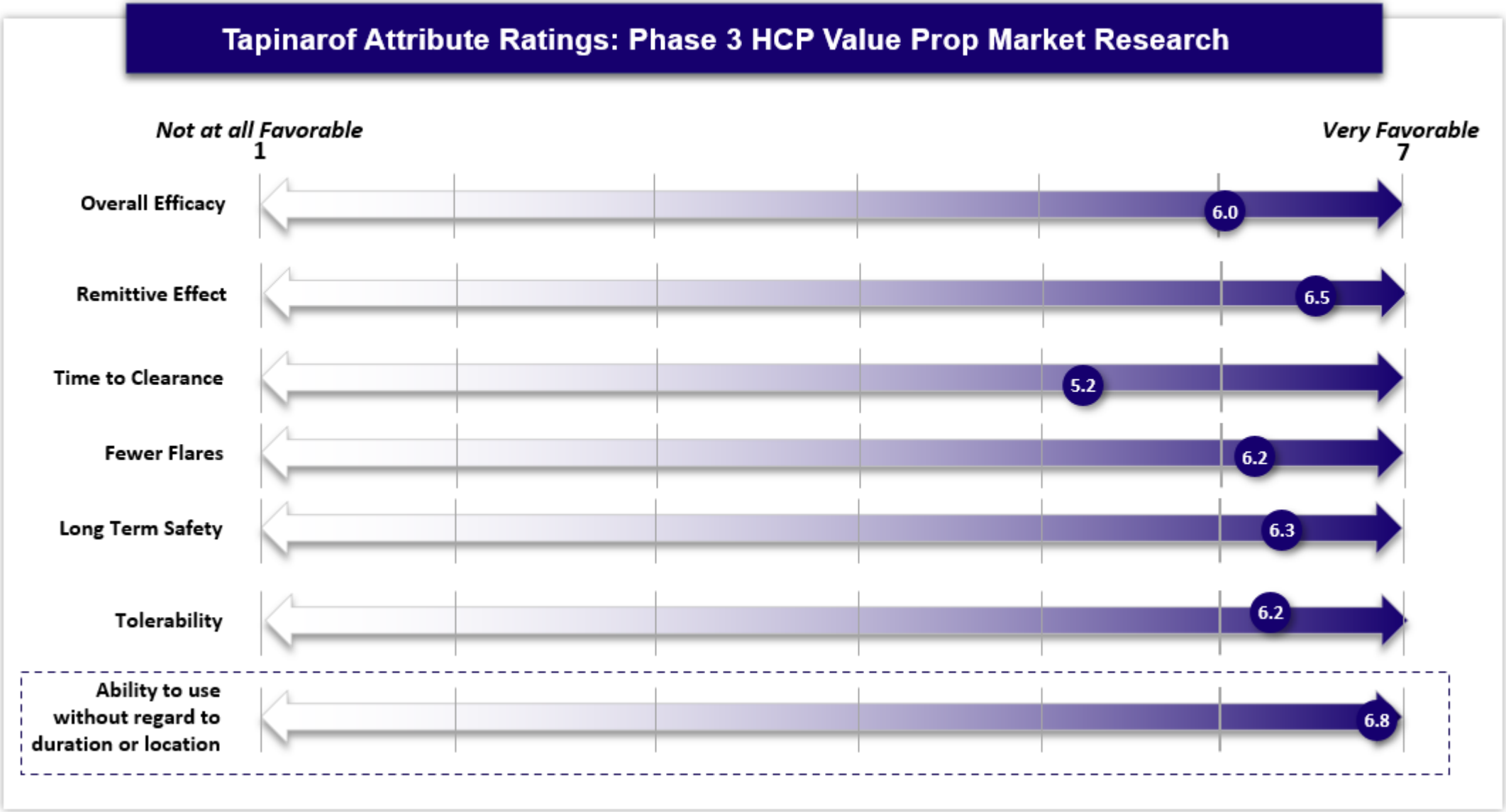
-National PBM

"I think the ***remittive effect is a very attractive*** aspect."

-Regional PBM

Source: N=17 payer interviews conducted by Triangle Insights Group, March & April 2021

Key Attributes Have Potential To Set New Benchmark for Topical Innovation



Source: Qualitative market research conducted by Triangle Insights, January 2021 with dermatologists (n = 50)
1. What aspect of this product do you find most attractive?

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Tapinarof's Prescriber, Payer & Patient Benefits are Uniquely Aligned

Versatility may fundamentally change the psoriasis treatment paradigm

Current PsO Treatment Paradigm[1]

	Mild Disease <3% BSA	Moderate Disease 3-10% BSA	Severe Disease >10% BSA
1st Line Treatment[2]	**1 *Chronic Monotherapy*** *"Breaking The TCS Flare Cycle/ Changing The Paradigm"*		**2 *Chronic Concomitant*** *"A Partner with Biologics"*
2nd Line Treatment[2]			
3rd Line Treatment[2]			

Tapinarof's profile may enable it to be used **in place of topical steroids** & may offer a **long-term solution to a chronic condition**[3]

Tapinarof may delay **the path to biologics, like the delay achieved by using oral agents**[5], therefore reducing reliance on expensive biologic therapies

Rationale:

- A retrospective study found that in patients prescribed a biologic therapy, almost **two thirds received a new topical prescription**[4]
- Topical medications were most often steroids, rather than Vitamin D

Potential to use without regard to location or duration could enable long-term monotherapy and concomitant use

Tapinarof has not been studied in combination with other drugs
No head-to-head trials of tapinarof have been conducted against other psoriasis treatments

Sources: 1. National Psoriasis Foundation (October 2020), retrieved from https://www.psoriasis.org/psoriasis-statistics/; 2. Takeshita, J., et al. Journal of Investigative Dermatology. 2015. 135. 2955-2963; 3. Interviews conducted by Triangle Insights, July 2020 with dermatologists (n = 19), NP/Pas (n = 7), & patients (n = 10). 4. Noe, M., et al. J Drugs Dermatol. 2019. 18(8): 745-750; 5. Wu, et al., Journal of Dermatological Treatment. 2019. 30 (5): 446-453


FINANCE, IP
AND SUMMARY
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Strategic Partnerships with GSK & Thermo Fisher Support Global Supply

Agreements ensure a high quality & predictable supply of drug substance and drug product

Drug Substance Manufacturing

ThermoFisher SCIENTIFIC

Cork, Ireland

Drug Product Manufacturing

gsk

Barnard Castle, UK

Experience with Tapinarof:
- Thermo Fisher: since 2016
- GSK: since 2015

Clinical Manufacturing:
- Thermo Fisher: Phase 3 clinical & registration batches
- GSK: Phase 3 clinical, registration batches, additional clinical & non-clinical studies

Commercial Production Readiness:
- Significant experience manufacturing at commercial scale
- Commercial sites with worldwide capabilities to support global registrations
- In good standing with global health agencies
- Commercial launch & supply sites for both drug substance & drug product

Capacity:
- Sites capacity sufficient to support tapinarof commercial demand

Governance:
- Structured metrics driven collaboration, solid compliance history, & quality management systems

Business Continuity:
- Robust site level business continuity programs & risk management planning

Raw Material Sourcing:
- Leverage global procurement & sourcing network at each site

Tapinarof IP Summary: Patent Protection Until at Least 2036

US Patent 10,195,160 expires 2036 (Formulation): covers all the viable emulsion/cream formulations that were studied by GSK, its predecessor & their CROs over many years of development

- Claims have very broad ranges regarding the critical components of the formulation
- Claims cover the commercial formulation and variations thereof

US Patent 10,426,743 also expires 2036 (Method of Use): covers treating inflammatory diseases, including specifically PsO & AD, using the formulations covered in the '160 patent

US Patent 10,647,649 expires in 2038: covers the commercial API synthesis, novel intermediates and high purity API crystal form produced by the synthesis

The '160, '743, & '649 Patents may be eligible for listing in FDA's Orange Book

- ANDA filers would have to invalidate or design-around these patents in order to obtain approval before the patents expire

Foreign counterpart applications to the '160 Formulation and '649 API Synthesis Patent Applications are issued or pending in other major market countries

- The Japanese formulation patent has issued and the European Examination Report indicated the claimed formulation subject matter is novel and inventive
- Once issued, natural expiration dates will be in 2036 for the formulation patents and in 2038 for the API synthesis patents

* The remittive effect encourages payers to consider innovative contracts that cap annual refills or involve risk-sharing for the patient outcomes.
Source: N=17 payer interviews conducted by Triangle Insights Group, March and April 2021

Summary

Dermavant poised to ***TRANSFORM*** Immuno-Dermatology

- $44.3B global opportunity across the two largest immuno-dermatology segments: psoriasis & atopic dermatitis (2026 forecast*)
- Tapinarof is a potentially transformational novel chemical entity that if approved may provide a combination of treatment effect, durability (on therapy), remittive effect (off therapy), safety & tolerability, in a once daily, cosmetically elegant non-steroidal cream
- PSOARING Phase 3 psoriasis program completed; PDUFA action expected 2Q 2022; Comprehensive commercial launch planning underway
- ADORING Phase 3 Program initiated 3Q 2021; topline results anticipated 1H 2023
- Development pipeline addressing additional disease states & indications

*Evaluate Pharma Data: Global Psoriasis and Atopic Dermatitis Prescription Drugs Market and Forecast 2019 – 2026 (excluding aesthetic indications); Psoriasis Indication Profile, USA Market Analysis; Atopic Dermatitis Indication Profile, USA Market Analysis (extracted September 2021).

Appendix

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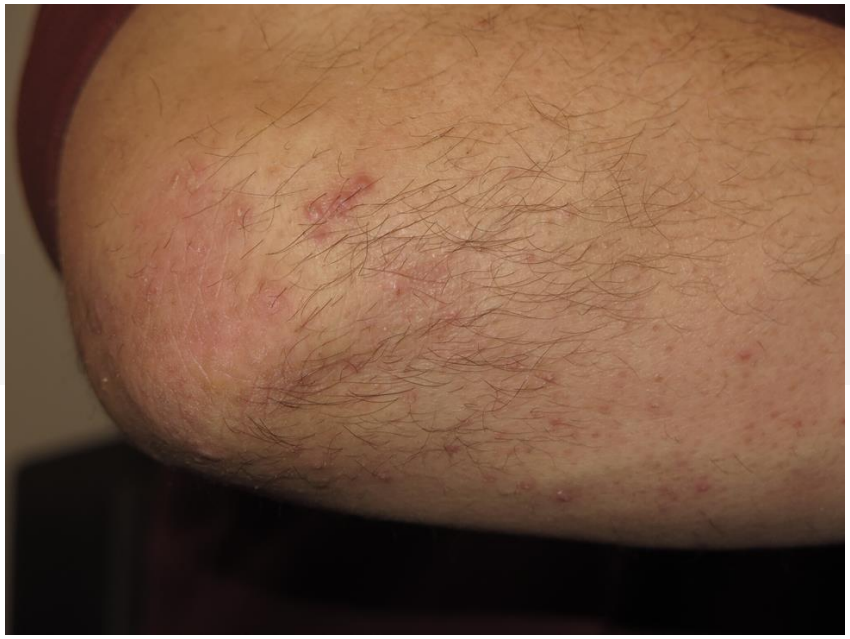
Folliculitis Examples From PSOARING 1 & 2

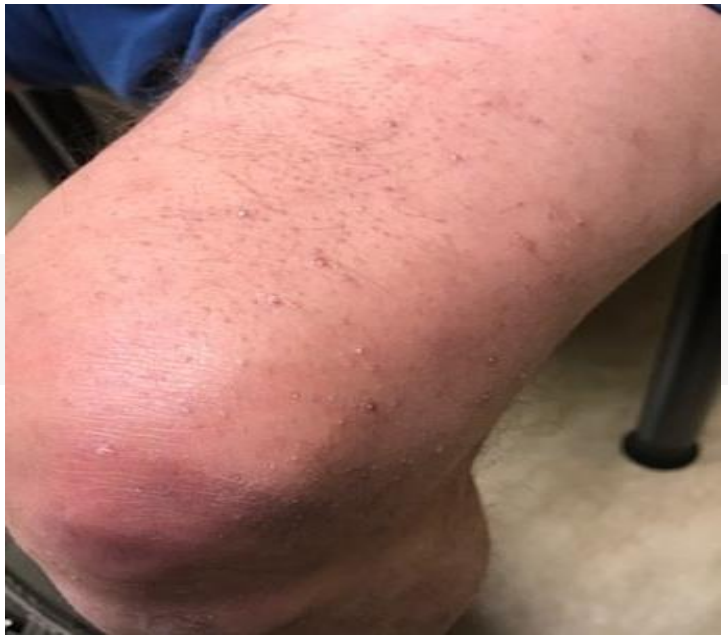
Most treatment-related events are localized to site of application & mild to moderate in nature

DMVT-505-3001_AE_1906_1906-007



CTCAE Grade 1 = Mild

DMVT-505-3002_AE_2016_2016_012



CTCAE Grade 2 = Moderate

Results shown for two patients are not necessarily indicative of results for other patients, additional trials or other uses

Examples of two representative target lesions of two tapinarof treated patients from the PSOARING 1 and 2 clinical trials.

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Roivant R&D Day

Investor Presentation

September 28, 2021

Forward-looking statements

This presentation contains forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as “may,” “might,” “will,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “intend,” “future,” “potential,” “continue” and other similar expressions (as well as other words or expressions referencing future events, conditions, or circumstances) are intended to identify forward-looking statements. For example, forward-looking statements include statements Immunovant makes regarding its business strategy, its plans to develop and commercialize its product candidates, the potential safety and efficacy of Immunovant’s current or future product candidates, including batoclimab for Myasthenia Gravis, Thyroid Eye Disease and Warm Autoimmune Hemolytic Anemia, its expectations regarding timing, the design and results of clinical trials of its product candidates, Immunovant’s plans and expected timing with respect to regulatory filings and approvals, the size and growth potential of the markets for Immunovant’s product candidates, and its ability to serve those markets. All forward-looking statements are based on estimates and assumptions by Immunovant’s management that, although Immunovant believes to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those expressed or implied by such forward-looking statements. Such risks and uncertainties include, among others: initial results or other preliminary analyses or results of early clinical trials may not be predictive final trial results or of the results of later clinical trials; the timing and availability of data from clinical trials; the timing of discussions with regulatory agencies, as well as regulatory submissions and potential approvals; the continued development of Immunovant’s product candidates, including the timing of the commencement of additional clinical trials and resumption of current trials; Immunovant’s scientific approach, clinical trial design, indication selection and general development progress; future clinical trials may not confirm any safety, potency or other product characteristics described or assumed in this presentation; any product candidates that Immunovant develops may not progress through clinical development or receive required regulatory approvals within expected timelines or at all; Immunovant’s product candidates may not be beneficial to patients, or even if approved by regulatory authorities, successfully commercialized; the potential impact of the ongoing COVID-19 pandemic on Immunovant’s clinical development plans and timelines; Immunovant’s business is heavily dependent on the successful development, regulatory approval and commercialization of its sole product candidate, IMVT-1401; Immunovant is at an early stage in development of IMVT-1401; and Immunovant will require additional capital to fund its operations and advance IMVT-1401 through clinical development. These and other risks and uncertainties are more fully described in Immunovant’s periodic and other reports filed with the Securities and Exchange Commission (SEC), including in the section titled “Risk Factors” in Immunovant’s Quarterly Report on Form 10-Q for the quarter ended June 30, 2021 filed with the SEC on August 9, 2021. Any forward-looking statement speaks only as of the date on which it was made. Immunovant undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

Rethinking possibilities in autoimmune disease

Our vision: Normal lives for people with autoimmune diseases

Love Trailblazing

Bolder Faster

All Voices

IMMUNOVANT

Anti-FcRn Market: Potential therapeutic benefit across wide range of indications

Fifteen indications announced by at least one anti-FcRn program

NEUROLOGY

Myasthenia Gravis
Chronic inflammatory demyelinating polyneuropathy
Myositis
Autoimmune encephalitis
Myelin oligodendrocyte glycoprotein antibody disorders (MOG-antibody disorder)

RHEUMATOLOGY

Primary Sjögrens Syndrome
Lupus Nephritis
Systemic lupus erythematosus
Rheumatoid arthritis

DERMATOLOGY

Bullous pemphigoid
Pemphigus foliaceus/
Pemphigus vulgaris

HEMATOLOGY

Warm autoimmune hemolytic anemia
Hemolytic disease of the fetus and newborn
Idiopathic thrombocytopenic purpura

ENDOCRINOLOGY

Thyroid eye disease

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Source: https://www.clinicaltrials.gov/

Despite available treatment options, people with Myasthenia Gravis report significant unmet needs

Reliable treatment options

- Variable time to response for existing treatments (e.g. steroids, immunosuppressants, IVIg)
- Trade-offs between safety risks and therapeutic benefit with some therapies

People-centered treatment delivery

- Desire to feel like a person not a patient
- Considerations for chronic disease management (i.e., simple, at-home self-administration)

Flexible treatment options

- Most patients feel that their condition is uncontrolled
- Different patients need more or less intensive therapy

Significant impact on quality of life

- Even well controlled patients report lifestyle accommodations
- Anxiety around response and duration

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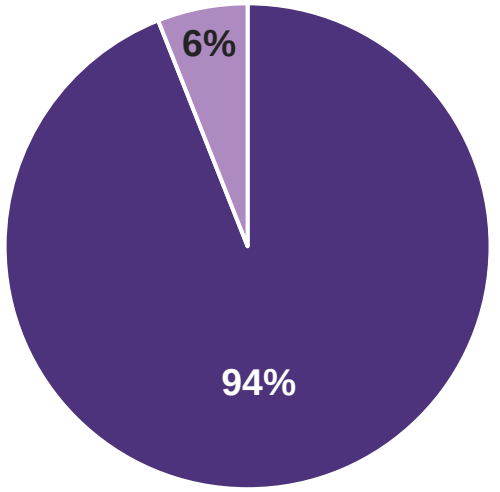
Source: Analysis – Social Media Review MG n=975 / Qualitative research – MG patient journey n=28 / MG Patient Advisory Council n=6 / MG Patient Quantitative Survey (n=50)

Dosing approach preferences

94% of respondents with Myasthenia Gravis prefer chronic versus intermittent dosing

Patient Survey Feedback:
Preferred Treatment Approach

- I want to stay on my MG treatment, even when my symptoms are under control, so that I can maintain a response and prevent potential symptom flares
- I only want MG treatment intermittently when my symptoms flare



Source: Analysis – MG Patient Quantitative Survey (n=50)

Batoclimab's (IMVT-1401) differentiated attributes provide a unique opportunity to address patients' unmet needs

Reliable treatment options

Flexible treatment options

People-centered delivery of treatment

Significant impact on quality of life

Batoclimab

Flexible dosing potential:
Deep, rapid IgG suppression in the short-term; adjustable IgG suppression in the long-term

Subcutaneous route of administration:
Designed and developed for simple subcutaneous injection to provide human-centric, give and go dosing experience

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Developing Gene Therapies for Rare Diseases

Aruvant represents a growth opportunity developing potentially curative gene therapies for rare diseases

ARU-1801

Lentiviral gene therapy for sickle cell disease

- Ongoing Phase 1/2 trial
- Clinical data demonstrating curative potential
  - Up to 100% reduction in vaso-occlusive events (VOEs)
  - Durable responses for more than three years
- Toxicity advantage vs other gene therapies: Requires non-myeloablative chemotherapy

ARU-2801

AAV gene therapy for hypophosphatasia

- Preclinical data: durable increases in tissue non-specific alklaline phosphatase (ALP) levels through 18 months
- Potential one time Rx to replace chronic ERT standard of care

Experienced team in gene therapy, clinical development and manufacturing

Will Chou, MD, MBA
Chief Executive Officer

NOVARTIS

- Global Commercial Head Kymriah
- Head Lymphoma Clinical Development Kymriah
- Clinical, CMC, regulatory and commercial leadership for first approved CAR-T

Palani Palaniappan, PhD
Chief Technology Officer

SAREPTA THERAPEUTICS

- Global Technical Operations Head
- 25 years technical ops leadership
- Multiple gene therapy development programs
- Successful rare disease approvals
- Novel assay development, CMO management

Stan Musial, MBA
Chief Financial Officer

ENIKOS rebalancing the immune system

- Chief Business Officer and Chief Financial Officer
- Financial executive with 25+ years experience
- CFO of multiple privately-held and publicly-held biotechnology companies
- Commercial launch and execution

E. Blair Clark-Schoeb
SVP, Communications

Zyla life sciences

- SVP, Communications
- 20+ years communications leadership (public relations, investor relations, patient advocacy & government affairs)
- Multiple rare disease programs (Friedreich's Ataxia, Hereditary Angioedema, Huntington's Disease)

Meghan Kelton
Executive Director, Human Resources

avexis

- Head, People, Organization & HR Site, Novartis Gene Therapies
- 15 years HR experience
- Senior Professional HR and Society or HR Management Senior certifications

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The major complication of sickle cell disease are vaso-occlusive events (VOEs) which are painful and costly

A person with sickle-cell disease with intensifying back pain receives a blood transfusion. Credit: Ilana Panich-Linsman/NYT/eyevine

- VOEs are episodes of extreme pain caused by vaso-occlusion that can last several days
- 95% of hospitalizations for SCD are due to VOEs[1]
- VOEs can lead to severe complications and progressive organ damage[2]
- Increased frequency of pain crises is associated with decreased survival[3]
  - Life expectancy of SCD remains in mid 40s

1. Ballas SK, Lusardi M. Am J Hematol. 2005;79(1):17-25; 2. Piel FB, Steinberg MH, Rees DC. N Engl J Med. 2017;376(16):1561-1573; 3. Elmariah H, Garrett ME, De Castro LM, et al. Am J Hematol. 2014;89(5):530-535

ARU-1801 is a one-time potentially curative therapy for SCD with a differentiated toxicity profile.

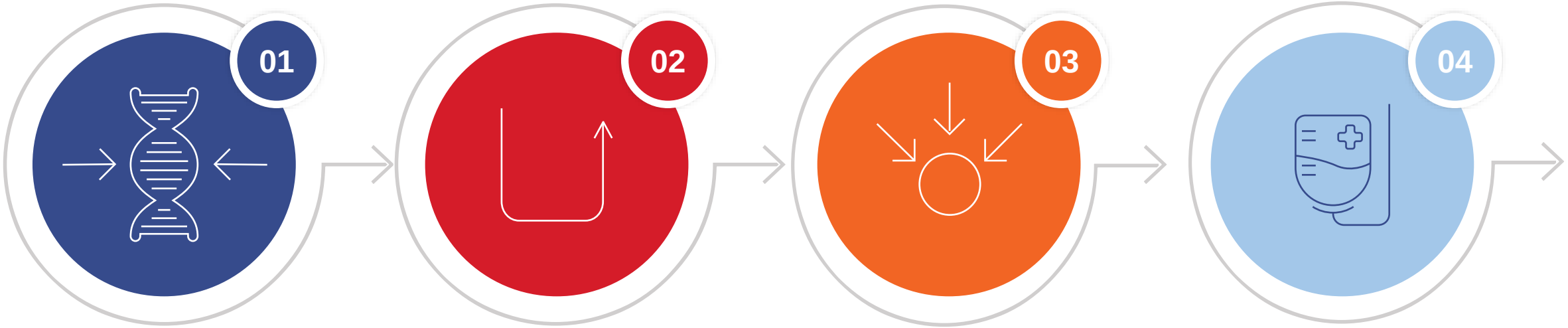
Uses self-inactivating lentiviral vector that contains a proprietary γ-globin gene for a novel, highly potent variant of fetal hemoglobin (HbF): HbF^{G16D}

Unique potency allows ARU-1801 to engraft with only reduced intensity conditioning (RIC).

Potential for curative reduction in disease burden.

- VOE reduction up to 100%
- Durable engraftment over three years

ARU-1801 uses a patient's own stem cells to make a unique fetal hemoglobin



Produce Lentiviral Vector

Collect CD34+ Stem Cells

Transduce CD34+ Cells *Ex Vivo*

Infuse Cells after a Single Dose of RIC

ARU-1801's unique attributes enable a potential differentiated product profile

More hemoglobin F per vector copy
Proprietary G16D point mutation drives higher HbF payload per vector copy

High HbF^{G16D} potency
HbF^{G16D} may have a more potent anti-sickling effect than endogenous HbF

Preserved stemness
Proprietary manufacturing component enables more true stem cells in each dose

Engraftment with RIC

Potential for clinical efficacy at lower VCN

ARUVANT

RIC has potential benefits for patients, providers, and payors

Reduced intensity conditioning (RIC) with melphalan 140mg/m^2 may provide significant clinical benefit compared to the busulfan-based regimen used by the other leading SCD gene therapy candidates, including the potential for lower risk of secondary malignancy

Note: no head-to-head studies of these products have been conducted

	Busulfan 3.2 mg/kg/day* (Used by myeloablative gene therapies)	Melphalan 140 mg/m^2 (Used by ARU-1801)
Neutropenia Recovery Time	20 days[1]	**7 days[2]**
Platelet Recovery Time	28 days[1]	**8 days[2]**
Neurotoxicity	Seizure prophylaxis required[3]	**No seizure prophylaxis required[4]**
Ovarian Failure	70 - 80%[5]	**30 - 40%[5]**
Chemo Administration	4 days[6] daily PK monitoring	**1-hour infusion[4]**
Days in Hospital (Median)	44 days[6]	**0-5 days[7]**
Potential for Outpatient Administration	Low[3] *(longer cytopenias, multiple infusions)*	**High[7]** ***(common in multiple myeloma)***
Backup Collection	Required[8]	**Not required[9]**
Risk if No Engraftment	Rescue transplant required[8]	**No rescue required[9]**

Table reflects combination of gene therapy protocols, reported results from gene therapy trials, and literature on the use of these conditioning agents in other settings.
*Dose adjusted to a targeted AUC for busulfan of 4200 μM*min. 1. bluebird bio ASGCT 2020. Resolution of Sickle Cell Disease (SCD) Manifestations in Patients Treated with LentiGlobin Gene Therapy: Updated Results of Phase 1/2 HGB-206 Group C Study. 2. Based on data from 3 ARU-1801 patients. 3. Busulfan label; seizure prophylaxis required but not with phenytoin due to PK interaction with busulfan. 4. ALKERAN label. 5. Estimated based on Kaplan-Meier plot in post-pubescent female children based on time to elevated FSH level with up to 8 years follow up (Panasuik et al. BJH 2015). 6. ZYNTEGLO EPAR. 7. Boston Medical Center. B Freeman et al. (2014) Bone Marrow Transplantation and Guru Murthy GS et al. (2019) Biol. Blood Marrow Transplant; outpatient autologous HSCT are already performed for multiple myeloma and AL amyloidosis 8. Rescue cell collection required per bluebird bio protocol. 9. Based on Aruvant protocol. Drugs are investigational and subject to regulatory approval.

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Recent events in 2021 reinforce importance of safety in GTx, an area where ARU-1801 is uniquely differentiated

BLUE events and findings

2nd AML case in SCD study

- Vector was very unlikely a factor in either AML/MDS case[1,2]
- Busulfan conditioning and baseline risk identified as possible causes[1,2]

MDS case in CALD study

- Known risk of specific retroviral promoter sequence in Skysona vector[3,4]

- ARU-1801 uses RIC melphalan[5]
- Lower exposure to alkylating chemotherapy associated with lower risk of oncogenesis[6-8]
- ARU-1801 does not use retroviral promoter sequences[5]
- Prior to CALD case, >250 patients treated with lentiviral gene therapies in autologous stem cells with no insertional oncogenic events[9]

Drugs are investigational and subject to regulatory approval.

1. Tisdale Blood Advances 2020
2. Bluebird bio press release and conference call March 2021
3. Bluebird bio Q2 earnings call, 8/9/2021
4. Eichler et alt. New England J of Medicine 2017
5. ARU-1801 IND
6. Greene MH et al. Ann Intern Med. 1986 Sep;105(3):360-7.
7. Tucker MA et al. J Natl Cancer Inst. 1987 Mar;78(3):459-64.
8. Cuzick J et al. Br J Cancer. 1987 May;55(5):523-9.
9. Tucci et al, poster presentation, EHA 2020

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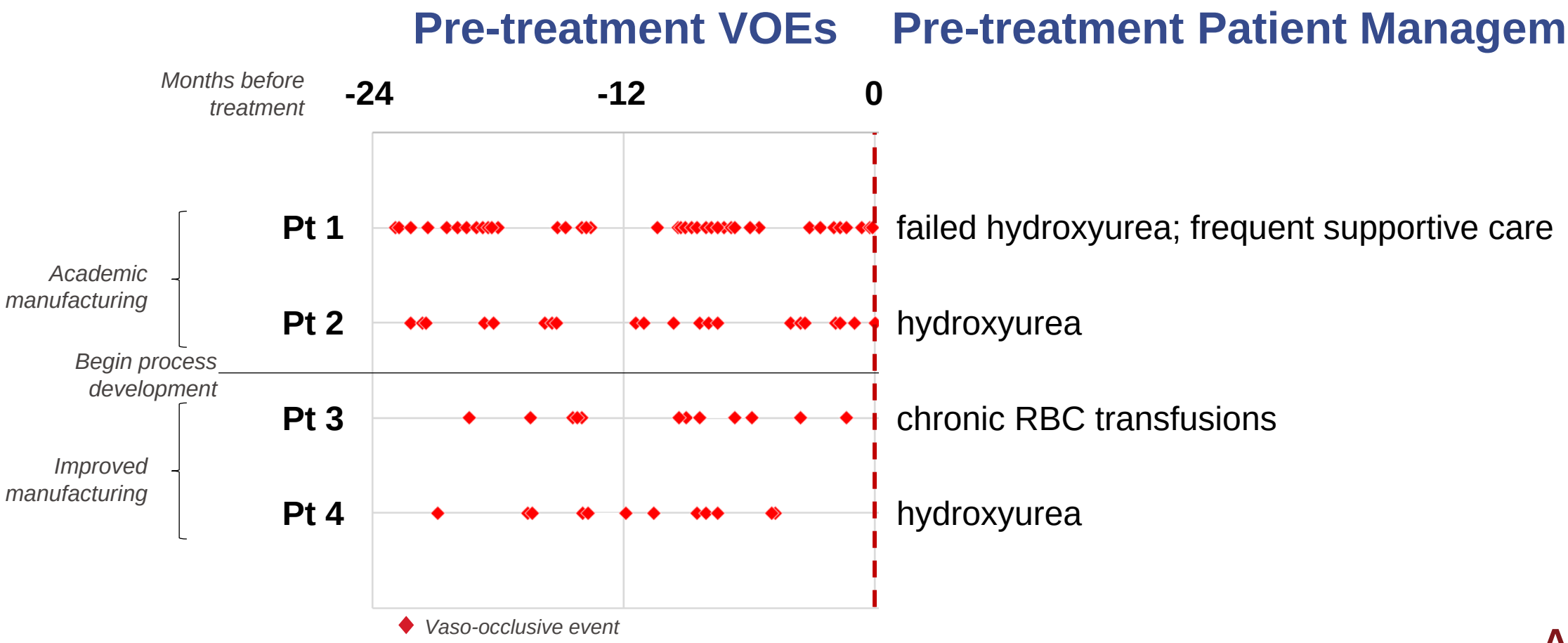
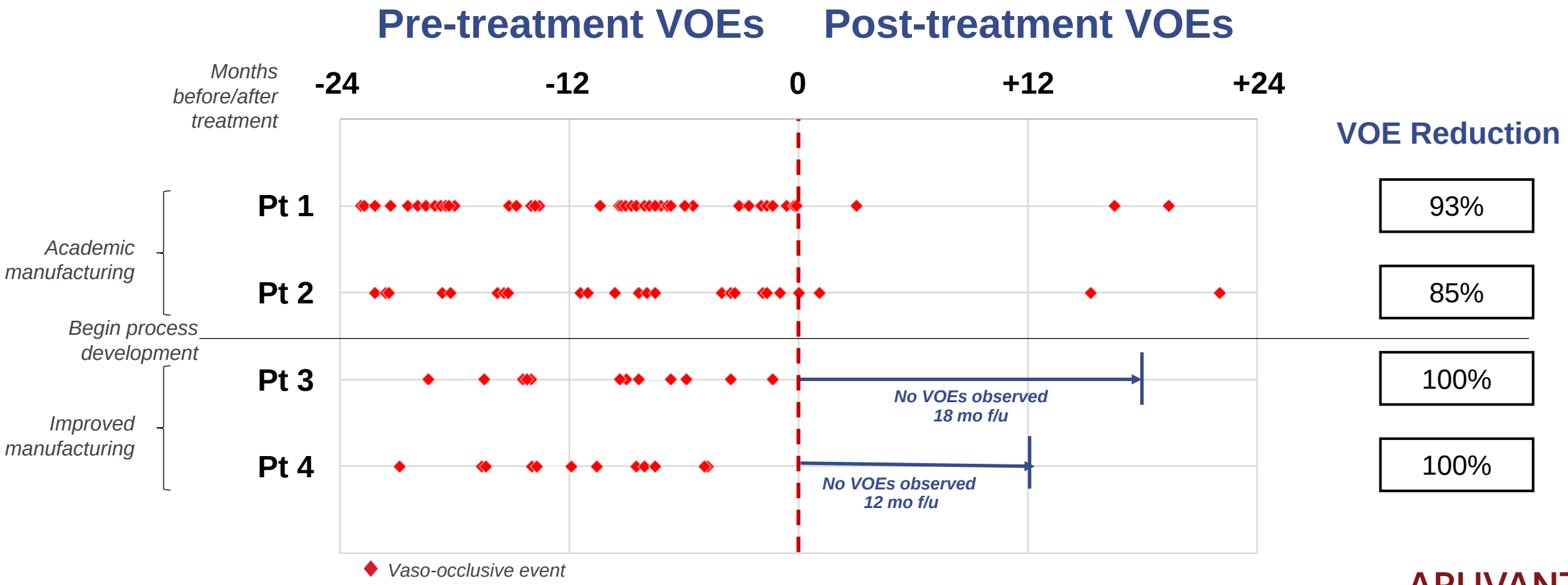
Before treatment with ARU-1801, patients had numerous VOEs despite SOC treatment

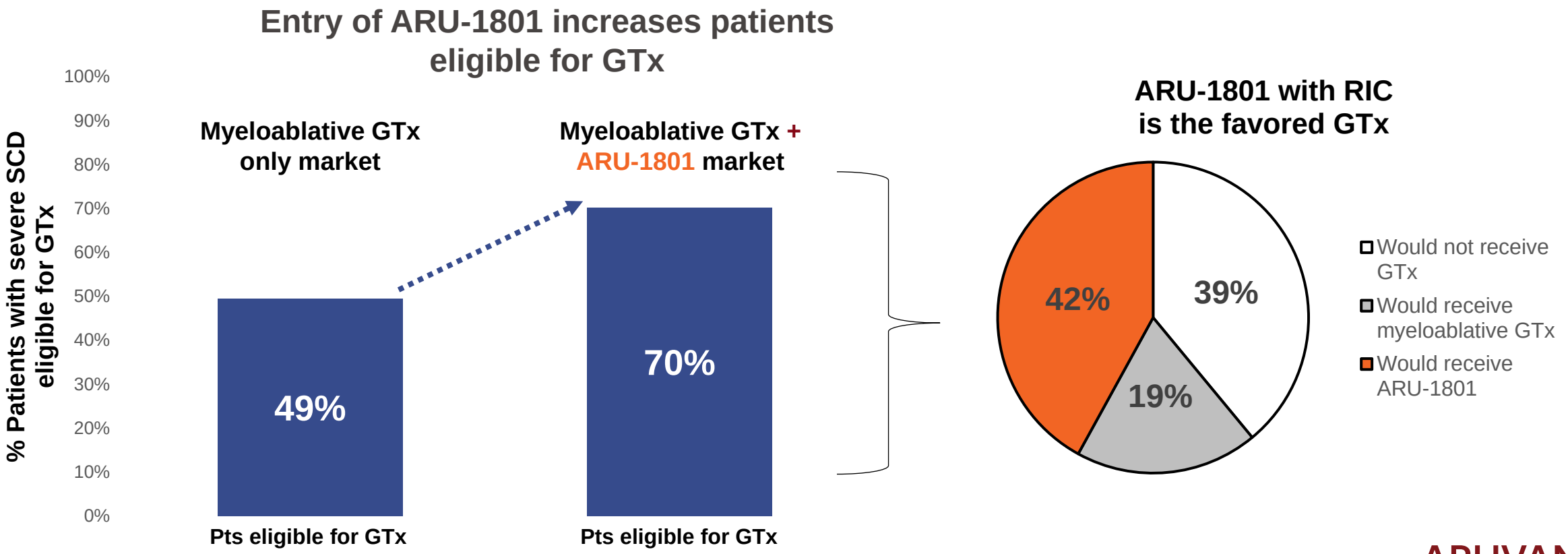


Significant improvement to date in VOEs including 100% resolution in recently treated patients



Market research showed GTx with RIC grows addressable population and is favored choice vs myeloablative options

225K SCD Population (US & EU) | **47% have severe SCD**



Results from market research of 75 physicians. Drugs are investigational and subject to regulatory approval.

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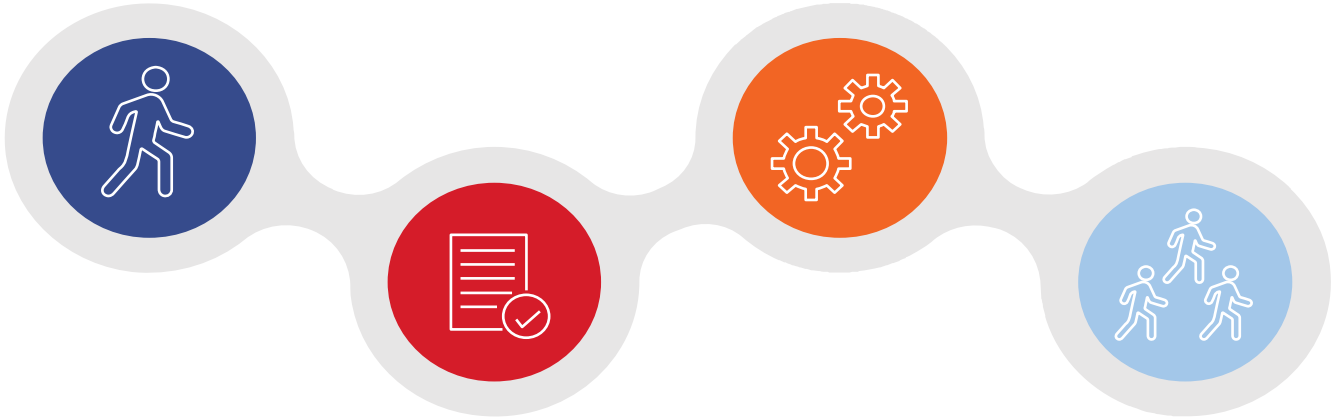
ARU-1801 Path Forward



✓	First patient dosed with updated manufacturing process	**H2**
✓	ARU-1801 Ph 1/2 data	**H2**
	Initiate ARU-1801 pivotal study	**H1:23**

ARU-2801 for Hypophosphatasia

Data presented in

Molecular Therapy Family of Journals

Journal of Bone and Mineral Research JBMR®

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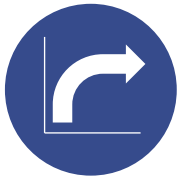
ARU-2801 is a one-time gene therapy for hypophosphatasia (HPP) that could replace a potential blockbuster enzyme replacement therapy (ERT) SOC and deliver potentially curative efficacy, without the limitations of chronic administration

ARU-2801 is an adeno-associated virus gene therapy designed to treat hypophosphatasia, a devastating, ultra-orphan disorder that affects multiple organ systems and leads to high mortality



Durable and sustainable increases in tissue non-specific alklaline phosphatase (ALP) levels through 18 months

Potential for reduction in disease burden

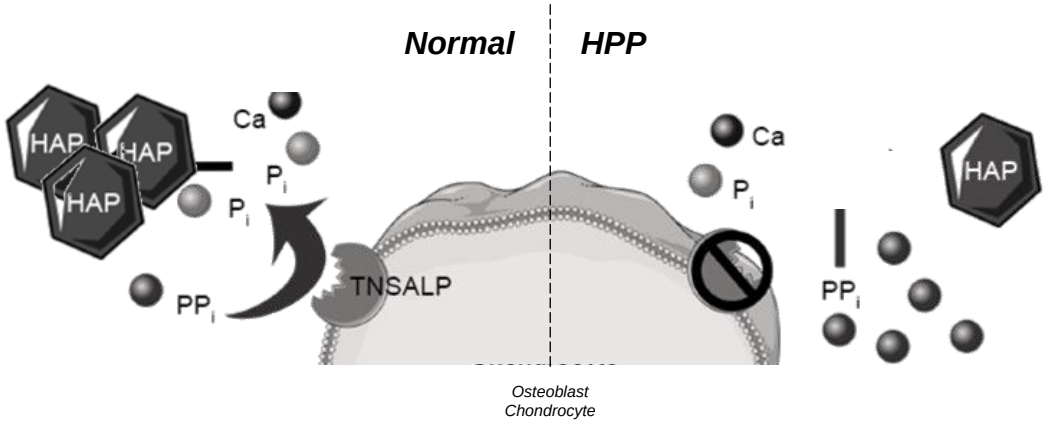
- Significant increase in survival and lifespan (18 months vs 3 weeks)
- Amelioration of bone defects with development of mature bone
- Normalization of body weight and bone density

Hypophosphatasia (HPP) is a devastating and potentially fatal orphan disorder with no gene therapy treatments available

HPP is caused by mutation in the *ALPL* gene and is characterized by low or no expression of tissue non-specific alkaline phosphatase (TNS-ALP)

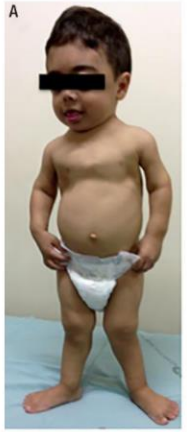
Mutant TNSALP impairs bone mineralization…

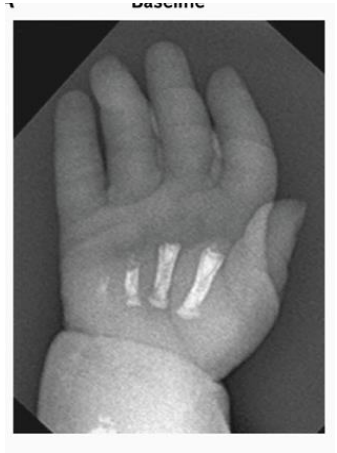
- In HPP, TNS-ALP, is mutated and cannot convert pyrophosphate (PPi) to phosphate (Pi)
- This results in limited hydroxyapatite formation, **and therefore limited bone mineralization**



…leading to severe musculoskeletal compromise

- Severe forms result in **respiratory failure** from chest hypoplasia, **seizures**, and **limb deformity**
- Left untreated, 50% of severe perinatal / infantile-onset patients die within first year of life





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2. Fraser D: Hypophosphatasia. Am J Med. 1957, 22: 730-46. 10.1016/0002-9343(57)90124-9.
3. Ann Hum Genet . 2011 May;75(3):439-45. doi: 10.1111/j.1469-1809.2011.00642.x. Epub 2011 Mar 24

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SOC ERT for HPP, Strensiq, requires chronic administration and patients experience injection site reactions leaving high unmet need

Chronic, frequent injections

- Up to 6x SC injections/week for a lifetime[1]
- Doses need to be matched with patient weight[1]

"Every injection is the most dreaded experience. It's like asking to inject fire into your body."

– HPP patient

AEs at injection site

- 74% injection site reactions[2]
- Lipodystrophy shown in 28% of patients, including 70% of juvenile-onset patients[1]

"I wouldn't hesitate with something new if it meant less injections."

– HPP patient

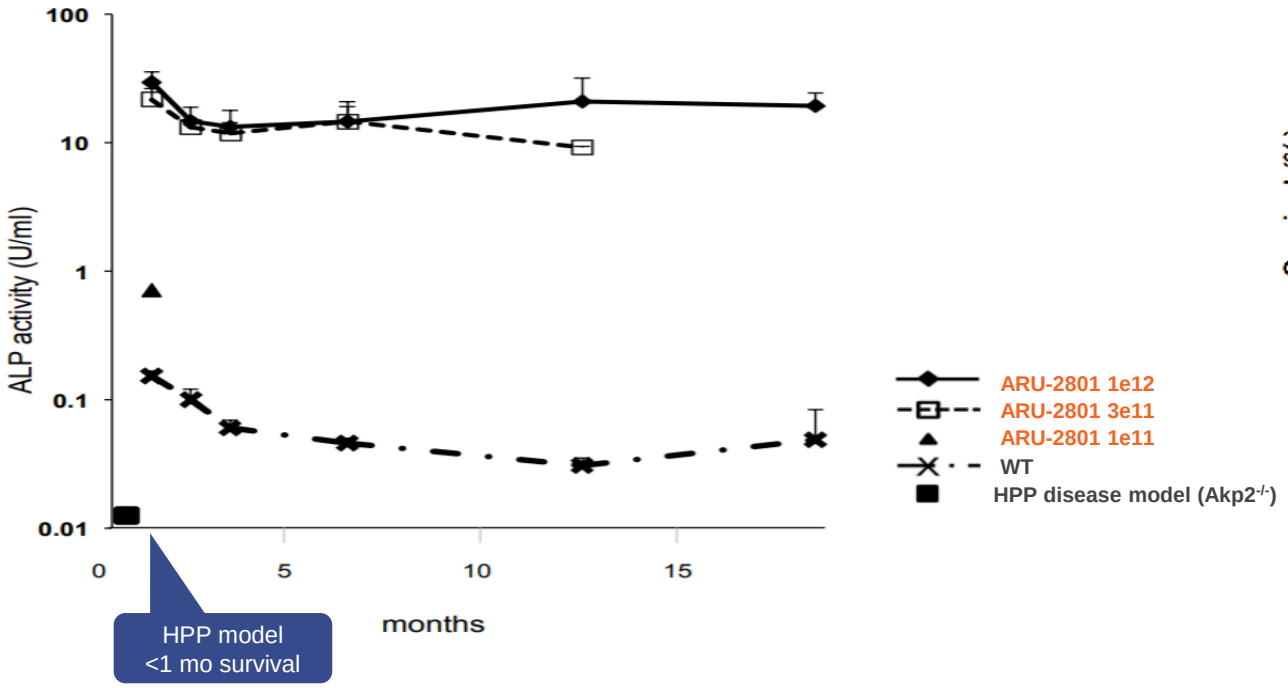
ARU-2801 can potentially eliminate these inherent chronic injection issues

1. Strensiq FDA Label
2. Strensiq EPAR Product Information

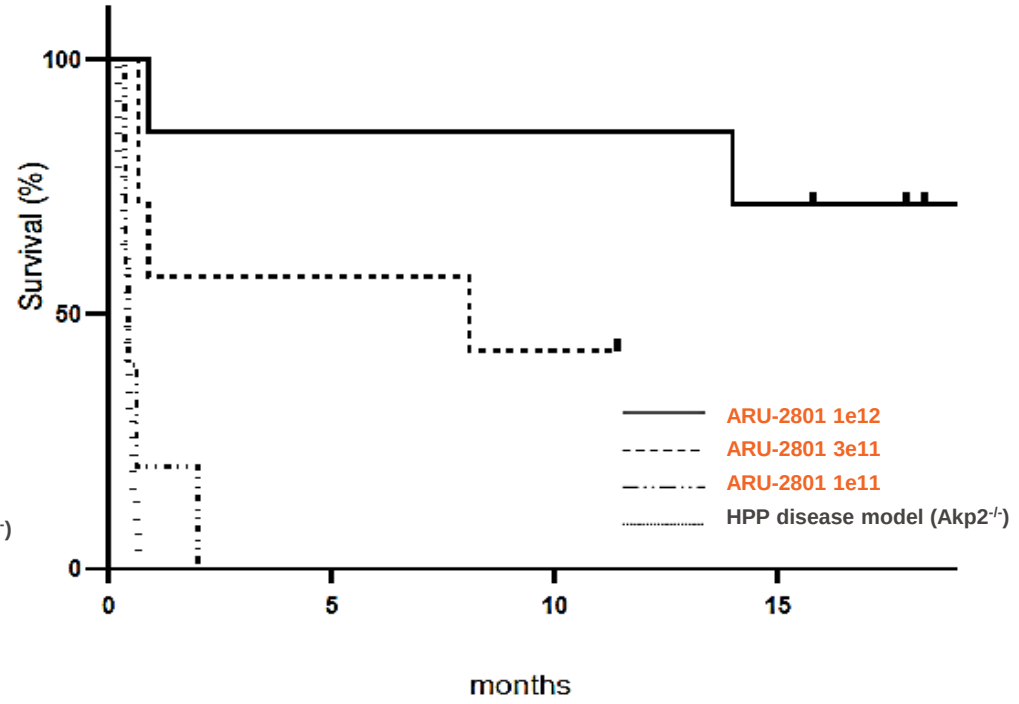
Drugs are investigational and subject to regulatory approval.

In HPP murine models, ARU-2801 treatment results in high, durable ALP levels and survival to 18 months (vs 3 weeks untreated)

High ALP levels in HPP model (Akp2$^{-/-}$ mice)



Durable 18-month OS of 70%



No evidence of ectopic calcifications at these therapeutic doses

All drugs are investigational and subject to health authority approval.

1. Matsumoto T et alt *Molecular Therapy Methods and Clinical Development* 2021

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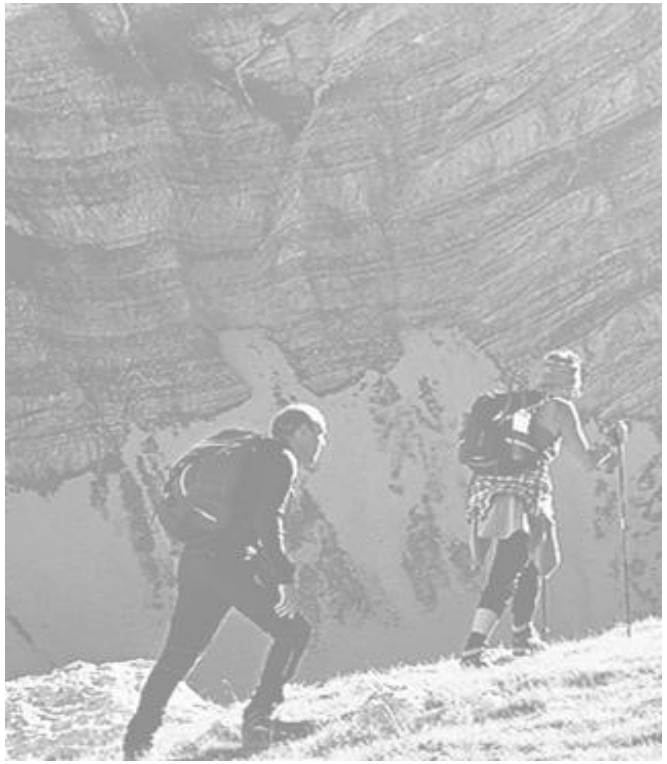
Targeting Rare Autoimmune Diseases

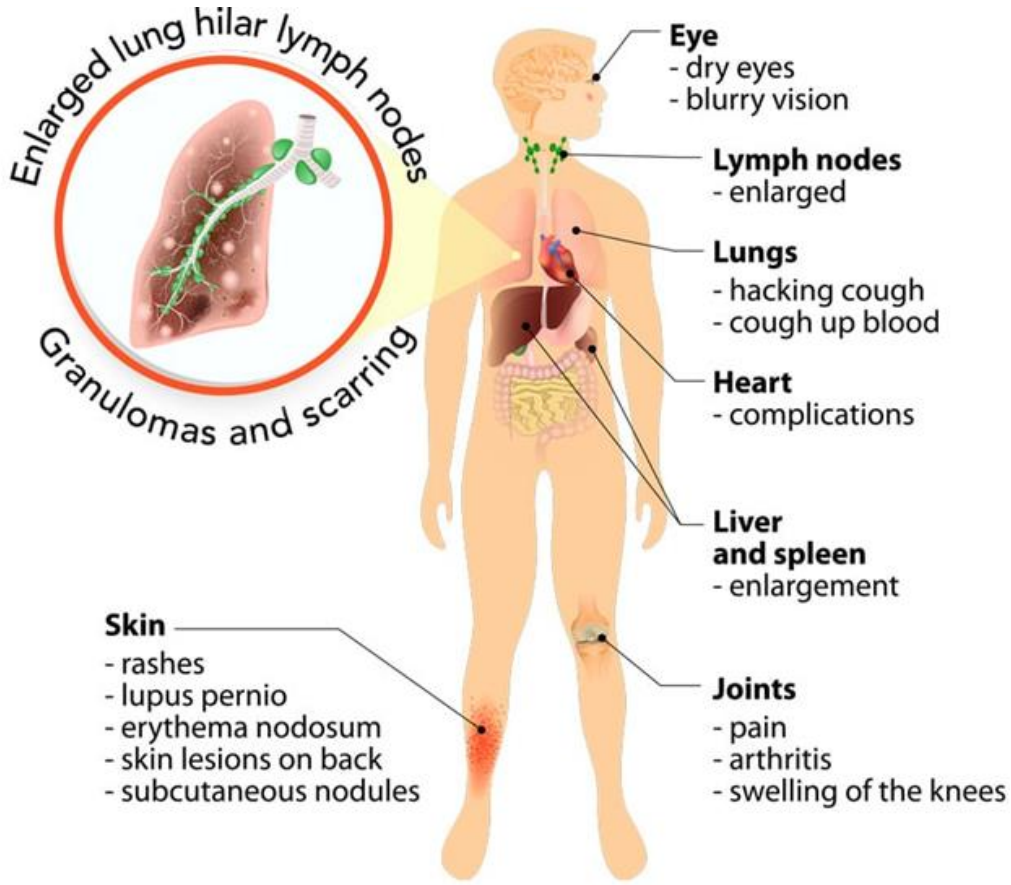
Introduction

- We are developing an anti-GM-CSF monoclonal antibody (namilumab) for sarcoidosis and potentially other autoimmune rare diseases
- Sarcoidosis is a systemic, multi-organ disease that results from a dysregulated immune response, with poor treatment options
- Our goal is to significantly improve the treatment of sarcoidosis with a convenient and well-tolerated 1x monthly injection
- We expect to initiate a Phase 2 clinical trial for pulmonary sarcoidosis in the first half of 2022



Sarcoidosis – Rare Autoimmune Disease

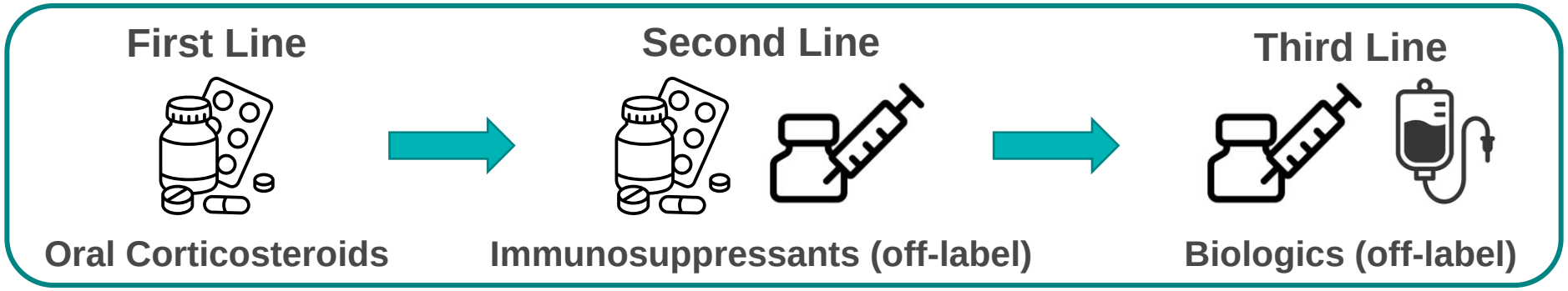
- Characterized by the accumulation of granulomas in organs and lymph nodes, believed to be due to an exaggerated antigen-driven immune response
- The resulting inflammation leads to organ dysfunction, irreversible scarring, and overall poor quality of life[1]
- ~200k have sarcoidosis in the US[2]
- Pulmonary sarcoidosis is the most common clinical manifestation (>90% of cases) and the most common cause of death[3]
  - Declining pulmonary function
  - Breathlessness, fatigue, cough, and pain



1. Baughman, et al. Annals ATS 2016
2. Denning, et al. European Respiratory Journal 2013
3. Sauer, et al. Annals ATS 2017; Baughman, et al. Sarcoidosis Vasculitis and Diffuse Lung Diseases 1997

Inadequate Treatment Options for Sarcoidosis

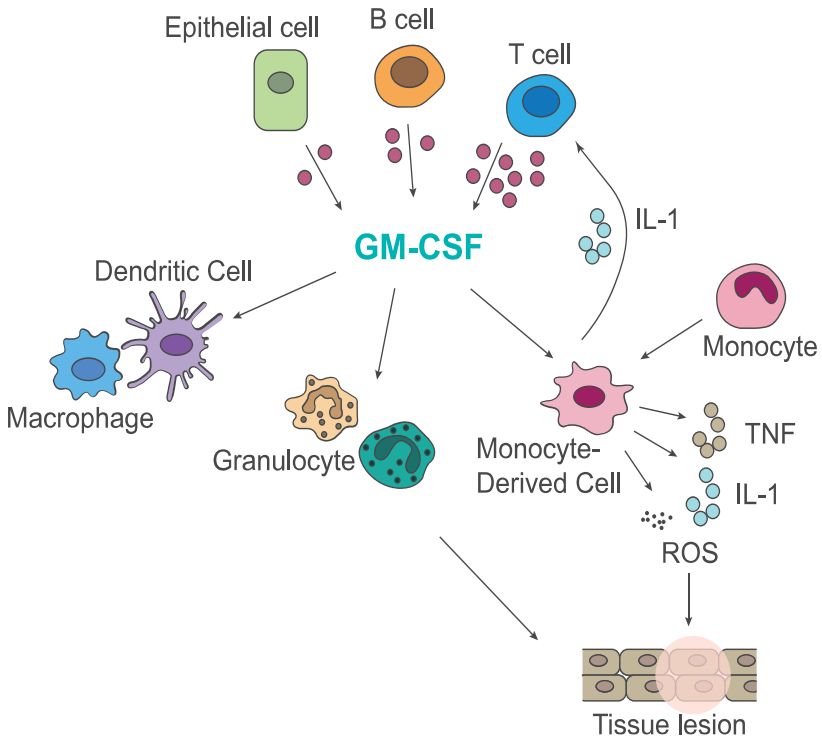
- Goal of therapy is to prevent or control organ damage, relieve symptoms and improve patients' quality of life
- Corticosteroids are first-line therapy, but have significant side effects with long-term dosing
- Immunosuppressive therapy (methotrexate, azathioprine) and biologics (TNF inhibitors) are steroid-sparing 2L and 3L options, but slow onset, poor tolerability, safety risks, inconsistent effectiveness, and/or reimbursement challenges limit their use
  - None are FDA approved for use in sarcoidosis[1,2]



1. Korsten, et. al Current Opinion in Pulmonary Medicine 2013
2. Foundation for Sarcoidosis Research: "Sarcoidosis Treatment Guidelines"

GM-CSF is a Key Pathogenic Cytokine in Sarcoidosis

- GM-CSF is a pro-inflammatory cytokine that plays a key role in the promotion and maintenance of sarcoid granuloma inflammation[1]
- GM-CSF activates macrophages and other immune cells, which drive inflammation and tissue damage[2]
- Upregulated GM-CSF forms granulomas in sarcoidosis *in vitro* models[3]
- GM-CSF knockout mice unable to form granulomas in response to tuberculosis and succumbed to the disease[4]
- GM-CSF over-expression in rat lung promotes macrophage granuloma formation, fibrosis, and tissue damage[5]
- GM-CSF is significantly elevated in patients' bronchoalveolar lavage fluid and lung tissue, and correlated with disease severity[6]



1. Ishioka S, et al. Sarcoidosis, Vasculitis, and Diffuse Lung Diseases 1996. 2. Itoh A, et al. Respirology 1998. 3. Crouser ED, et al. Am J Respir Cell Mol Biol 2017. 4. Szeliga J, Daniel DS, Yang CH, et al. Tuberculosis 2008; Beecher et al. Immunity 2016. 5. Xing Z, et al. J. Clin. Invest 1996. 6. Itoh A, Yamaguchi E, Furuya K, et al. Thorax 1993; Crouser ED, et al. Am J Respir Crit Care Med 2009; Itoh A, et al. Respirology 2008

Namilumab

- Namilumab is a fully human anti-GM-CSF monoclonal antibody with broad potential in autoimmune diseases
- In multiple Phase 2 studies, anti-GM-CSFs have been well-tolerated and have demonstrated the potential to improve symptoms in autoimmune diseases including rheumatoid arthritis and giant cell arteritis[1]
- Namilumab has been studied in ~300 patients to date and was demonstrated to be well-tolerated with decreased disease activity compared to placebo in rheumatoid arthritis[2]
- Namilumab has been studied using the least frequent subcutaneous dosing in the anti-GM-CSF class (Q4W)
- Namilumab has the potential to be the preferred option for pulmonary sarcoidosis
- Kinevant has completed a robust planning campaign for a Phase 2 trial of namilumab in pulmonary sarcoidosis expected to be initiated in the first half of 2022

Drugs are investigational and subject to regulatory approval.

1. Kiniksa Announces Positive Data from Phase 2 Trial of Mavrilimumab in Giant Cell Arteritis, October 2020. GSK Presents New Efficacy and Safety Data of an Anti GM-CSF Antibody in Patients with Rheumatoid Arthritis, October 2018.
2. Taylor P, et al. Arthritis Res Therapy 2019; Tanaka S et al. International J Pharmacol Therapy 2018; Papp KA et al. J Dermatol 2019; Huizinga TW et al. Arthritis Res Ther. 2017; Unpublished Ph 2 results ankylosing spondylitis

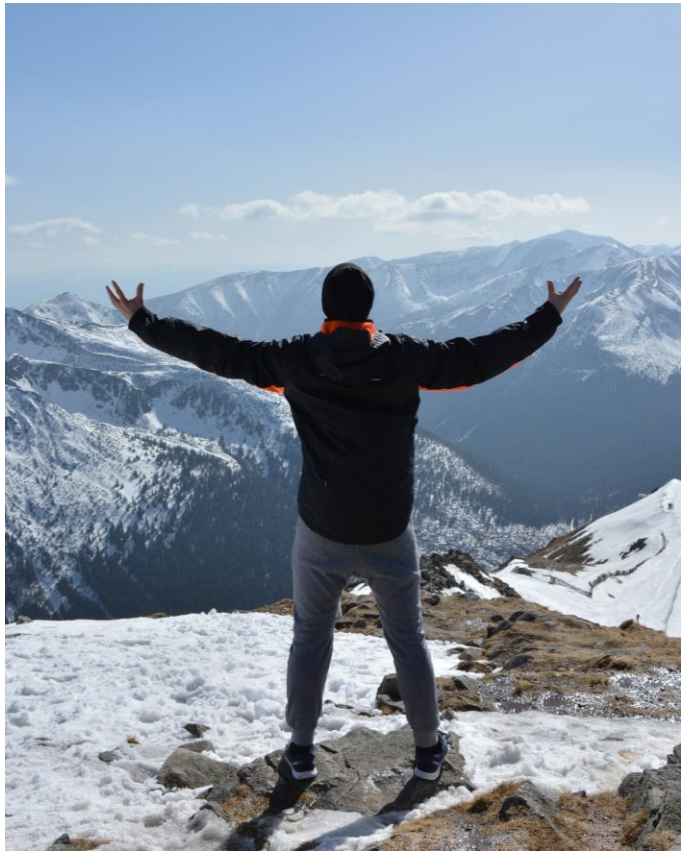
Limited Pipeline Competition for Pulmonary Sarcoidosis

Candidate	Sponsor	Mechanism of Action	Development Phase	
			Phase 1/2	Phase 2
ATYR1923	aTyr	NRP2 modulator	Completed	
CMK389	Novartis	IL-18 Antibody		Initiated
Inhaled VIP	Relief	Immunosuppressant		Announced

Sources: clinicaltrials.gov; aTyr Pharma press release dated September 13, 2021; Relief Therapeutics press release dated September 2, 2021

Summary

- Sarcoidosis is a significant unmet clinical need
- Preclinical studies and patient samples indicate GM-CSF likely contributes to the pathogenesis of sarcoidosis
- Namilumab has the potential to significantly improve the treatment of sarcoidosis
- We are building a world class team with drug development expertise in respiratory and autoimmune diseases
- A well-tolerated and effective, steroid-sparing, therapy for sarcoidosis has blockbuster commercial potential[1]
- We plan to initiate a Phase 2 study in pulmonary sarcoidosis in first half of 2022
- We plan to evaluate indication expansion opportunities for namilumab beyond pulmonary sarcoidosis



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1. Market research.


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