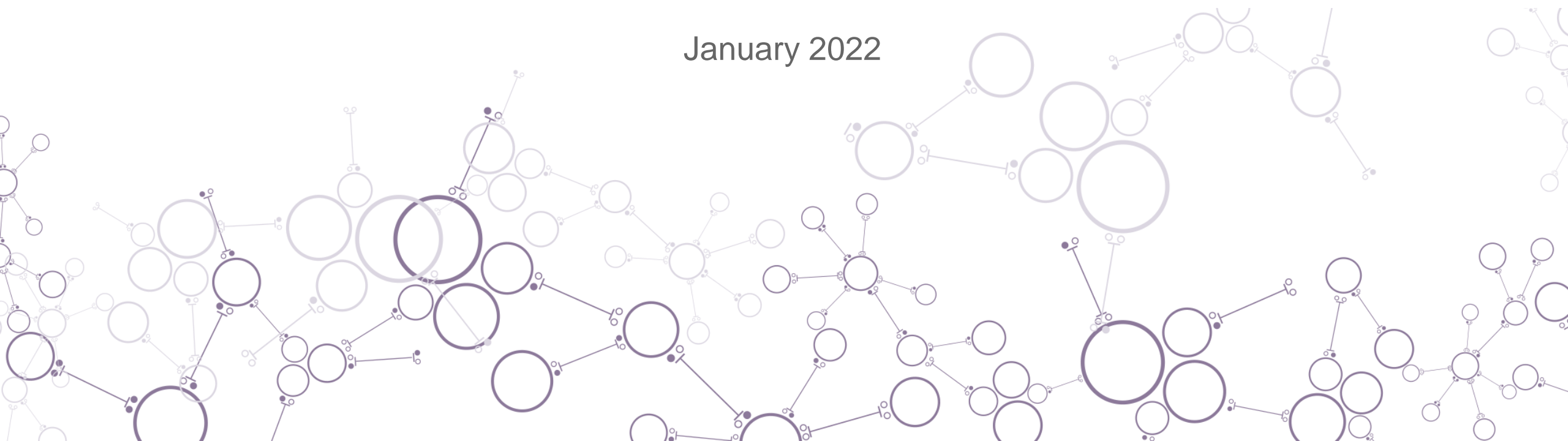# Oncology Overview

January 2022

Forward-Looking Statements

Forward–Looking Statements and Disclaimer

This presentation will include forward-looking statements that are subject to substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Our forward-looking statements include, but are not limited to, statements regarding our or our management team's expectations, hopes, beliefs, intentions or strategies regarding the future, and statements that are not historical facts, including statements about the clinical and therapeutic potential of our product candidates, the availability and success of topline results from our ongoing clinical trials and any commercial potential of our product candidates. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements.

Although we believe that our plans, intentions, expectations and strategies as reflected in or suggested by those forward-looking statements are reasonable, we can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved. Furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a number of risks, uncertainties and assumptions, including, but not limited to, those risks set forth in the sections captioned "Risk Factors" and "Forward-Looking Statements" of our filings with the U.S. Securities and Exchange Commission, available at www.sec.gov and investor.roivant.com. We operate in a very competitive and rapidly changing environment in which new risks emerge from time to time. These forward-looking statements are based upon the current expectations and beliefs of our management as of the date of this presentation, and are subject to certain risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. Except as required by applicable law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

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Roivant: Redefining "Big Pharma" from End to End

We are a biopharmaceutical company discovering, developing and commercializing transformative medicines faster by building technologies and deploying talent in creative ways
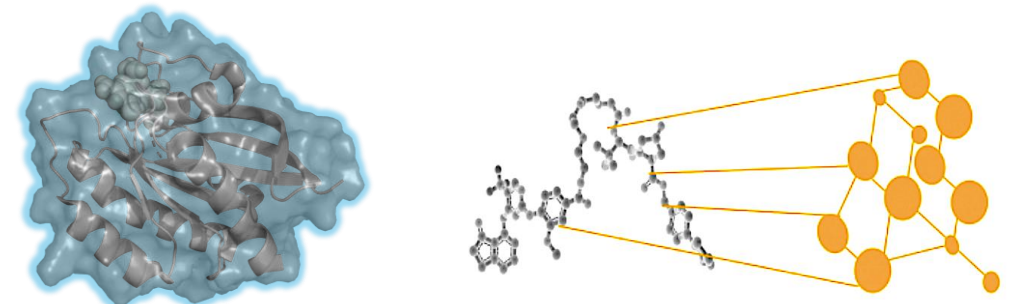
Vant Model

Aligning incentives to promote successful execution, with Vants benefiting from support of the Roivant platform
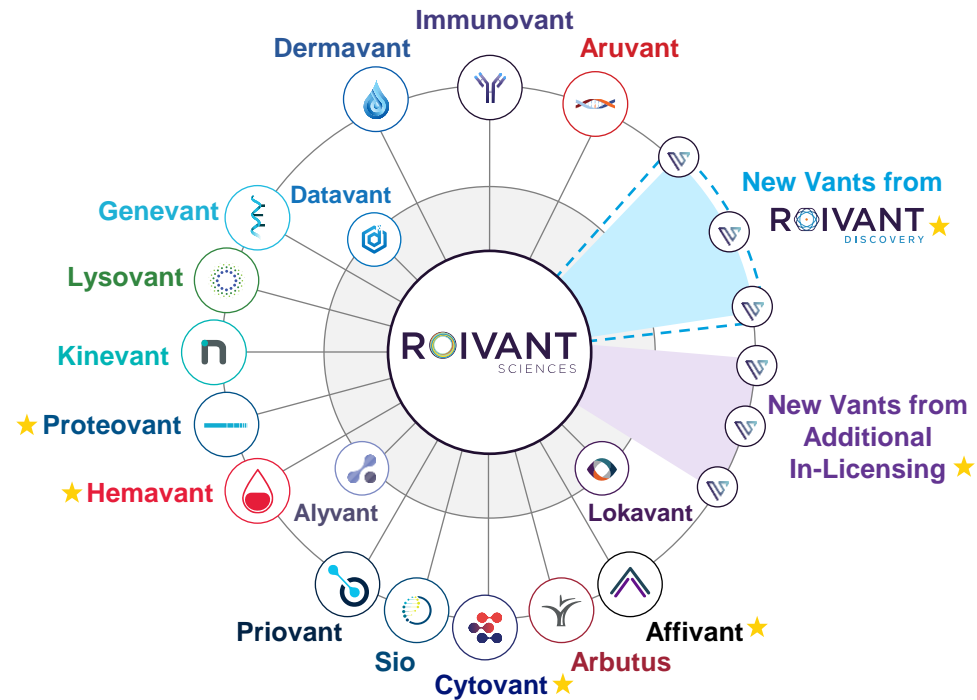

Computational Tools

Technologies built to address inefficiencies in drug discovery, development and commercialization processes

★ Indicates Vant or strategy with oncology relevance

Select Discovery and Development Pipeline in Oncology to Address Unmet Patient Needs

			Modality	Discovery	Preclinical	Phase 1/2
🩸	**RVT-2001**	Transfusion-Dependent Anemia in Patients with Lower-Risk MDS				▶
	AFM32	Solid Tumors			▶	
	CVT-TCR-01	Oncologic Malignancies			▶	
	AR	Prostate Cancer			▶	
	STAT3	Oncology, Immunology			▶	
	Undisclosed	Oncology		▶		
	CBP/p300	Oncology		▶		
	SMARCA2/4	Oncology		▶		
	Undisclosed	Oncology		▶		
	Multiple Additional Targets	Oncology, Immunology		▶		
	WRN	Oncology		▶		
	CRAF	Oncology		▶		
	HIF2A	Oncology		▶		
	ADAR1	Oncology		▶		
	Multiple Additional Targets	Oncology, Immunology, Neurology		▶		
	KRAS G12D	Oncology		▶		

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

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Cytovant · Hemavant · Affivant · Proteovant · Roivant Discovery · Degrader · Inhibitor/Modulator · Biologic

RVT-2001: Potential First-in-Class Small Molecule SF3B1 Modulator for the Treatment of Transfusion-Dependent Anemia in Patients with Lower-Risk MDS

Lower-Risk MDS is a Commercially Validated Market

Encouraging Proof-of-Concept Data

Multipronged Strategy to Optimize RVT-2001's Clinical Impact

Expect Fast, Well-Established Path to Potential Approval

Strong Intellectual Property Position

Transfusion-dependent anemia in MDS has limited treatment options

Luspatercept (Reblozyl), approved for RS+ MDS in 2020, annualizing at >$500M 5 quarters after launch; BMS potential projected peak >$4B[1]

First-in-class potential as the only known SF3B1 modulator currently in clinical development

Compelling data in a highly refractory population

80+ subjects treated in Phase 1/2 study; generally well-tolerated to date[2]

Planned development strategy optimizing dosing, utilizing precision medicine enrollment, and excluding certain refractory patients

Precedent suggests minimal data decay between Phase 2 and Phase 3[3]

Intend to conduct a robust open-label expansion of an ongoing Phase 1/2 trial in 2022

Precedent in the space is a single pivotal study with approximately 200-250 patients[4]

Composition of matter IP protection expected until 2035, before any potential patent term extensions

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High Unmet Need for an Oral Therapy in Transfusion-Dependent Anemia in Lower-Risk MDS

Current treatment options fail in multiple segments of the patient population

~17K new MDS cases/year,
~115K MDS patients total in US[1]

Lower-risk patients
(~2/3 of new patients)[2]

Transfusion-Dependent Anemia in Lower-Risk MDS

RS+	RS-	del(5q)

ESAs	ESAs	Lenalidomide

Luspatercept	**RVT-2001**

RVT-2001
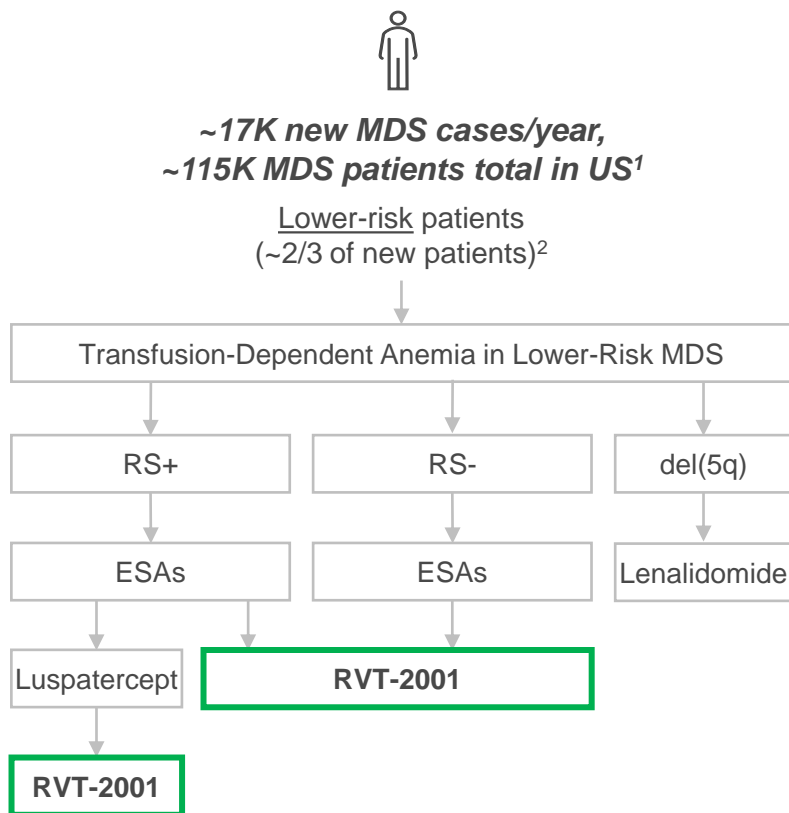
- Lower-risk MDS is a chronic condition; therapy is focused on management of symptoms
  - Goal of treatment is to reduce or eliminate red blood cell (RBC) transfusion dependence with minimal toxicity

- Erythropoiesis-stimulating agents (ESA) used in 1L
  - Ineffective in >50% of patients, primarily used in patients with low transfusion burden and EPO levels[3]

- Luspatercept is ineffective in >50% of patients and is most effective in patients with low transfusion burden[4]

- Lenalidomide is associated with significant toxicities and is only approved for 10-15% of MDS patients[5]

- RVT-2001 is a potential oral therapy targeting SF3B1, a genetically validated target mutated in up to 80% of certain MDS patient subsets[6]
  - Mutations cause alterations in mRNA splicing thought to be an initiating event in MDS[7]
  - *In vitro* and *in vivo,* RVT-2001 corrects splicing defects caused by SF3B1 mutations in mRNA transcripts that encode proteins that are thought to be associated with the development of MDS[8]

**Initial plan to target second line in SF3B1-mutated patients,
with potential to expand to other spliceosome mutations and first line**

Encouraging Early Data Demonstrate RVT-2001's Clinical Potential

Meaningful Clinical Impact in Refractory Patient Population to Date

- **RVT-2001: RBC-TI rate of >30%** in Phase 1/2 study in subset of 19 patients with lower-risk, transfusion-dependent MDS, 15 of whom had documented prior treatment with lenalidomide and/or HMAs[1]

  - Median duration of treatment for responders of approximately 2 years[1,2]

  - **Luspatercept: 13% RBC-TI** among patients with prior lenalidomide exposure in Phase 2 trial[3]

  - **Lenalidomide: 12% HI-E** among patients with prior HMA exposure in investigator-sponsored trial[4]

- RVT-2001 was generally well-tolerated in Phase 1/2 study (n=84 in patients with MDS, AML, and CMML), with the majority of events classified as Grade 1[1]; significant need remains for additional tolerable, effective therapies

Note: No head-to-head studies of RVT-2001 have been conducted

Potential for Improved Therapeutic Effect in Earlier-Line Patients

- Hemavant plans to enroll earlier-line patients in RVT-2001 trials, who have been more responsive in trials for other therapies to treat anemia associated with lower-risk MDS

  - Luspatercept Phase 3 trial excluded prior lenalidomide exposure following reduced RBC-TI responses in Phase 2[3]

    - In luspatercept's Phase 2 trial, **44% RBC-TI** in patients **without prior lenalidomide exposure** vs. **13% with prior lenalidomide exposure**[3]

  - In a lenalidomide investigator-sponsored trial of patients with lower-risk, non-del(5q) MDS, **HI-E of 38% prior to HMAs** vs. **12% post-HMAs**[5]

Plan to Amend Ongoing Open-Label Phase 1/2 Trial to Target Improved and Extended Responses

Robust signal-enhancing design can provide multiple paths to demonstrate value through potential high response rates and/or long duration either in the overall population or in genetically defined subsets

Target Genetically Defined Subpopulations

- Selectively enroll lower-risk MDS patients with *SF3B1* mutations (~30% of MDS patients)[1]

- Expand dataset in high TMEM14C ratio subset

  - **RBC-TI of 71% (5/7) to date** among patients in RVT-2001 Phase 1/2 study with the highest levels of aberrant TMEM14C transcripts (as measured by elevated AJ/CJ ratios)[2]
  - High ratios of aberrantly spliced TMEM14C transcripts were associated with SF3B1 mutations[2]

Improve Dosing

- Strengthen pharmacodynamic effect by optimizing dosage of RVT-2001

Minimal Data Decay

- Minimal data decay observed historically from Phase 2 to Phase 3 in precedent trials for other therapies in MDS

All product candidates are investigational and subject to regulatory approval.
AJ/CJ: Ratio of aberrant splicing junction to canonical splicing junction.
1. Malcovati et al., 2015
2. Steensma et al., 2021

Collaboration with Affimed To Develop Bispecific Antibodies for Solid Tumors

- Affimed's ROCK platform technology generates diverse, tetravalent, bispecific antibodies known as innate cell engagers (ICE) which can be customized to target specific binding domains on hematologic and solid tumor cells

- The partnership grants Roivant a license to AFM32, a preclinical ICE candidate

  - In a head-to-head preclinical study, AFM32's potency exceeded that of a monoclonal antibody that has been clinically validated against the same tumor target

  - AFM32's potency also exceeded that demonstrated in published preclinical studies of an antibody-drug conjugate agent that has been clinically validated against the same tumor target

  - Based on preclinical and clinical experiences with other ICE antibodies in separate studies, the tolerability of AFM32 has the potential to be superior to that observed to date with antibody-drug conjugates in published literature

  - AFM32 is potentially applicable to several highly prevalent solid tumor indications

- Beyond an exclusive license to AFM32, Roivant has the option to license from Affimed additional ICE molecules directed against targets that are not (a) currently licensed or optioned to third parties or (b) directed against targets included in Affimed's current pipeline

All drugs are investigational and subject to health authority approval.

9

Affivant Overview

Bispecific Antibodies: A Novel Class that Directs the Immune System to Kill Tumors
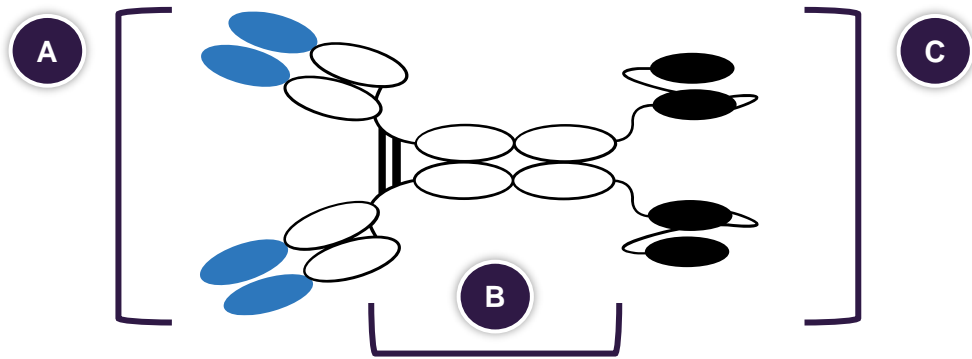
A **Tumor Associated Antigen (TAA) binding domain:**
Causes high affinity, high specificity binding to tumor surface

B **Linker region:**
Improves pharmaceutical properties. Size and flexibility can be modulated to fine tune activity

C **Immune cell binding domain:**
Binds and activates specific immune cell subsets, resulting in tumor cell death

Unique Approach to Engaging Natural Killer (NK) Cells and Macrophages Kills Tumor Cells

CD16A	CD16B	CD16A	+ IgG
✓ Binding	✗ **No** Binding	✓ Binding	
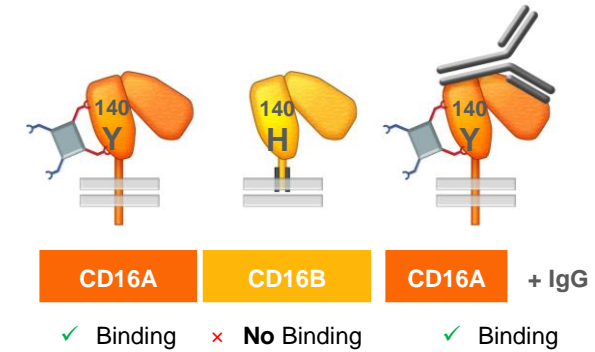
- Affimed's Innate Cell Engagers (ICE) bind CD16A with a unique epitope
- CD16A is sufficient to fully activate cell killing by NK cells and macrophages
  - Differentiated from platforms that can engage NK cells
- Highly selective for CD16A
  - No dilution and sink effect through neutrophils (CD16B+)
- High affinity binding with minimal serum IgG competition
  - Superior to monoclonal antibodies (mAbs) and Fc-enhanced mAbs

Proteovant Positioned to Lead in Protein Degrader Discovery and Development

World class Proteovant team to drive discovery and development of optimized protein degraders

Well-financed to advance pipeline of protein degraders to the next level of value creation

Exclusive long-term discovery research partnership with the University of Michigan Lab of Dr. Shaomeng Wang (founder of Oncopia Therapeutics)
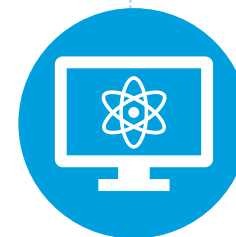
Significant investments in internal discovery; exclusive partnership with VantAI to access a unique and proprietary degrader-optimized machine learning and systems biology platform

VantAI: A Novel Paradigm For Rational Degrader Discovery

proteovant THERAPEUTICS

Classical small molecule machine learning starts chemistry first - VantAI flips this script
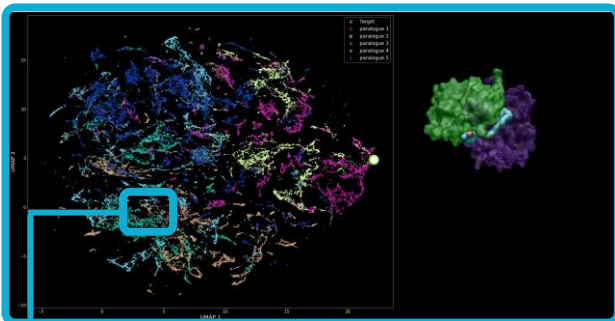
Protein-Contacts First, Learning From Evolution

I) Look at every possible interface

II) Evolutionary scoring

Interface
E3 → K S H K → POI → DL model → **0.7** VantAI-score

III) Chemistry to fill the gap

Degrader
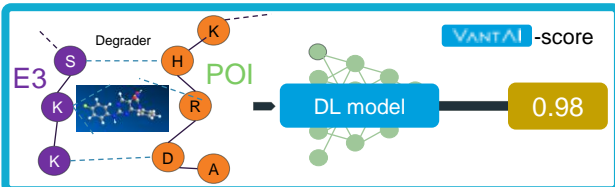E3 → K S H K → POI → DL model → **0.98** VantAI-score

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

Without VantAI method[1]   With VantAI method

72.9%

6.4%

>11x

Enrichment

- 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

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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

Roivant Discovery Approach to End-to-End Heterobifunctional Drug Discovery is Anchored on Five Core Components

Target mapping and selection:
Our translational cheminformatics and multi-omics capabilities stratify the proteome to select targets for our pipeline, based on therapeutic and degradability potential

Degradability demonstration and E3 ligase fitness:
We deploy our biology and degradomics platforms to measure the key characteristics of each protein of interest and then demonstrate its degradability experimentally

New proprietary ligands:
We exploit our leading physics-based platform to evolve ligands for E3 ligases and Proteins of interest, from starting points identified by integrated hit finding
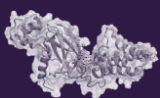
**Predictive heterobifunctional assembly**:
We apply our industry-leading ternary complex modeling directly as part our design-predict-make-test cycle to design and optimize linkers and ligands
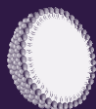
Enhanced delivery:
We apply our development degrader expertise and emerging technologies for advanced delivery of heterobifunctionals

Heterobifunctional expansion
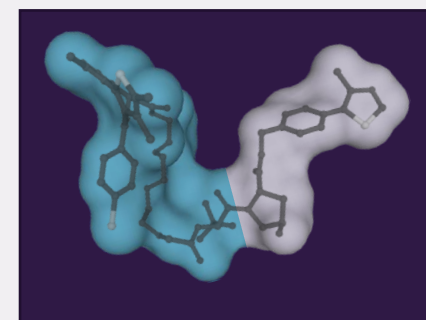
Catalysts

Vant	Catalyst	Expected Timing
dermavant	FDA approval decision on tapinarof for psoriasis	2Q 2022
	Topline data from tapinarof Phase 3 trials in atopic dermatitis	1H 2023
IMMUNOVANT	Batoclimab pivotal trial initiation in MG	1H 2022
	Initiate three pivotal programs, including MG	2022
	Progress TED, WAIHA, and two new indications to be announced	2022
ARUVANT	ARU-1801 Phase 3 initiation	1H 2023
kinevant	Namilumab Phase 2 initiation in sarcoidosis	1H 2022
lysovant	LSVT-1701 MAD initiation	1H 2022
HEMAVANT	Expand ongoing RVT-2001 Phase 1/2 trial in lower-risk MDS	2022
proteovant THERAPEUTICS	Phase 1 initiation for first degrader candidate	2022
ROIVANT DISCOVERY proteovant THERAPEUTICS	Multiple additional degrader candidates entering IND-enabling studies each year	Starting 2022

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All timelines reference calendar year.