



# Pioneering Computational Molecular Design

November 2024

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These forward-looking statements reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. Actual results may differ materially from those described in the forward-looking statements and are subject to a variety of assumptions, uncertainties, risks and important factors that are beyond our control, including the demand for our software solutions, the reliance upon our third-party drug discovery collaborators, the reliance upon Novartis to perform its obligations to develop and commercialize any development candidates discovered by us under the collaboration, the uncertainties inherent in drug development and commercialization, such as the conduct of research activities and the timing of and our ability to initiate and complete preclinical studies and clinical trials, uncertainties associated with the regulatory review of clinical trials and applications for marketing approvals, factors adversely affecting the life sciences industry, and other risks detailed under the caption "Risk Factors" and elsewhere in our Securities and Exchange Commission ("SEC") filings and reports, including our Quarterly Report on Form 10-Q for the quarter ended September, 2024, filed with the SEC on November 12, 2024, as well as future filings and reports by us. Any forward-looking statements contained in this presentation speak only as of the date hereof. Except as required by law, we undertake no duty or obligation to update any forward-looking statements contained in this presentation, future events, changes in expectations or otherwise.

This presentation includes statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this presentation involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. We have not independently verified such third-party data, and we undertake no obligation to update such data after the date of this presentation.



# **Recent Highlights**

#### **3Q24 Financial Results**

- \$35.3M total revenue
- \$31.9M software revenue
- Received \$48M from sale of equity in Morphic\*

#### **Novartis Collaboration**

- \$150M upfront
- \$2.3B in potential milestones plus royalties
- Multi-year, multi-target
- Expanded software contract

#### **Data Presentations**

- SGR-3515 preclinical data presented at ENA24
- PRMT5-MTA preclinical data presented at ENA24

#### **FY24 Financial Commentary**

- Narrowed software revenue guidance
- Lowered drug discovery revenue guidance

#### **Predictive Toxicology**

- Broadening and accelerating initiative
- \$9.5M additional funding

# Phase 1 Data Readouts on Track

- SGR-1505 1H 2025
- SGR-2921 2H 2025
- SGR-3515 2H 2025





# Schrödinger

# Pioneering Digital Chemistry



30+ years of innovation



Over 850 employees worldwide; >40% Ph.D.



>50% of employees dedicated to R&D

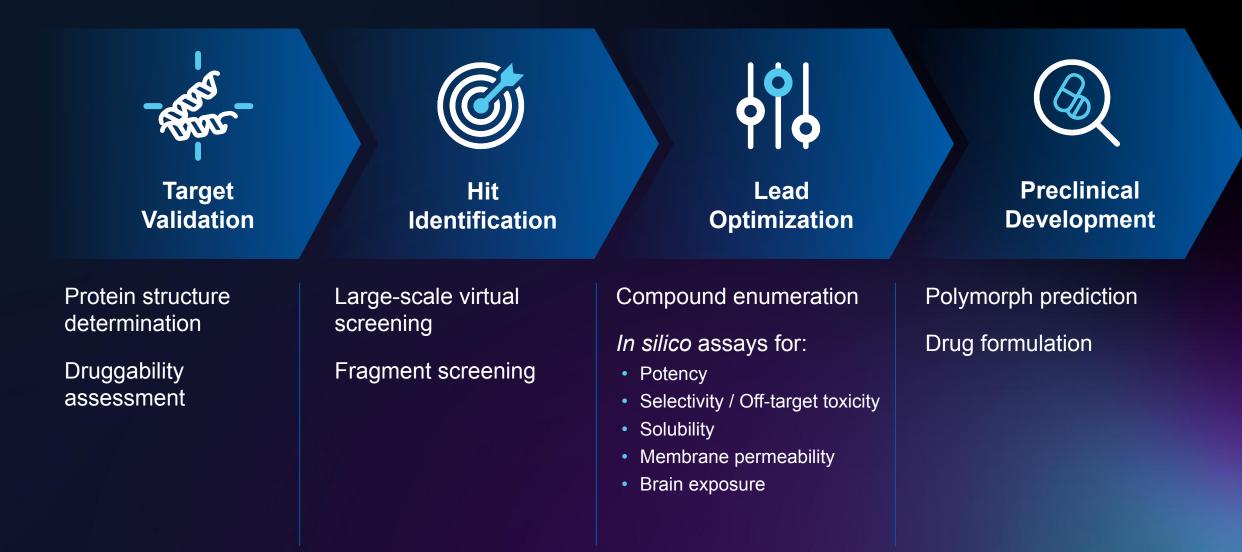


~1,785 customers, including top 20 biopharma<sup>1</sup>



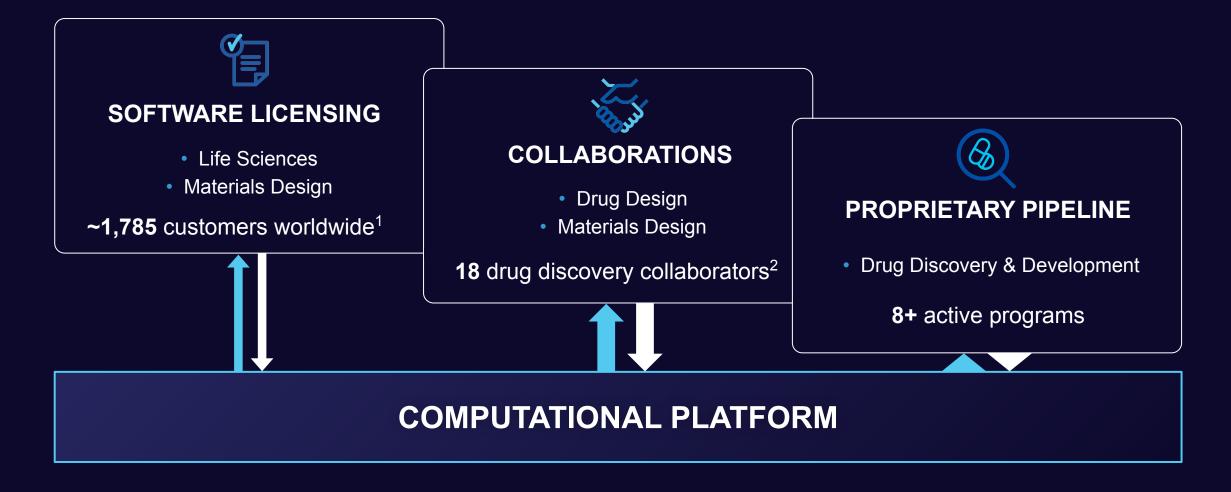
Pipeline of 25+ collaborative and proprietary programs

# **Our Target-to-Clinic Digital Chemistry Laboratory**





### Multi-Pronged Business Enabled by Highly Differentiated Computational Platform





# Computational Platform



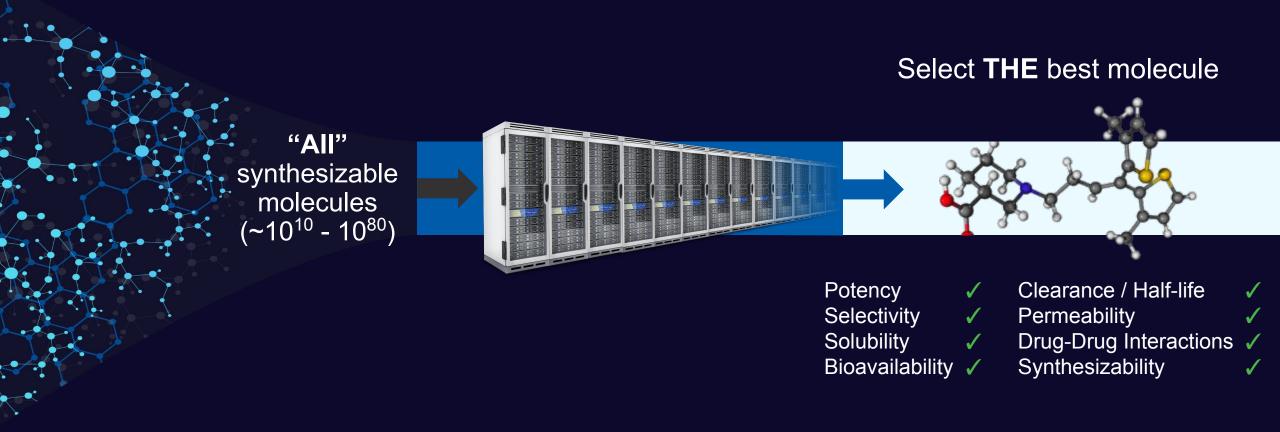
### Designing Drugs Is a Highly Challenging Multi-Parameter Optimization Problem

Need to identify a molecule that balances many anti-correlated properties:	~~Q	~ <del>?</del> \$		dyD	d <sub>t</sub> o		
Potency	$\checkmark$	×	$\checkmark$	×	$\checkmark$	$\checkmark$	33%
Selectivity	×	<ul> <li>Image: A start of the start of</li></ul>	$\checkmark$	$\checkmark$	×	<b>√</b>	success
Solubility	×	×	×	<b>√</b>	<b>√</b>	X	IND delivery
Bioavailability	×	×	×	×	×	×	66%
Clearance / Half-life	×	×	×	×	×	×	failure
Permeability	×	×	×	×	×	×	
Drug-drug interactions	×	×	×	×	×	X	
Synthesizability	×	×	×	×	×	×	



# Schrödinger's Vision for the Future of Drug Discovery

If all properties can be calculated with perfect accuracy, designing drugs would have a much **higher success rate**, be much **faster** and **cheaper**, and would produce much **higher-quality** molecules.





# **Digital Chemistry Laboratory Leverages Physics + Al**



#### Physics-based Methods

- ✓ No training set required
- Can extrapolate into novel chemical space
- ✓ Accurate
- × Slow



#### Physics + Al

#### Training Set for AI/ML Generated Using Physics

- ✓ Fast
- ✓ Accurate
- ✓ Can handle very large datasets
- Can extrapolate into novel chemical space

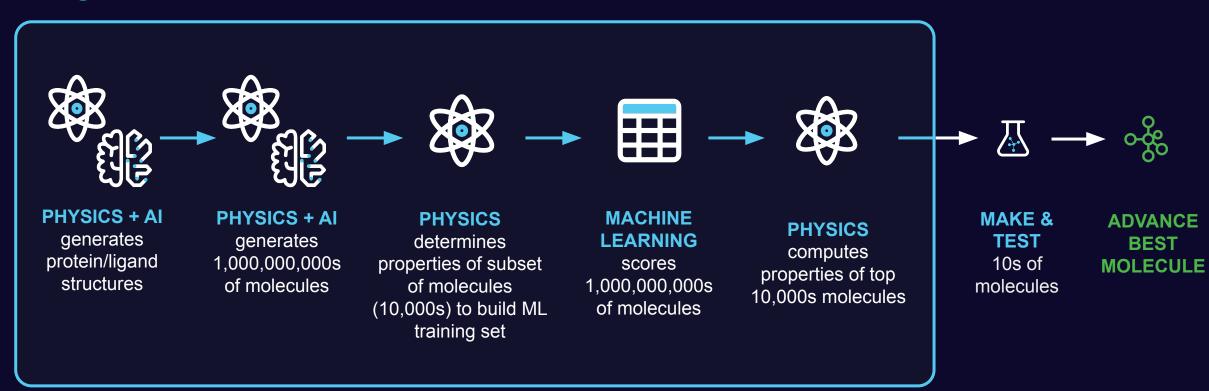


#### Artificial Intelligence / Machine Learning

- ✓ Effective at interpolation
- Fast
- ✓ Can handle very large datasets
- K Requires massive training sets



# **Physics-Enabled AI/ML Platform**

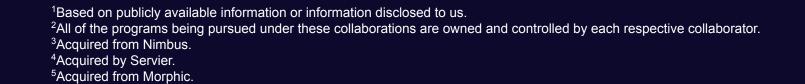




# A Broad Portfolio of Advancing Collaboration Programs<sup>(1)(2)</sup>

Phase 1 Phase 2		Phase 3		FDA-Approved			
nimbus THERAPEUTICS	Immuno-oncology	🕼 GILEAD	Metabolic Diseases <sup>3</sup>	Takeda	Psoriasis <sup>3</sup>	≁ agios	TIBSOVO⁴ IDHIFA⁴
	Obesity	Lilly	Inflammatory Bowel Disease <sup>5</sup>				
Undisclosed	Undisclosed						
Undisclosed	Undisclosed						





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### A Multi-Target Drug Discovery Collaboration and Expanded Software Licensing Agreement



# Schrödinger & Novartis Collaboration Leverages Synergies

#### Schrödinger

- Licensing certain existing early-stage discovery programs outside oncology
- World class experts in physics-based molecular design and drug discovery joining forces with Novartis teams
- \$150M upfront payment, \$2.3B in potential milestones and tiered royalties on global net sales
- Expanded software contract and real-time knowledge transfer to Novartis

Combining expertise and existing efforts to jointly pursue novel medicines

#### Novartis

- Advance discovery efforts in core therapeutic areas
- Development, regulatory and commercial expertise
- Global commercial rights to resulting development candidates
- Adoption and onboarding of Schrödinger physics-based platform, AI/ML solutions, and enterprise informatics



# **Collaboration Details & Financial Implications**

<section-header></section-header>	<ul><li>\$150M upfront</li><li>Up to \$2.3B in development, regulatory and commercial milestones</li><li>Royalties on global net sales</li></ul>	<ul> <li>Upfront recognized over duration of research period</li> <li>Milestones begin in discovery and escalate</li> <li>Mid-single to low-double digit tiered royalties on net global sales</li> </ul>
Software Agreement	Significantly expands existing license agreement Software deployed at industry-leading scale Full suite of physics-based modeling and enterprise informatics	<ul> <li>Initial license deployment in 4Q24</li> <li>Multi-year purchase commitment</li> <li>Mix of upfront and ratable revenue</li> </ul>

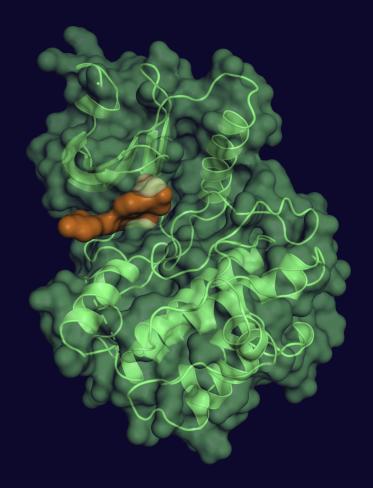


# Predictive Toxicology Initiative



# **Off-Target Toxicity Is a Major Challenge in Drug Discovery**

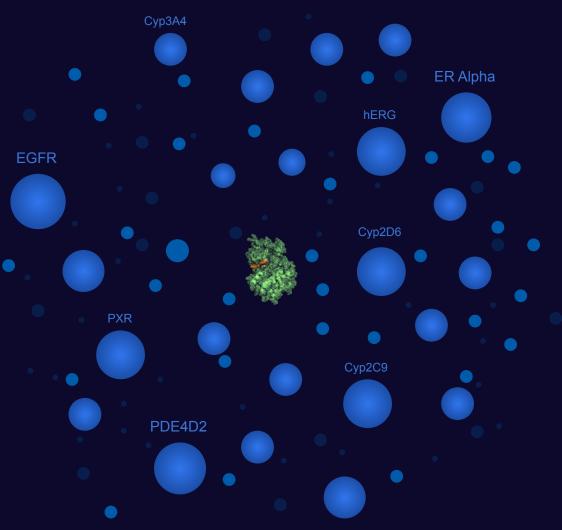
- Toxicity associated with binding to off-target proteins is a significant cause of development failures
- Current drug discovery is focused primarily on ligand binding to therapeutic target protein
- Experimental toxicity screening is slow, costly and usually assessed late in the discovery process





### Predicting Off-Target Toxicity Can Dramatically Improve Drug Discovery Productivity

- Predictive Toxicology Initiative: Determine structure of off-target proteins and build accurate structure-based models for ligand binding to off-targets
- Expanded focus to optimize ADME
- A predictive, computational, approach offers multiple advantages:
  - Early de-risking
  - Faster ligand evaluation
  - Greater throughput
  - Lower cost
  - Improved toxicity profile





# Schrödinger's Predictive Toxicology Initiative



- Determines off-target protein structures
- Develops accurate predictive models
- Incorporates models into platform

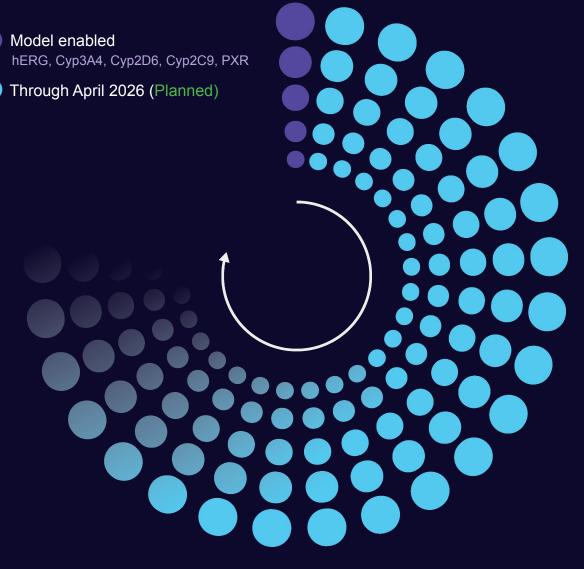
#### BILL& MELINDA

GATES foundation

- Committed \$10M initial grant July 2024
- Additional \$9.5M grant November 2024

### 📀 NVIDIA.

Provides enabling AI technologies





# **Proprietary Pipeline**



# **Advancing Multiple Clinical and Preclinical Programs**

		DISCOVERY	PRECLINICAL	PHASE 1
SGR-1505 (MALT1)	R/R B-cell Malignancies <sup>*</sup>			
SGR-2921 (CDC7)	R/R AML/MDS <sup>*</sup>			
SGR-3515 (Wee1/Myt1)	Solid Tumors			
SOS1	Solid Tumors			
PRMT5-MTA	Solid Tumors			
EGFR <sup>C797S</sup>	Solid Tumors			
NLRP3	Immunology			
LRRK2	Neurology			
Undisclosed Programs	Multiple Areas			

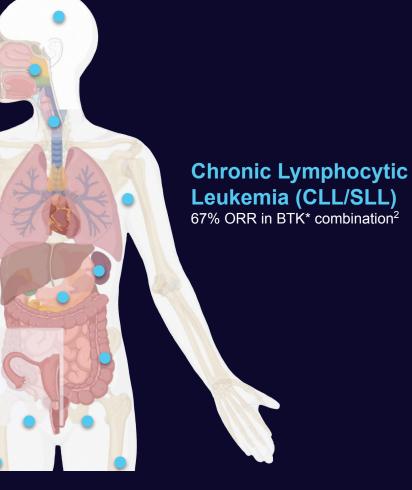


<sup>\*</sup>Definitions: R/R: Relapse/refractory; AML: Acute myeloid leukemia; MDS: Myelodysplastic syndromes.

## MALT1 Protease Inhibition Clinically Validated in 3<sup>rd</sup> Party Study



Solid Tumors Third Party Phase 1 Study Ongoing<sup>5</sup>



#### Allosteric Inhibition of MALT1

- Clinically validated by 3<sup>rd</sup> party MALT1 inhibitor showed monotherapy and combination activity in human B-cell malignancies
- Opportunity for well-tolerated, potent, optimized inhibitors in NHL and CLL
- Potential in autoimmune disease

\*Definitions: ORR: overall response rate; BTK: Bruton tyrosine kinase.



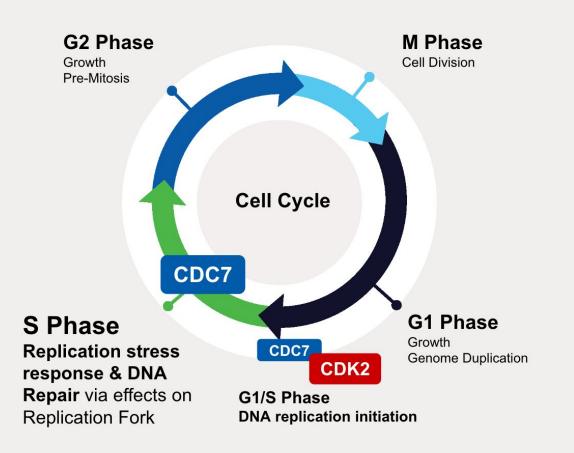
<sup>1</sup>WO2022184716 Combination Therapy using MALT1 Inhibitor and BTK Inhibitor. <sup>2</sup>WO2022185097 Method of treating a condition using a therapeutically effective dose of the MALT1 inhibitor JNJ-67856633. <sup>3</sup>Kalac M. et. al, EHA Abstracts HemaSphere 7(S3):p e60782b9, August 2023. <sup>4</sup>Hertzberg et. al. *Hematological Oncol* June 2023. <sup>5</sup>Naing et al., *Ann Oncol* 2023, 34 (suppl\_2): S619-S650.

# SGR-1505 Status and Next Steps





# CDC7 Is an S-phase Kinase That Regulates DNA Replication and the Replication Stress Response



#### CDC7

- Maintains DNA replication fork progression, activates fork protection and restart mechanisms<sup>1,2</sup>
- Activates BRCA1-A and Cohesin complexes<sup>1</sup>
- Required for protection and restart of stalled replication forks<sup>1,3,4</sup>



<sup>1</sup>*Mol Cell* 2021 Feb 4;81(3):426-441. <sup>2</sup>*Oncogene* 2008 May 29;27(24):3475-82. <sup>3</sup>*Genes Dev* 2015 Sep 15;29(18):1955: 2506. <sup>4</sup>*J Biol Chem* 2020 Jan 3;295(1):146-157.

# SGR-2921 Status and Next Steps

Strong preclinical rationale	<ul> <li>High replication stress in AML</li> <li>Potent and selective CDC7 inhibition shows strong anti-proliferative activity in AML samples, including those resistant to standard-of-care therapies</li> </ul>
Phase 1 study in AML or MDS ongoing	<ul> <li>Primary objectives: Evaluate safety, tolerability and RP2D</li> <li>Secondary objectives: Evaluate PK, preliminary anti-tumor activity</li> <li>Initial clinical data presentation expected 2H 2025</li> </ul>
Future opportunities	<ul> <li>Explore combination potential with existing and emerging agents</li> <li>Expansion opportunities in solid tumors</li> </ul>

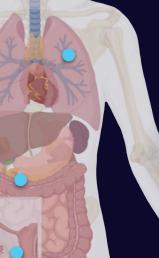


# Wee1 Inhibition Clinically Validated in 3<sup>rd</sup> Party Studies

**Breast Cancer 26% ORR (**cisplatin combination)<sup>1</sup>

> \*Uterine Cancel 30% ORR monotherapy

\*Ovarian Cancer Up to 50% ORR monotherapy <sup>3,4-6</sup>



Head and Neck Cancer 50% ORR (chemo combination)<sup>7</sup>

#### Lung Cancer

Monotherapy and combo responses<sup>8-9</sup>

#### Pancreatic Cancer

Increased PFS and OS (gemcitabine combination)<sup>10</sup>

Colorectal Cancer Responses and increased PFS<sup>8,11,12</sup>

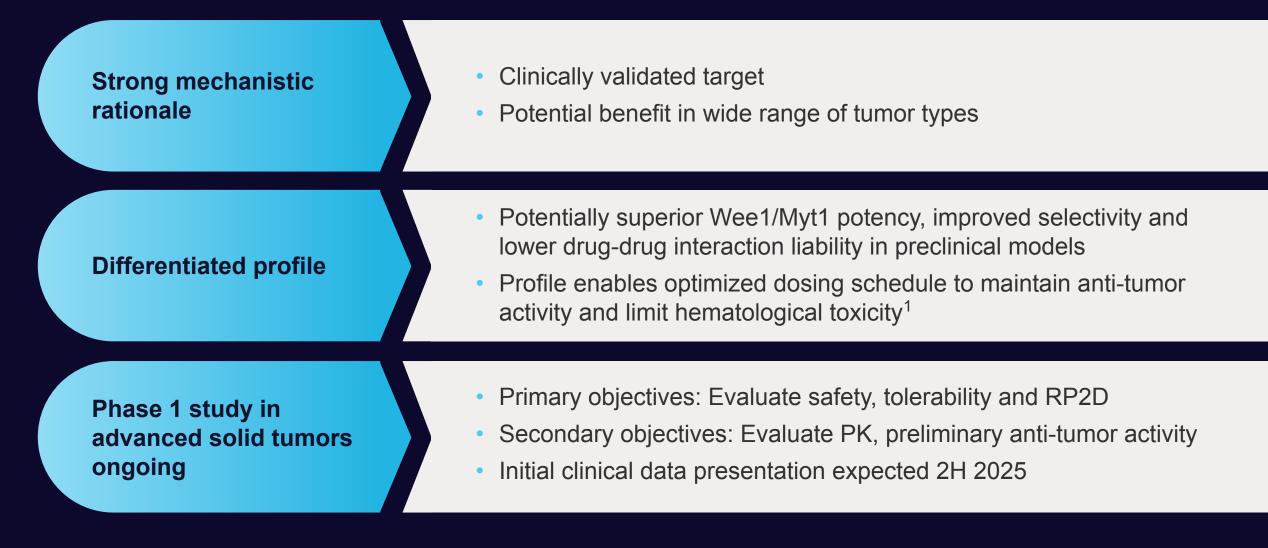
#### SGR-3515 Combines Wee1/Myt1 Activity

- Opportunity for improved therapeutic index
- Demonstrates durable activity from intermittent dosing in preclinical models<sup>13</sup>
- Myt1 activity offers opportunity to benefit from synthetic lethal relationship



<sup>1</sup>*Clin Cancer Res* 2021: 27(4). <sup>2</sup>*J Clin Oncol* 2021: 39(14):1531-1539. <sup>3</sup>*J Clin Oncol* 40, no. 16\_suppl (June 01, 2022) 5515. <sup>4</sup>*Lancet* 2021: 398:281-92. <sup>5</sup>*J Clin Oncol* 2016: 34:4354-4361. <sup>6</sup>*Clin Cancer Res* 2018: 24(120): 2740-8. <sup>7</sup>*Clin Cancer Res* 2018: 15;24(12):2740-2748. <sup>8</sup>*Zentalis investor deck*. <sup>9</sup>*Ann Oncol* 2020: 31 (suppl\_4). <sup>10</sup>*J Clin Oncol* 2019 Oct 10;37(29). <sup>11</sup>*Cancer Res* (2019) 79 (13\_Supplement): CT02. <sup>12</sup>*J Clin Oncol* 2021 Nov 20;39(33). <sup>13</sup>Sun et al., AACR 2022.

# SGR-3515 Status and Next Steps





# **Advancing Multiple Discovery Programs**

#### EGFR<sup>C797S</sup>

- Optimizing a wild-type-sparing, CNS-penetrant molecule<sup>\*</sup>
- Potential to address brain metastases and deepen responses through new combination regimens

# PRMT5-MTA

- Leads display MTAP<sup>KO</sup> selective anti-proliferative effects, and favorable solubility and ADME profiles<sup>\*</sup>
- Rapidly advancing novel, selective, potent molecules with optimized brain-penetration

#### NLRP3



- Advancing leads in two series with excellent *in vivo* potency and ADME profiles
- Both peripheral and CNS penetrant leads being optimized

Expect to file at least one IND in 2025 from discovery pipeline



# Materials Science



# **Leveraging Platform Synergies: Materials Science**

- Materials Science business launched in 2012
- Leverages 30+ years of innovation in atomic-scale simulation solutions

#### **Initial Collaborations: Next-Gen Batteries**



- Developing atomistic simulations to improve battery performance
- Agreement renewed for a second three-year term in 2023

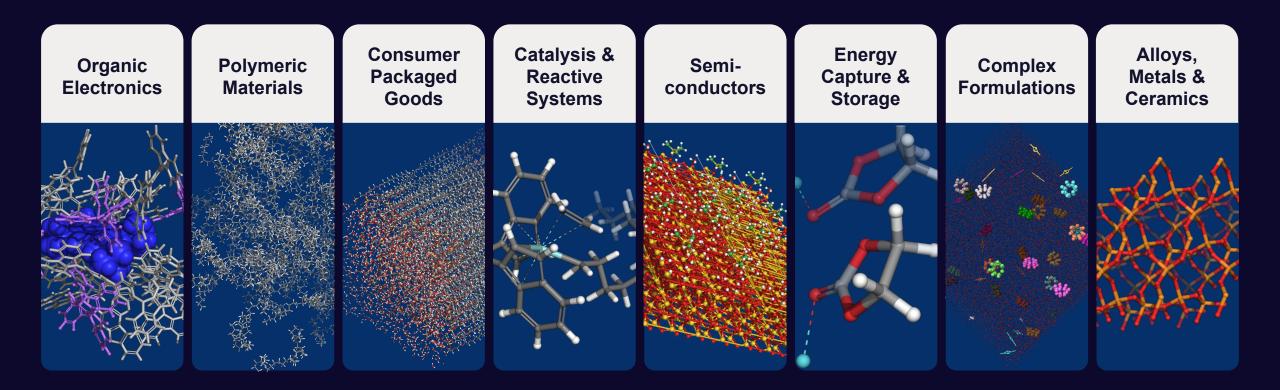
#### +EONIX

- Accelerating materials discovery and design for next gen Li-ion batteries
- 3-year collaboration





## Platform Has Broad Application Across Industrial Materials Design and Development



Tailored solutions designed to reduce cost, risk, and shorten timelines



# Financial Overview



# 3Q24 Financial Highlights vs. 3Q23

			Three Months Ended Sept.30
	Q3 2023	Q3 2024	% Change
Total revenue	\$42.6	\$35.3	(17%)
Software revenue	\$28.9	\$31.9	10%
Drug discovery revenue	\$13.7	\$3.4	(75%)
Gross profit	\$23.6	\$17.7	(25%)
Software gross margin	76%	73%	
Operating expenses	\$79.8	\$86.2	7.9%
Other income/(expense)	(\$8.7)	\$30.2	
Net loss	(\$62.0)	(\$38.1)	
	as of 9/30/23	as of 9/30/24	
Cash and cash equivalents, restricted cash, and marketable securities	\$502.5	\$398.4	(21%)
Deferred revenue, current and long term	\$55.4	\$47.0	(15.2%)
	• (in mi	llions)	,



### Four-Quarter Trailing Average Software Quarterly Revenue Trend





## **2024 Financial Guidance**

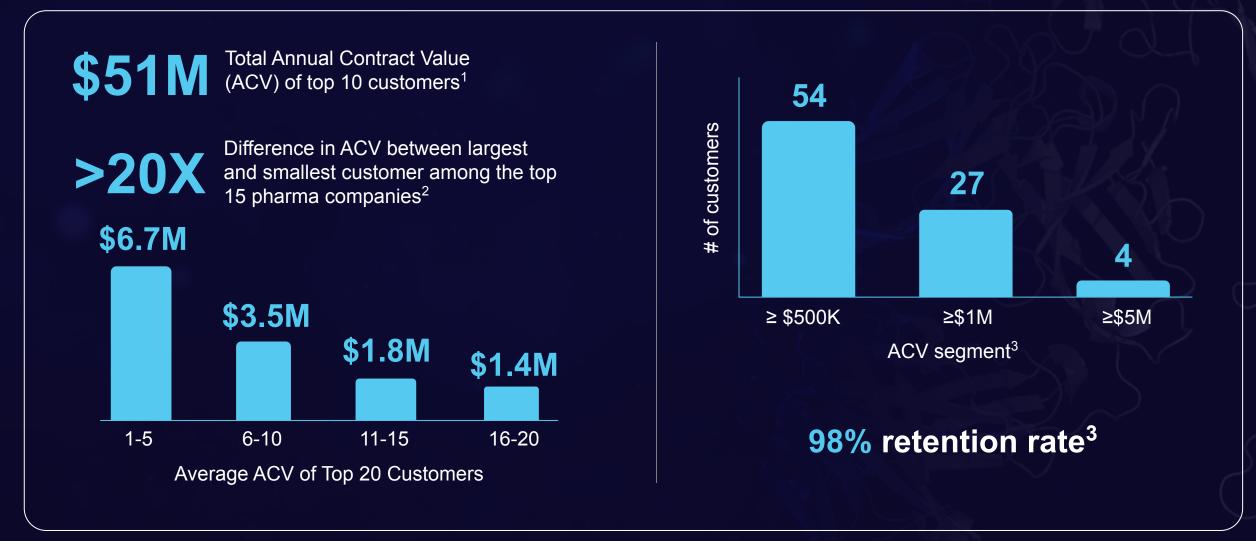
(As of November 12, 2024)

	2023 Actual	Year-to-Date 3Q24	Updated 2024 Guidance
Total revenue	\$216.7	\$119.2	
Software revenue	\$159.1	\$100.7	8% – 13%
Drug discovery revenue	\$57.5	\$18.5	\$20 – \$30
Software gross margin	81%	77%	Similar to 2022*
Operating expense growth	28.4%	10.5%	8% – 10%
Cash used in operating activities	\$136.7	\$126.3	Above 2023

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(in millions)

# **2023 Key Performance Indicators**





# Full Year 2023 Key Performance Indicators (KPIs)

	2022	2023
Software KPI		
Total annual contract value (ACV)	\$140.6M	\$154.2M
ACV of Top 10 Customers	\$46.5M	\$51.0M
Number of customers with ACV ≥\$5M	4	4
Number of customers with ACV ≥\$1M	18	27
Number of customers with ACV ≥\$500K	52	54
Number of customers with ACV ≥\$100K	227	222
Customer retention rate with ACV ≥\$500K	100%	98%
Customer retention rate with ACV ≥\$100K	96%	92%
Number of customers with ACV ≥\$1K	1,748	1,785
	as of 12/31/22	as of 12/31/23
Drug Discovery KPI		
Ongoing programs eligible for royalties	15	12
Number of collaborators since 2018	17	17



# Software and Drug Discovery Revenues: 2019-2023





# **Capital Allocation Strategy Built on Proprietary Insights** and Competitive Advantages in Computational Chemistry

Aiming to Generate Positive Returns from **Deployment of Technology, Expertise and Capital** 

**Opportunities that leverage:** 

#### Validated Target or **Development Goal**

- Academia
- Entrepreneurs
- Investors
- Industry

- The

...

at Scale

Computation Schrödinger Proprietary Technology

Schrödinger Scientific Team



Unique

Scientific

Insight or

Observation

Commercially Useful Innovation

- Proprietary Asset
- Venture / NewCo
- License IP / Program



# **Strategic Priorities**

- Drive increased customer adoption of computational software platform
- Advance science underlying computational platform
- Expand portfolio of collaborations
- Achieve clinical proof of concept for proprietary programs
- Progress additional proprietary programs toward IND

# **Timelines for Therapeutics Milestones**

- Present initial clinical data from Phase 1 study of SGR-1505 in 1H 2025
- Present initial clinical data from Phase 1 study of SGR-2921 in 2H 2025
- Present initial clinical data from Phase 1 study of SGR-3515 in 2H 2025





# Pioneering Computational Molecular Design

November 2024

# Appendix

Annual Contract Value (ACV). With respect to contracts that have a duration of one year or less, or contracts of more than one year in duration that are billed annually, ACV is defined as the contract value billed during the applicable period. For contracts with a duration of more than one year that are billed upfront, ACV in each period represents the total billed contract value divided by the term. ACV should be viewed independently of revenue and does not represent revenue calculated in accordance with GAAP on an annualized basis, as it is an operating metric that can be impacted by contract execution start and end dates and renewal rates. ACV is not intended to be a replacement for, or forecast of, revenue.

*Customer Retention for our customers with an ACV of at least \$500,000.* We calculate year-over-year customer retention for our customers in this cohort by starting with the number of such customers we had in the previous fiscal year. We then calculate how many of these customers were active customers in the current fiscal year. We then divide this number by the number of customers with an ACV of at least \$500,000 that Schrödinger had in the previous fiscal year to arrive at the year-over-year customer retention rate for such customers.

