SCHRÖDINGER®

Transforming Discovery of
Therapeutics and Materials

March 23, 2021

# *Cautionary Note and Disclaimer*

*This presentation contains certain "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this presentation, including, without limitation, statements regarding the potential advantages of our physics-based computational platform, our strategic plans to accelerate the growth of our software business, our research and development efforts for our internal drug discovery programs and our computational platform, the initiation, timing, progress, and results of our internal drug discovery programs or the drug discovery programs of our collaborators, our plans to discover and develop product candidates and to maximize their commercial potential by advancing such product candidates ourselves or in collaboration with others, our plans to leverage the synergies between our businesses, our outlook for the fiscal year ended December 31, 2021, our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents, and marketable securities, our marketing capabilities and strategy, and our expectations related to the key drivers of our performance, are forward-looking statements. The words "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "will," "would" or the negative of these words or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.*

*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 factors that are beyond our control, including those risks detailed under the caption "Risk Factors" and elsewhere in our Securities and Exchange Commission filings and reports, including the Annual Report on Form 10-K for the year ended December 31, 2020, filed with the Securities and Exchange Commission on March 4, 2021, as well as future filings and reports by us. Except as required by law, we undertake no duty or obligation to update any forward-looking statements contained in this presentation as a result of new information, 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. Neither Schrödinger nor its affiliates, advisors or representatives makes any representation as to the accuracy or completeness of that data or undertakes to update such data after the date of this presentation.*

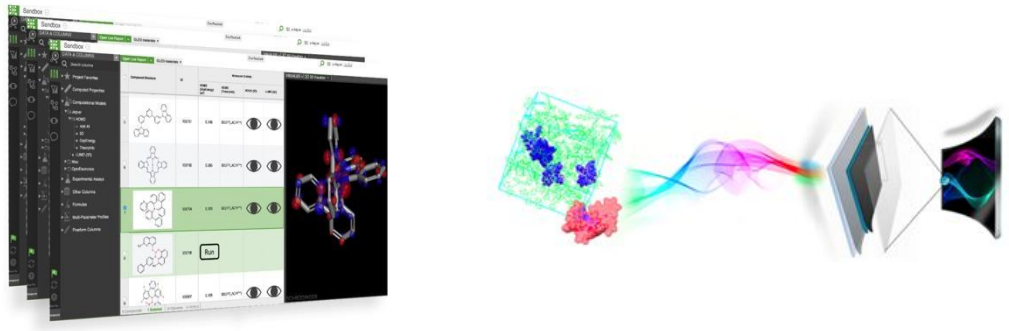
# Schrödinger

## We are transforming the way therapeutics and materials are discovered

We have developed an industry-leading physics-based computational platform that enables discovery of high-quality molecules for drug development and materials applications faster than traditional methods, at a lower cost, and with a higher likelihood of success

### Software Business

Preclinical Drug Discovery & Materials Design



~1,450 customers worldwide[1]

### Drug Discovery Business

Collaborative Programs

**Programs Progressed by Collaborator**

| Collaborator | Indication | Status |
|---|---|---|
| agios | Oncology | FDA Approved |
| | Oncology | FDA Approved |
| AJAX | Oncology | Discovery |
| | Oncology | Discovery |
| BRIGHT ANGEL THERAPEUTICS | Antifungal | Discovery |
| FAIXAN THERAPEUTICS | Undisclosed | Discovery |
| MORPHIC THERAPEUTIC | Fibrosis | IND Enabling |
| | Inflammatory Bowel Diseases | Phase 1 |
| | Undisclosed no. of add'l programs | – |
| NIMBUS THERAPEUTICS | Metabolic Diseases | Phase 2[3] |
| | Autoimmune Disease | Phase 1 |
| | Immuno-oncology | Discovery |
| | Oncology | Discovery |
| | Oncology | Discovery |
| | Undisclosed no. of add'l programs | – |

| Collaborator | Indication | Status |
|---|---|---|
| ONO PHARMACEUTICAL | Undisclosed | Discovery |
| *Undisclosed* | Oncology/Metabolic Disease | IND Enabling |
| PETRA PHARMA | Oncology/Metabolic Disease | Discovery[4] |
| SANOFI | Autoimmune Disease | Phase 1 |
| | Autoimmune Disease | Discovery |
| SHIONOGI | Oncology | Discovery |
| | Cardiopulmonary Diseases | IND Enabling |
| sparc | Metabolic Diseases | Discovery |
| TB ALLIANCE | Oncology | Discovery |
| | Tuberculosis | Discovery |

**Programs Progressed by Schrödinger**

| | | |
|---|---|---|
| Takeda | Neurodegenerative Disease | Discovery |
| | Oncology | Discovery |

Internal Pipeline

| PROGRAM | DISCOVERY | IND-ENABLING | CLINICAL | RIGHTS |
|---|---|---|---|---|
| **CDC7** Hematological Cancers and Solid Tumors | | | | SCHRÖDINGER. |
| **WEE1** Gynecological Cancers and other Solid Tumors | | | | |
| **MALT1** Relapsed/Resistant Non-Hodgkin's Lymphoma | | | | |
| **HIF-2a** Renal Cell Carcinoma | | | | SCHRÖDINGER. Bristol Myers Squibb |
| **SOS1/KRAS** KRAS-Driven Cancers | | | | |
| **Undisclosed targets** Oncology, Immunology, and Neurology | | | | |

~25 programs



*(1) Active customers as of Dec 31, 2020. We define active customers as the number of customers who had an ACV of at least $1,000 in a given fiscal year.*

# Designing drugs is extremely hard!

## Lengthy, capital-intensive, and prone to high failure rates

Need to identify a molecule that balances a large number of anti-correlated properties:

- Potency
- Selectivity
- Solubility
- Bioavailability
- Clearance / half-life
- Permeability
- Drug-drug interactions
- Synthesizability
- Toxicity



*(1) Based on average, industry-wide success rates*

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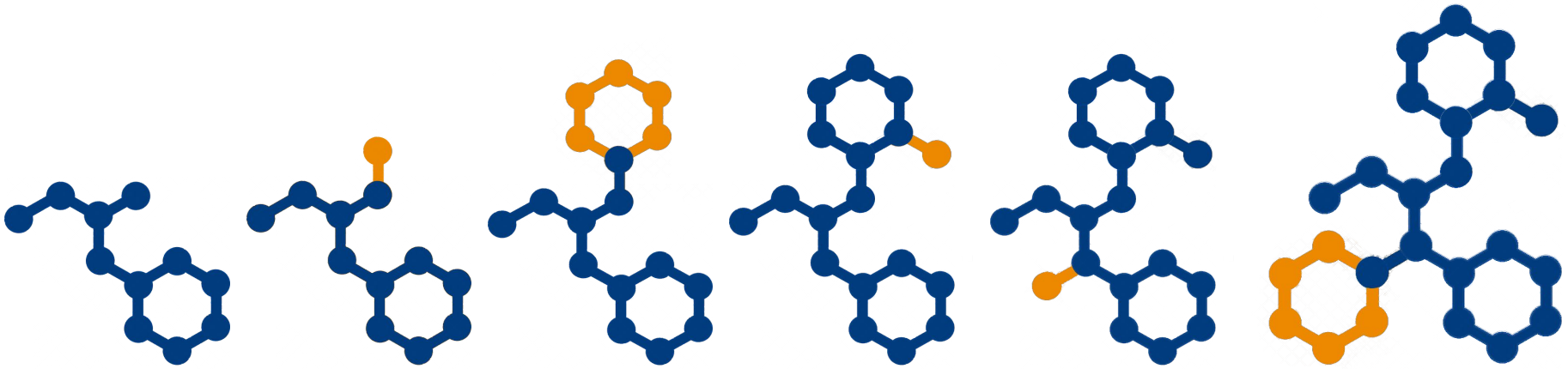
- Synthesizability
- Toxicity



...

| | | | | | | |
|---|---|---|---|---|---|---|
| Potency | ✓ | x | ✓ | x | ✓ | ✓ |
| Selectivity | x | ✓ | ✓ | ✓ | x | ✓ |
| Solubility | x | x | x | ✓ | ✓ | x |
| Clearance | x | x | x | x | x | x |
| Permeability | x | x | x | x | x | x |

2/3rd of programs never succeed in delivering an IND(1)



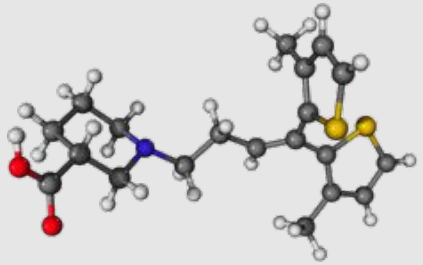
(1) Based on average, industry-wide success rates

# Drug discovery – vision for the future

If we could calculate all the properties with perfect accuracy, designing drugs would have a higher success rate, be faster and cheaper, and would produce higher-quality molecules

"All" synthesizable molecules

Select THE best molecule



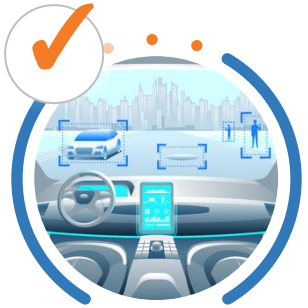
- Potency ✓
- Selectivity ✓
- Solubility ✓
- Clearance ✓
- Permeability ✓
- Drug-Drug Interactions ✓
- Synthesizability ✓
- Toxicity ✓

# Potential solutions to the drug discovery problem

Decades long challenge – two major approaches:

- Knowledge-based machine learning (often referred to as AI)
  - If AI can beat humans at chess and Go, recognize faces in photos, autonomously drive cars, can it be used to design drugs?

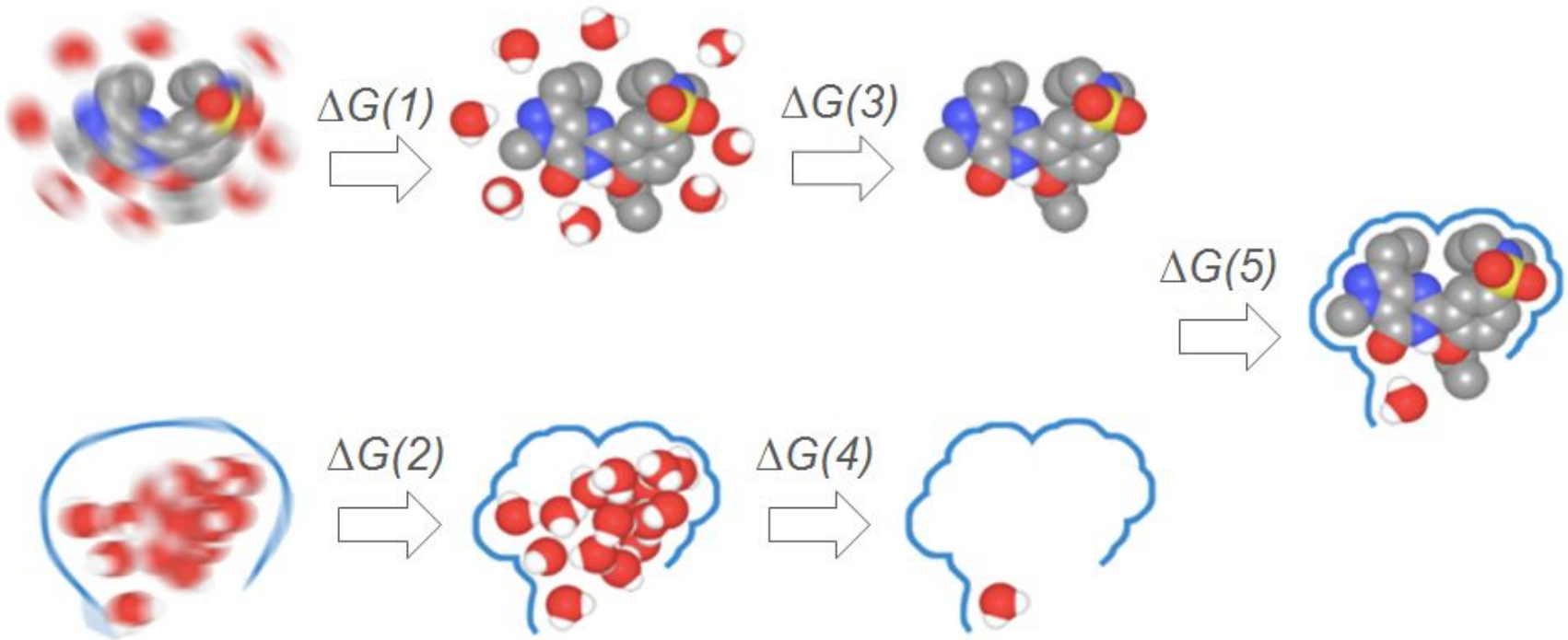





- Rigorous, first principles physics-based modeling
  - Requires deep understanding of the physics underlying highly complex molecular interactions

$$i\hbar\frac{d}{dt}|\Psi(t)\rangle = \hat{H}|\Psi(t)\rangle \qquad i\hbar\frac{\partial}{\partial t}\Psi(\mathbf{r},t) = \left[\frac{-\hbar^2}{2m}\nabla^2 + V(\mathbf{r},t)\right]\Psi(\mathbf{r},t)$$

# Physics-based methods required to capture complexity of molecular properties



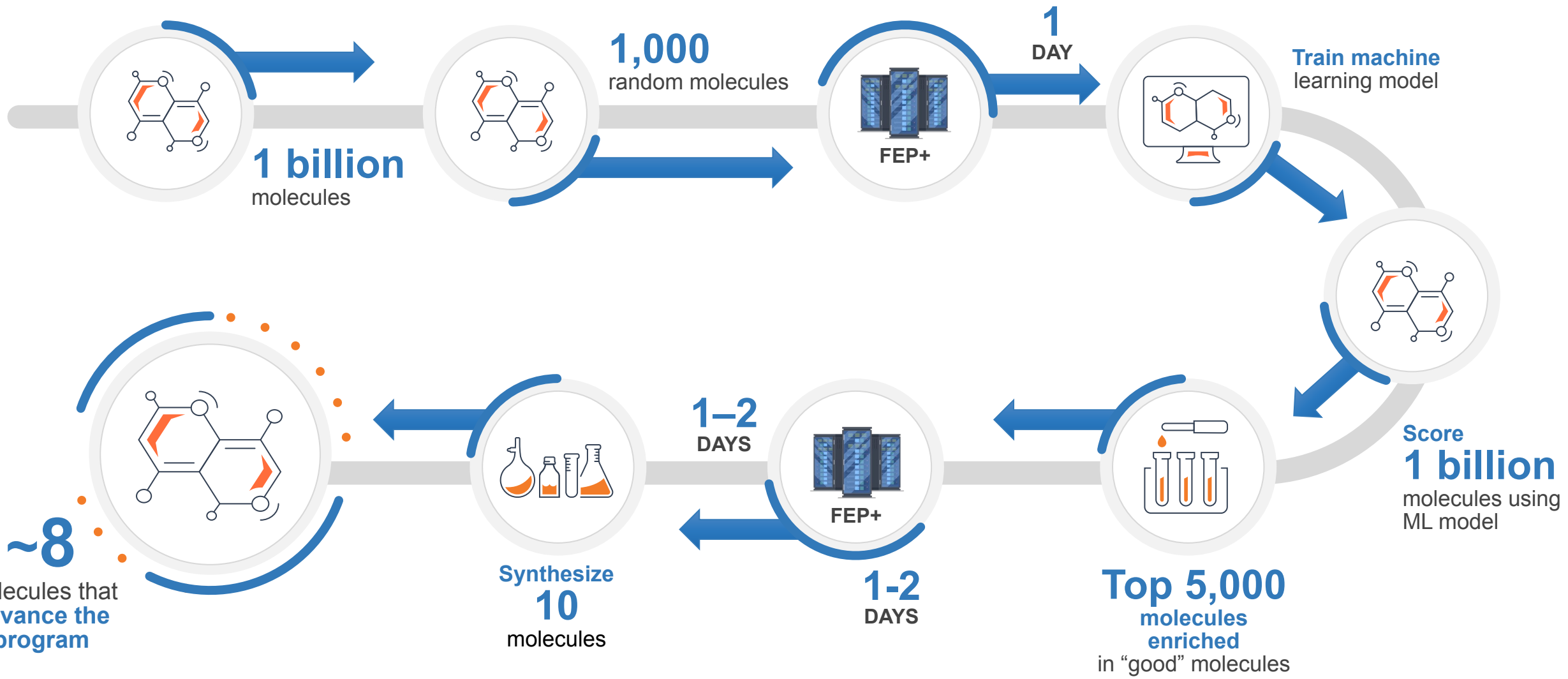

$$\Delta G_{bind} = \Delta G(1) + \Delta G(2) + \Delta G(3) + \Delta G(4) + \Delta G(5)$$

$$\Delta G = \Delta H - T\Delta S$$

*(free energy = enthalpy minus temperature times entropy)*

# Schrödinger platform combines accuracy of physics with speed of machine learning

## Enables ultra-large scale exploration of chemical space

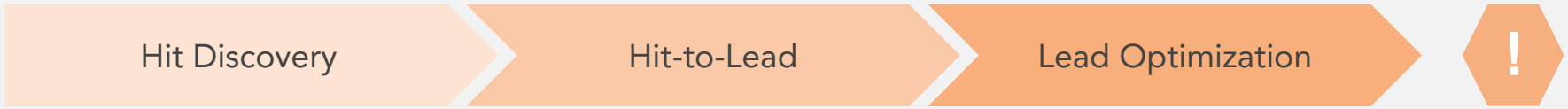


# Demonstrated benefits of Schrödinger drug discovery platform

## Reduces time and cost and increases quality vs. traditional drug design

### Traditional Drug Design

- Manual molecule design
- ~5,000 molecules synthesized and tested over ~4 – 6 years




Drug development candidate with Property issues

### SCHRÖDINGER


Drug development candidate with Optimal property profile

- Billions of molecules tested in computational assays
- ~1,000 molecules synthesized and tested over ~2 – 3 years

# Drug Discovery

# Our strategy: Expand and advance collaborative and internal drug discovery programs

- Apply our latest technologies to the discovery of small molecules and biologics
- Add new collaborations that offer scientific synergies
- Maximize the value and commercial opportunities generated by program IP
- Advance our wholly-owned programs into clinical development ourselves or in partnership to maximize success and commercial opportunities

# Broad pipeline of collaborative programs[1][2]

## Programs Progressed by Collaborator

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| agios | Oncology | FDA Approved |
| | Oncology | FDA Approved |
| AJAX | Oncology | Discovery |
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| BRIGHT ANGEL THERAPEUTICS | Antifungal | Discovery |
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| | Inflammatory Bowel Diseases | Phase 1 |
| | Undisclosed no. of add'l programs | – |
| NIMBUS THERAPEUTICS | Metabolic Diseases | Phase 2[3] |
| | Autoimmune Disease | Phase 1 |
| | Immuno-oncology | IND Enabling |
| | Oncology | Discovery |
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| | Autoimmune Disease | Discovery |
| | Oncology | Discovery |
| SHOU TI | Cardiopulmonary Diseases | IND Enabling |
| | Metabolic Diseases | IND Enabling |
| sparc | Oncology | Discovery |
| TB ALLIANCE | Tuberculosis | Discovery |

## Programs Progressed by Schrödinger

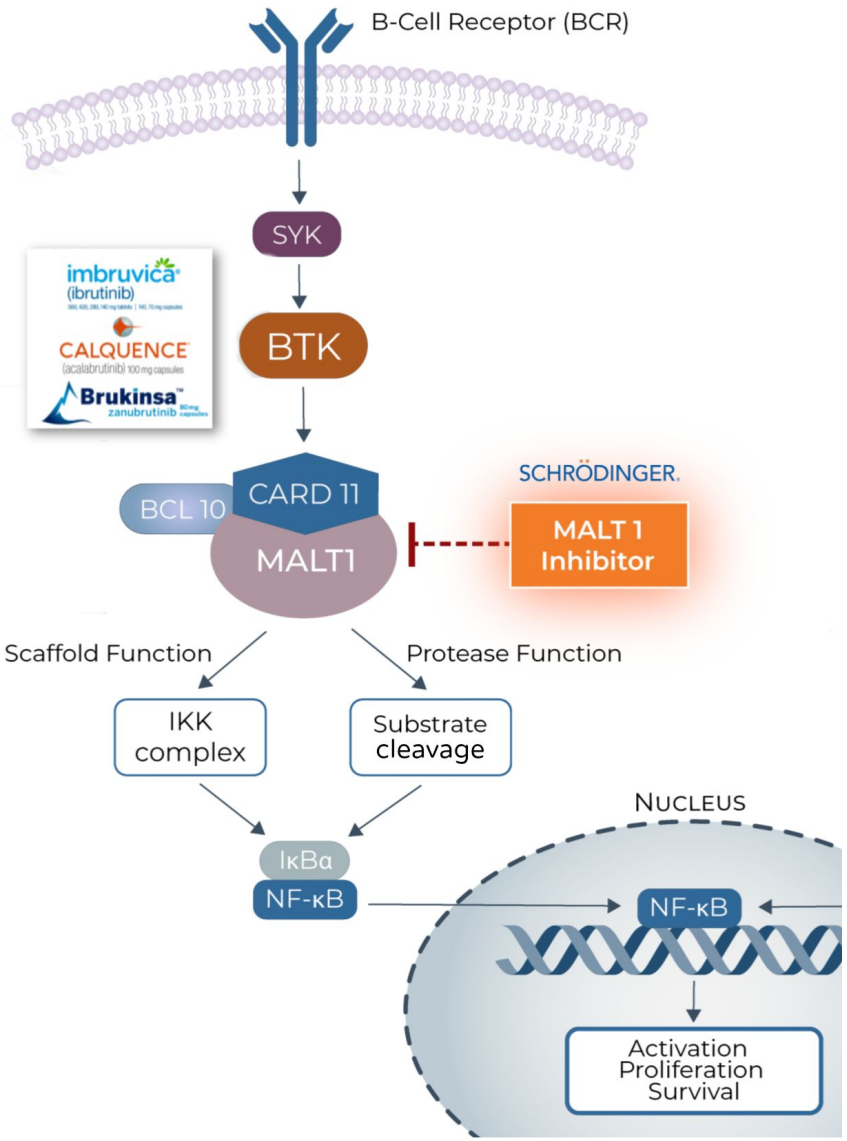
| | | |
|---|---|---|
| Takeda | Neurodegenerative Disease | Discovery |
| | Oncology | Discovery |

*(1) As of March 2021. Based on publicly available information or information disclosed to us. Excludes programs from any undisclosed collaborations.*
*(2) With the exception of Takeda, where we retain all intellectual property rights until Takeda exercises its option to acquire a program, all of the programs being pursued under these collaborations are fully owned and controlled by each respective collaborator. (3) Acquired by Gilead Sciences, Inc. (4) Petra was acquired by a third party in May 2020.*

# Internal drug discovery programs

| PROGRAM | DISCOVERY | IND-ENABLING | CLINICAL | RIGHTS |
|---|---|---|---|---|
| **CDC7**<br>Hematological Cancers and Solid Tumors | | | | SCHRÖDINGER. |
| **WEE1**<br>Gynecological Cancers and other Solid Tumors | | | | |
| **MALT1**<br>Relapsed/Resistant Non-Hodgkin's Lymphoma | | | | |
| **HIF-2a**<br>Renal Cell Carcinoma | | | | SCHRÖDINGER.<br>Bristol Myers Squibb™ |
| **SOS1/KRAS**<br>KRAS-Driven Cancers | | | | |
| **Undisclosed targets**<br>Oncology, Immunology, and Neurology | | | | |

# MALT1 inhibitors are additive to covalent and non-covalent BTK inhibitors

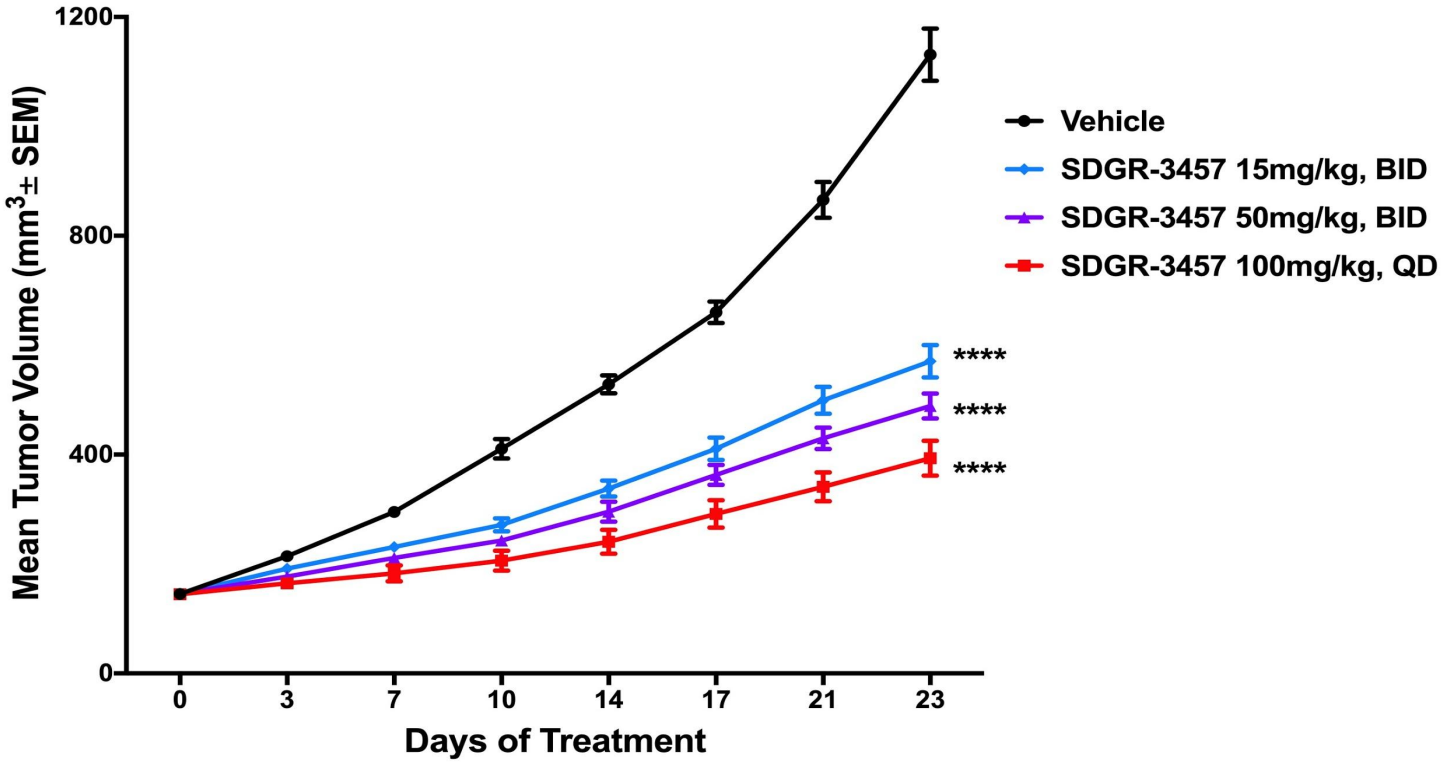



- MALT1 is one of the key regulators of physiological antigen receptor signalling in B cells and T cells, also the only component of the CARMA1-BCL10-MALT1 (CBM) signalosome which has proteolytic activity
- 30-40% of DLBCL patients experience progression or relapse following R-CHOP treatment
- Mutations that trigger constitutive MALT1 protease activity and MALT1 fusions with cellular inhibitor of apoptosis (cIAP) are associated with aggressive forms of non Hodgkin B-cell lymphoma\avage *in vivo*.
- Our data suggest that targeting MALT1 may expand therapy options for patients with selected B-cell lymphomas, such as ABC-DLBCL

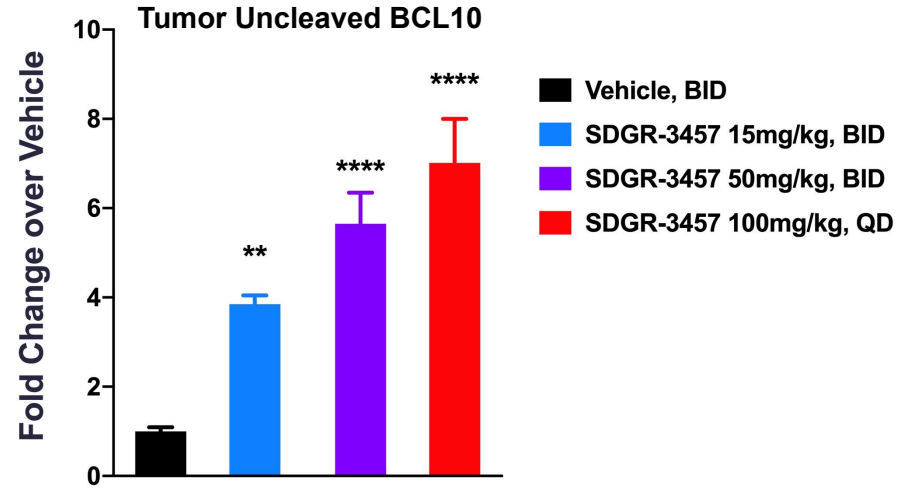

*Studies conducted using versions of Ibrutinib, Acalabrutinib, and ARQ-531 synthesized by third-party contract research chemists, using publicly available information*

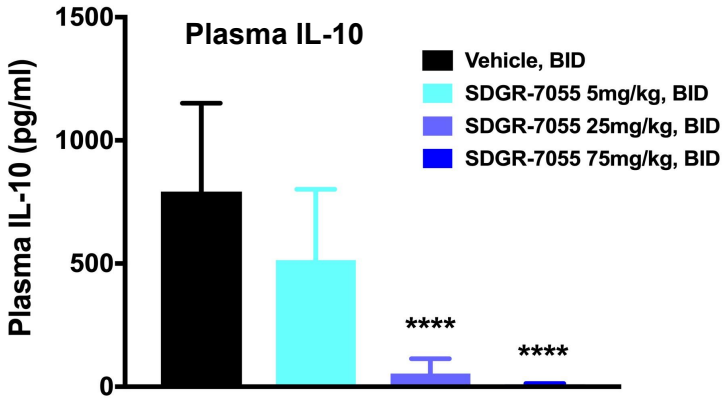
# MALT1: Anti-tumor potency as single agent in mouse model

Tumor growth inhibition in an OCI-LY3 CDX Xenograph model



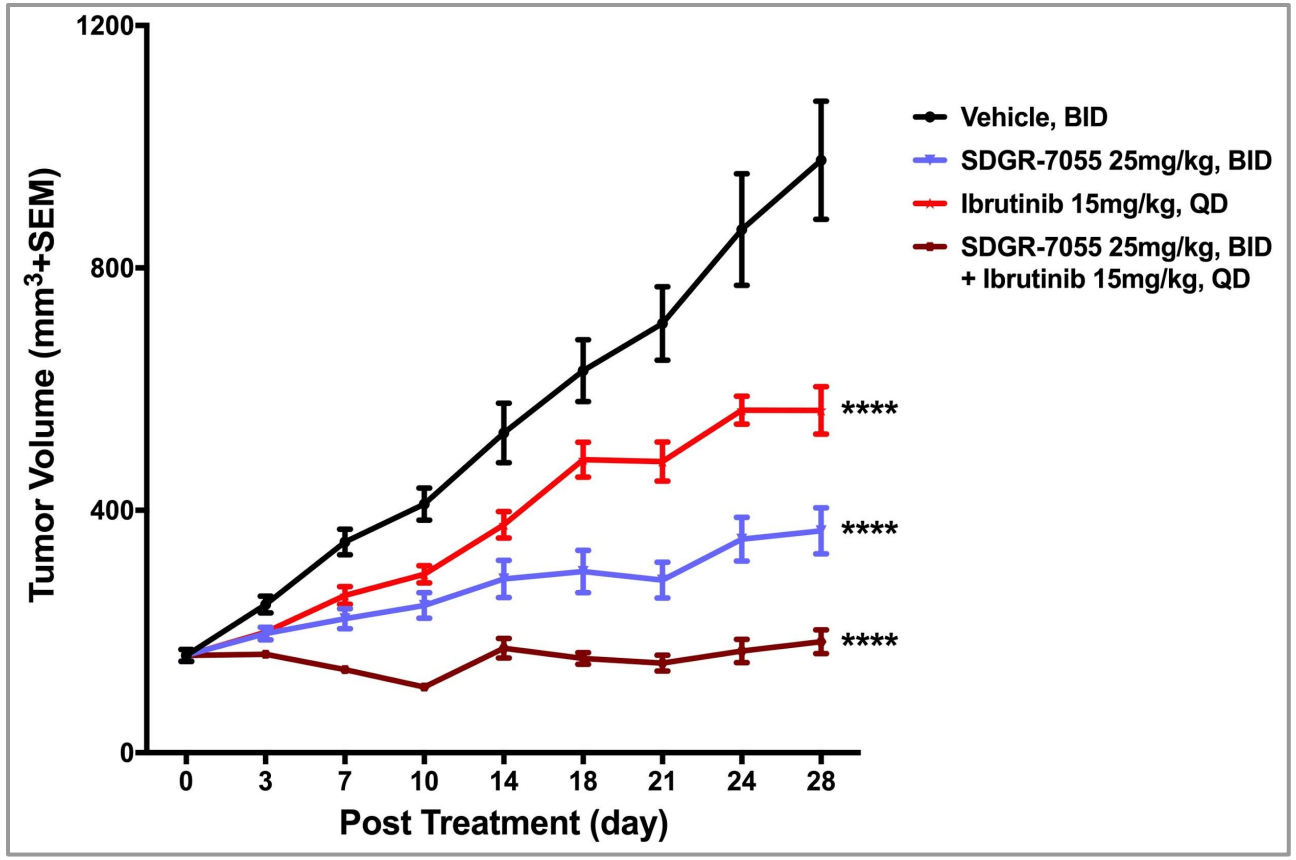

Dose responsive changes in BCL-10 cleavage and serum IL-10 confirm post treatment target engagement and reduced NF-Kappa B signaling



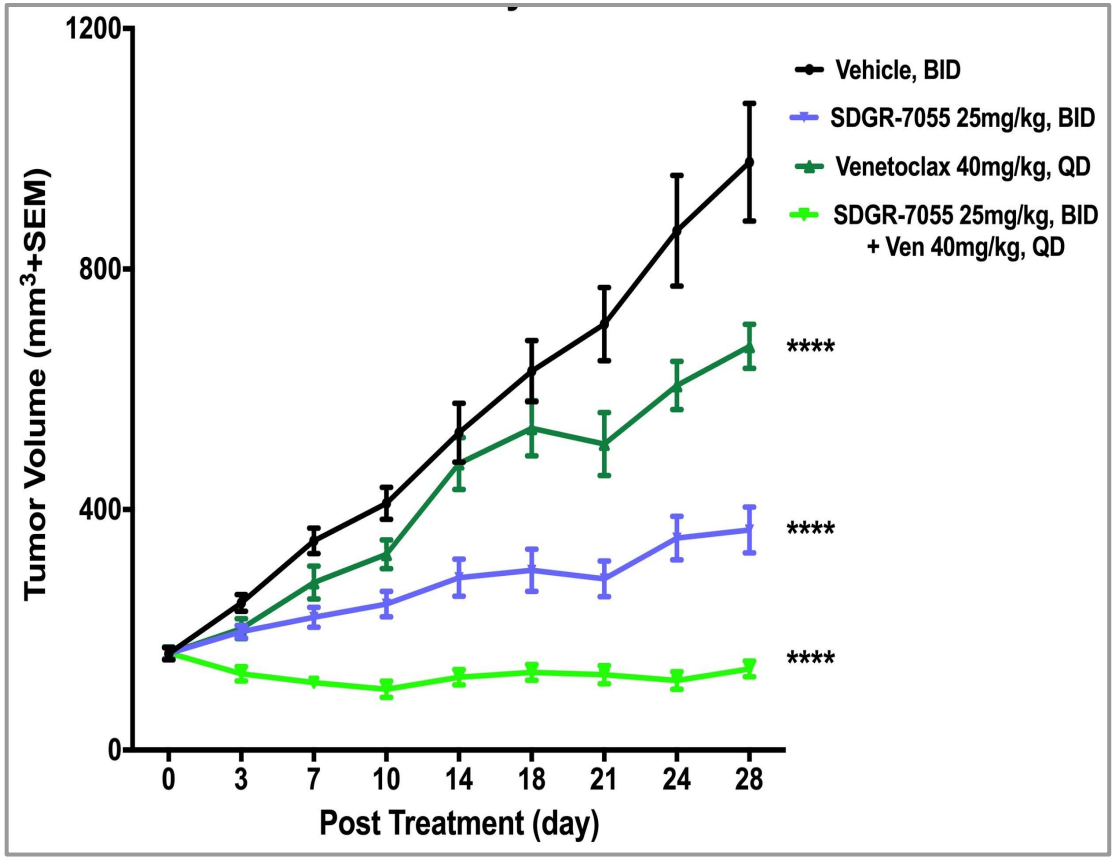



# MALT1: Potent anti-tumor effects observed in combination with ibrutinib or venetoclax

SDGR molecule + ibrutinib drives significant reduction in tumor volume in animal model compared to either therapy alone

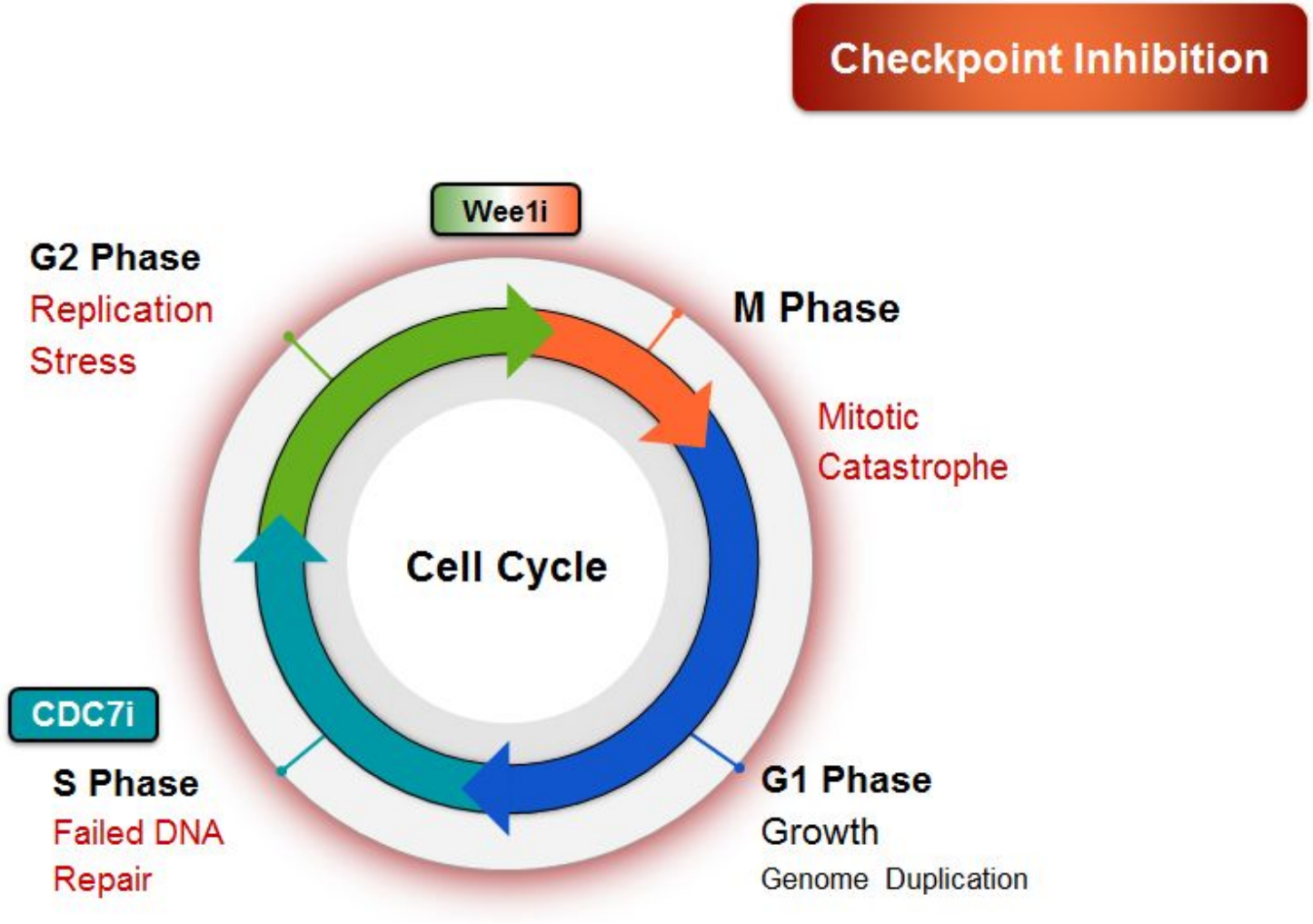



Similar results with venetoclax through at least 28 days post-treatment



# CDC7 & WEE1 target cancer through replication stress and DNA repair mechanisms

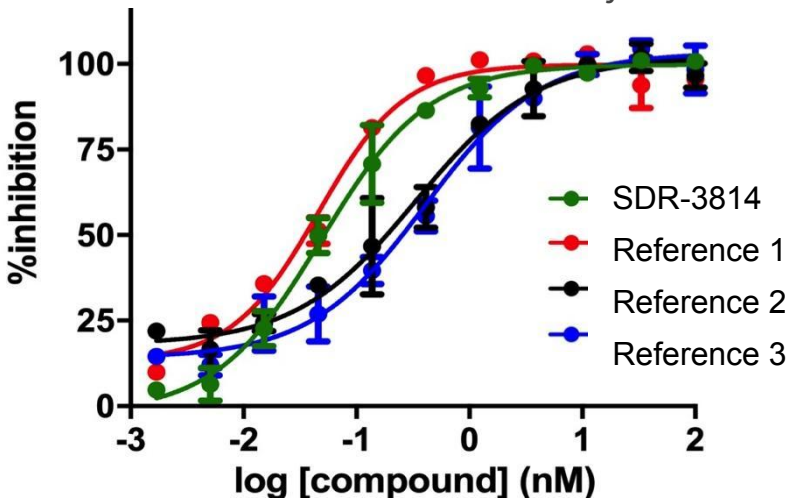
- Cancer cells depend on checkpoint kinases to repair DNA damage and adapt to genotoxic stress
- Inhibition of these kinases leaves cancer cells vulnerable to failed DNA damage repair and high levels of replication stress, failure of cell division, and cell death
- Combining multiple DNA damage response mechanisms can heighten damage and lead to durable anti-proliferative efficacy



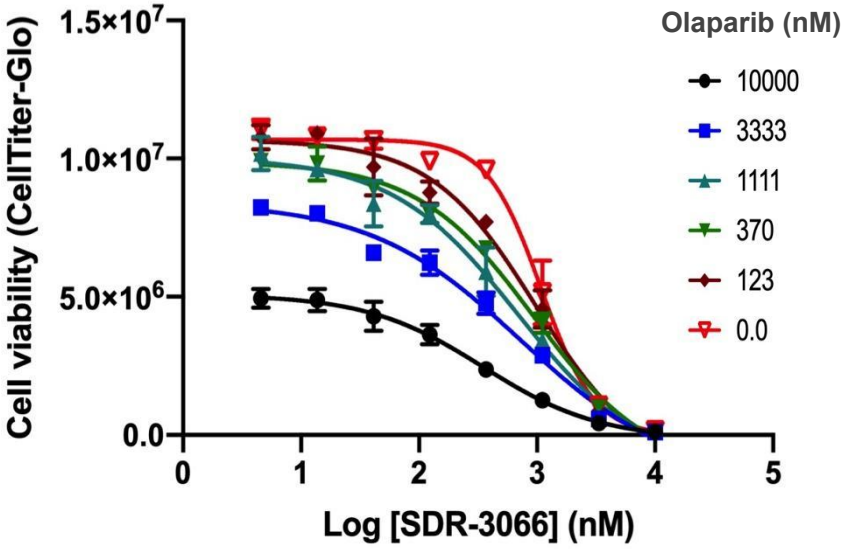
# CDC7 inhibitors show additive anti-proliferative effects with PARP inhibitors

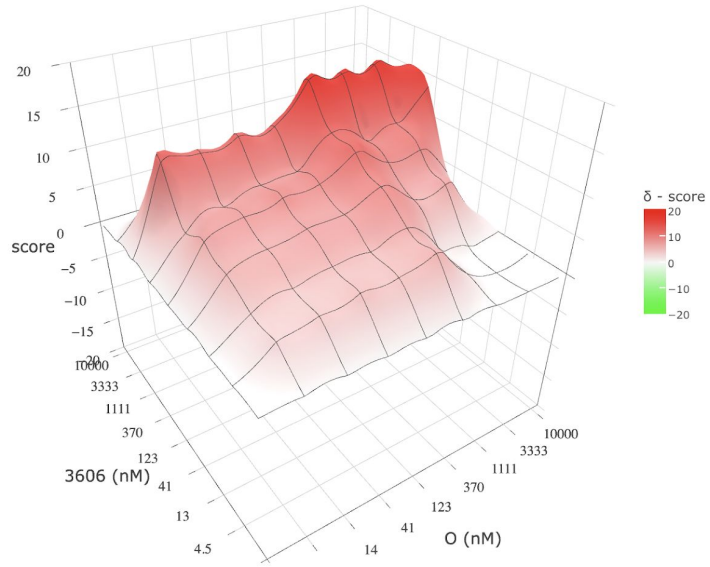
- We have identified tight-binding, selective, novel CDC7 inhibitor series
- When combined with olaparib or other cell cycle inhibitors, our CDC7 inhibitors resulted in additive anti-proliferative effects in human non-small-cell lung cancer H460 cells and at least one other solid tumor cell line

CDC7 biochemical assay data

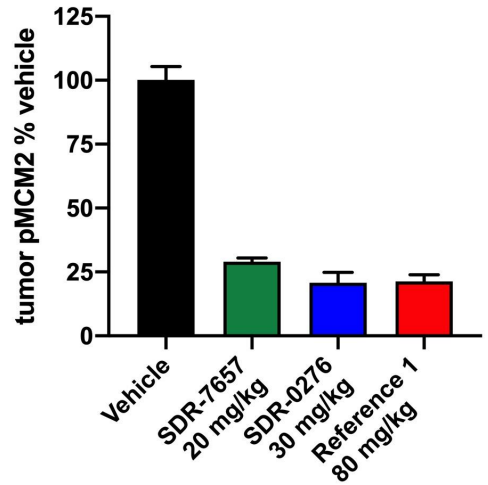



Combination of SDR-3066 and olaparib showing synergy in H460 lung cancer cells




Tumor phosphorylated MCM2



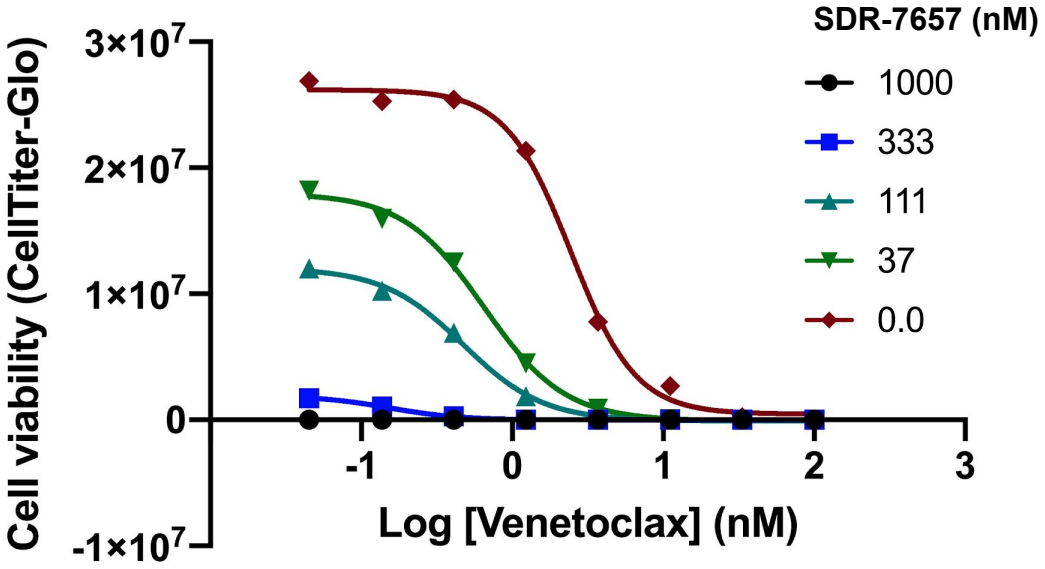


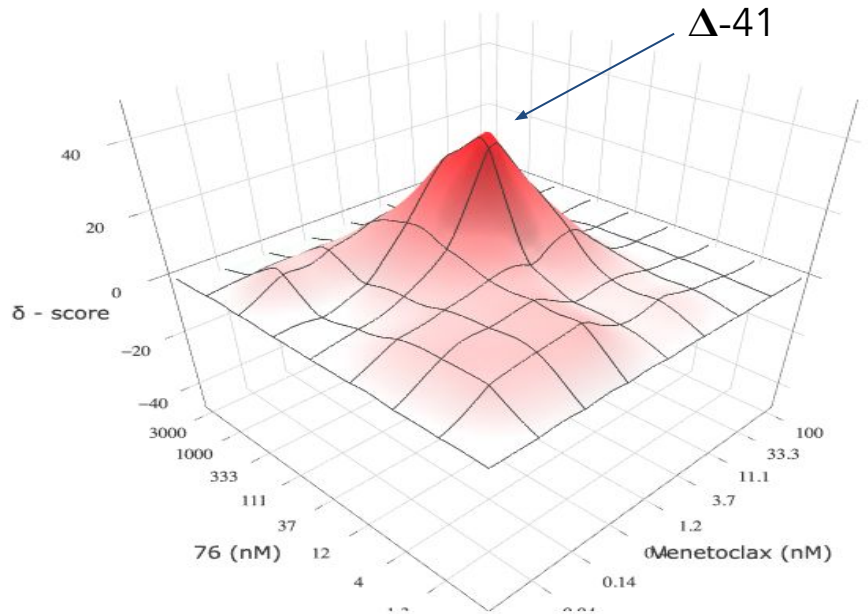

*Studies conducted using versions of clinical references and olaparib synthesized by third-party contract research chemists, using publicly available information*

# CDC7 inhibitors show additive anti-proliferative effects in AML models

- Our novel CDC7 inhibitor series combined with venetoclax, a BCL2 inhibitor, resulted in additive anti-proliferative effects in human acute myeloid leukemia cells.

Combination of SDR-7657 and venetoclax showing synergy in AML cells



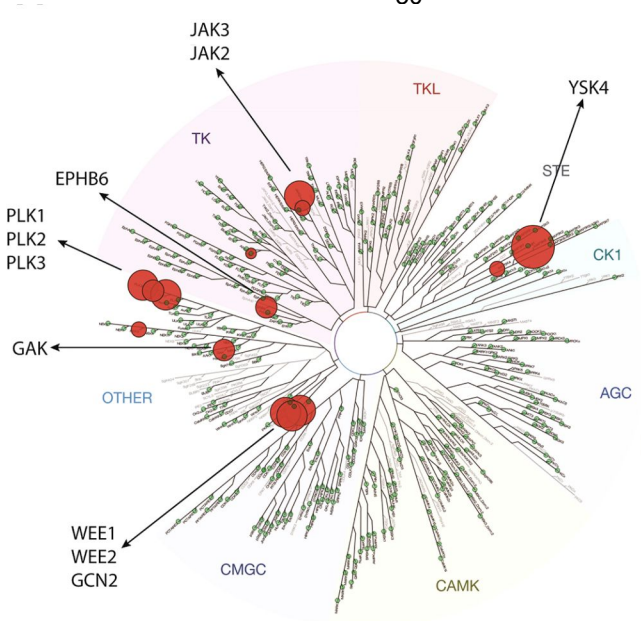



# WEE1 inhibitors have optimized selectivity and physicochemical properties

- Existing WEE1 inhibitors inhibit polo-like kinase 1 (PLK1). We have identified lead molecules that achieve ~100-fold greater selectivity versus PLK1 relative to AZD1775
- Using Protein FEP+ technology we rapidly achieved very high level of broad kinome selectivity for multiple lead series
- Lead molecules from our chemical series show no CYP3A4 TDI liability and exhibit favorable ADME/DMPK properties

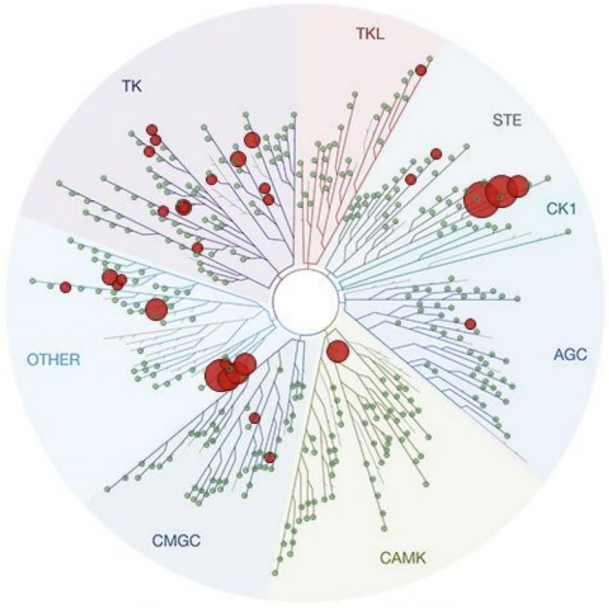
**AZD-1775**

Wee1 $IC_{50}$ 0.25nM
OVCAR3 CTG, $EC_{50}$ 330nM



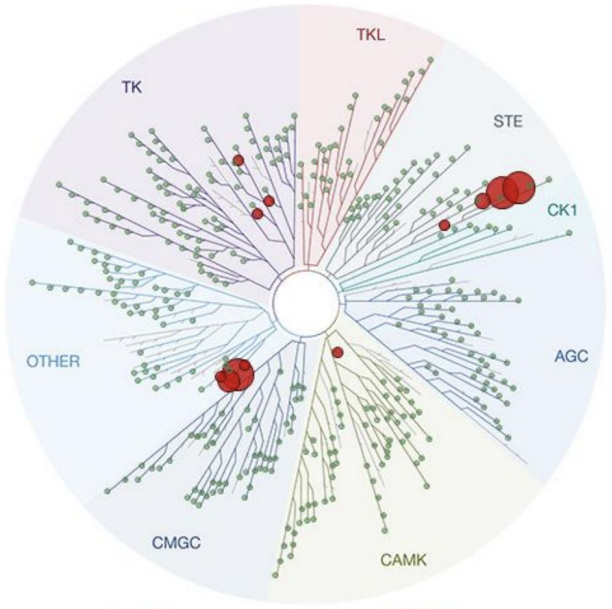

**SDR-7995**

Wee1 $IC_{50}$ 0.06nM
OVCAR3 CTG, $EC_{50}$ 90nM




**SDR-7778**

Wee1 $IC_{50}$ 0.8nM
OVCAR3 CTG, $EC_{50}$ 190nM






*Studies conducted using versions of AZD1775 synthesized by third-party contract research chemists, using publicly available information*

# Rapidly progressing pipeline

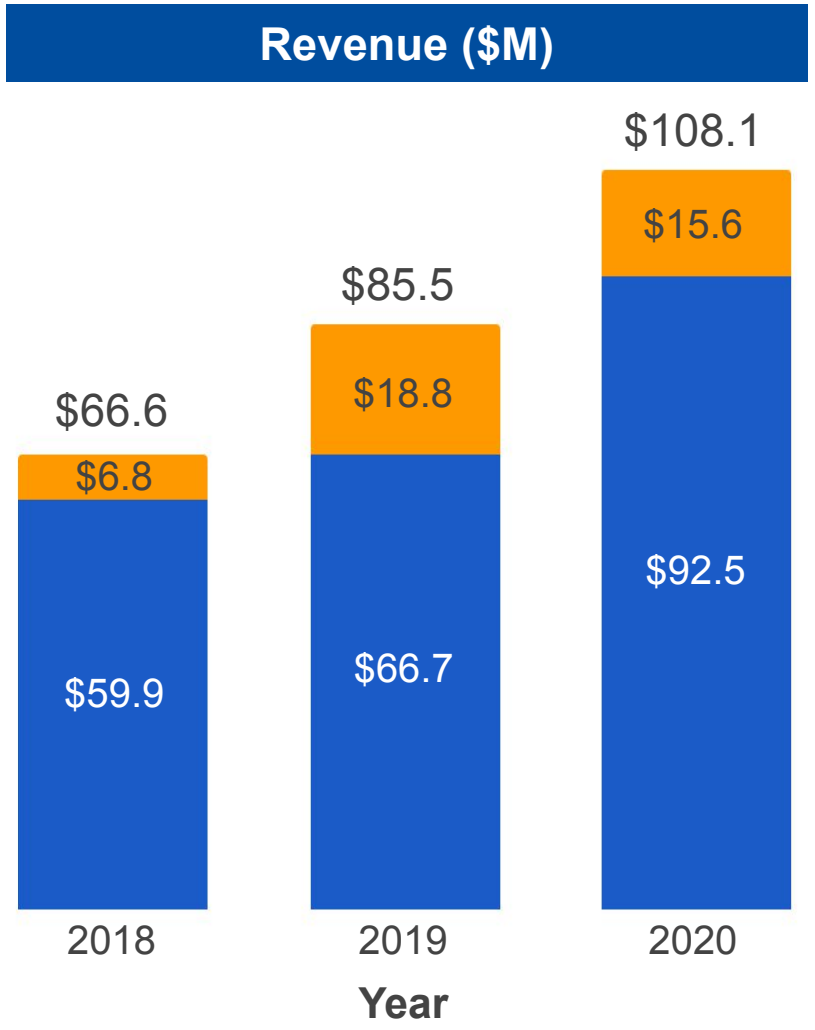
- Internal deployment of physics-based methods has accelerated the advancement of our programs
- Building capabilities to support our clinical program execution
- Anticipate advancing IND-enabling studies to support up to three IND* applications next year
  - First IND submission expected in H1 2022
- Expanding into additional disease areas and expect to initiate new programs this year



*IND: Investigational New Drug

# Key Financials

# Strong operating momentum across the business




Continued momentum in 2020

- Total revenue of $108.1 million, 26% y/y growth
- Software revenue of $92.5 million, 39% y/y growth

Strong cash position to advance the business

- $643.2 million in cash* at Dec. 31st 2020
- $16.8 million in net cash generated from operating activities in 2020

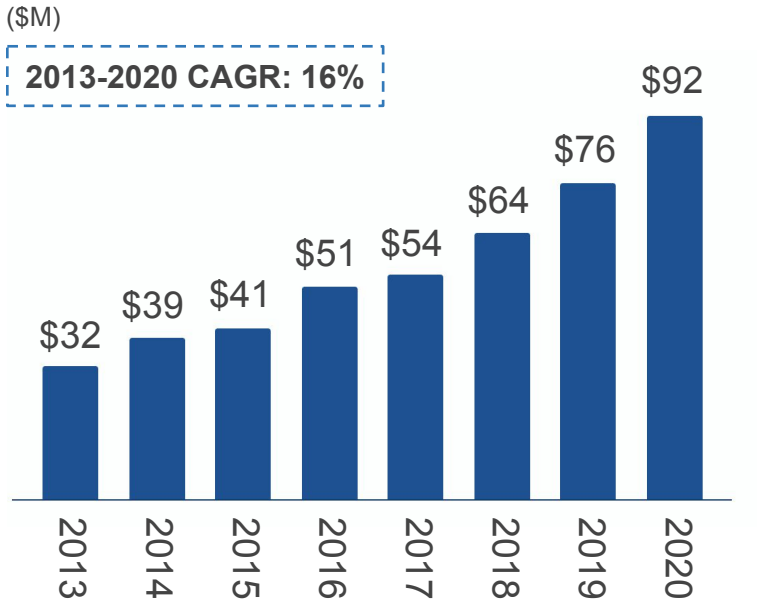


** Cash, cash equivalents, restricted cash and marketable securities. In February 2020, we received net proceeds of $209.6M from our IPO after deducting underwriting discounts, commissions, and offering expenses. In August 2020, we received net proceeds of $325.6M from our follow-on public offering after deducting underwriting discounts, commissions, and offering expenses.*

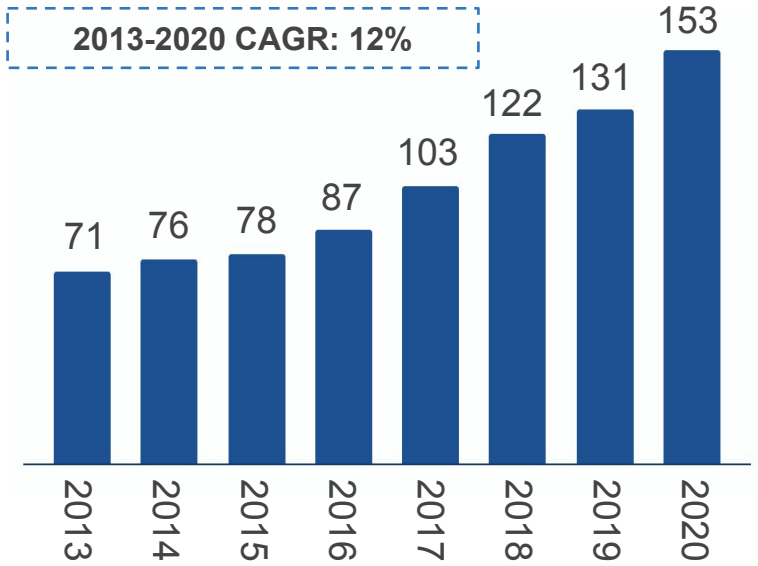
# Key performance indicators show strength of software business

- Software annual contract value (ACV) was $92.1 million in 2020, up 22% vs. 2019
- 16 customers with >$1 million in ACV in 2020 vs. 10 in 2019
- 153 customers with >$100,000 in ACV in 2020 vs. 131 in 2019
- Customer retention in this cohort was 99% in 2020

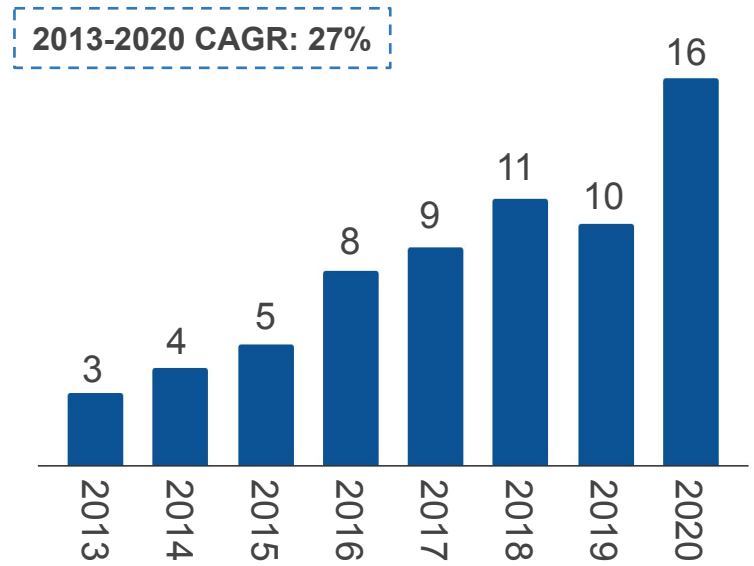
**Total Annual Contract Value (ACV)**




**Customers with ACV >$100K**




**Customers with ACV >$1M***




*For the fiscal year ended December 31, 2020, we had two customers with an ACV between $950,000 and $1,000,000, which is not included in the chart above; we had 3 such customers for the fiscal year ended December 31, 2019 and 1 such customer for the fiscal year ended December 31, 2016.*

# Driving value from our collaborations and partnerships

## Equity positions in our collaborators and co-founded companies[1][4]

| Company | Equity |
|---|---|
| Ajax Therapeutics, Inc. | 8.7% |
| Bright Angel Therapeutics Inc. | 33.3% |
| Faxian Therapeutics, LLC (JV) | 50.0% |
| Morphic Holding, Inc.[2] | 2.6% |
| Nimbus Therapeutics, LLC[3] | 6.9% |
| Ravenna Pharmaceuticals, Inc. | 3.1% |
| ShouTi Inc. | 6.1% |

Revenue generation:

Research fees, discovery and clinical milestones and potential future commercial milestones and single-digit royalties from many of these programs

Equity value:

Received over $50 million in cash distributions from equity in Nimbus and Petra*

Morphic and Relay IPOs led to significant equity gains

1. *Equity stakes in our collaborators on an issued and outstanding basis as of December 31, 2020, except as noted otherwise*
2. *Based on the number of shares of common stock outstanding as of February 24, 2021, as reported on Morphic's Annual Report on Form 10-K, for the year ended December 31, 2020, as filed with the SEC on March 1, 2021*
3. *On a fully diluted unit basis*
4. *In January 2021, Schrödinger sold its equity stake in Relay Therapeutics, Inc. for aggregate consideration of $15.7 million*



** $46 million in 2016/2017 related to acquisition of one Nimbus program by Gilead; $4.6 million from share of upfront acquisition fee of Petra in 2020*

# Key financial data: Full-year 2020 and 2019

| Financial Results Data ($M) | 2020 | 2019 | Y/Y % |
|---|---|---|---|
| Software revenue | $92.5 | $66.7 | *39 %* |
| Drug discovery revenue | 15.6 | 18.8 | *(17) %* |
| **Total revenues** | **$108.1** | **$85.5** | ***26 %*** |
| | | | |
| Gross profit | $63.5 | $49.1 | *29 %* |
| *Software gross margin* | *81 %* | *80 %* | *na* |
| | | | |
| Research and development expense | 64.7 | 39.4 | *64 %* |
| Sales and marketing expense | 17.8 | 21.4 | *(17) %* |
| General and administrative expense | 41.9 | 27.0 | *55 %* |
| **Total operating expenses** | **$124.4** | **$87.8** | ***42 %*** |
| | | | |
| Operating loss | (60.9) | (38.7) | *57 %* |
| Total other income* | 34.6 | 12.7 | *172 %* |
| Net loss** | (24.5) | (24.6) | *(1) %* |
| **Balance Sheet Data ($M)** | | | |
| Cash, cash eq., restricted cash and marketable securities | 643.2 | 86.3 | *645 %* |
| Deferred revenue, current and long-term | 86.6 | 27.3 | *217 %* |



**Includes gains on equity method investments, changes in fair value and interest income*
***After adjusting for non-controlling interests*

# 2021 financial outlook *(as of March 23, 2021)*

| Revenue Expectation | Range | Percent Increase Year-Over-Year |
|---|---|---|
| **Total revenue** | $124-142M | 15-31% |
| **Software revenue** | $102-110M | 10-19% |
| **Drug discovery revenue** | $22-32M | 41-106% |

Software revenue

- Growth expected to be higher in the second half of the year with the majority of second half growth in Q4
- Q1 growth rate vs. Q1 2020 expected to be high single digits

Discovery revenue

- $54 million in deferred revenue from BMS agreement expected to be recognized over the next four years
- Q1 growth rate vs. Q1 2020 expected to be 30-40%; highly variable quarter to quarter

Expenses

- Continue to aggressively fund R&D to advance our technology and progress our drug discovery pipeline
- Expect operating expense growth to be higher than the 42% annual growth rate reported in 2020
- Expect software gross margin to be lower than the 81% reported in 2020

# Schrödinger

- We have developed a leading computational platform that is transforming discovery of therapeutics and materials
- We have a strong track record of software revenue growth
- We are advancing a pipeline of drug discovery programs internally and through collaborations to bring new medicines to patients
- We have established a strong financial position to enable continued investment in our computational platform and therapeutic pipeline

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Transforming Discovery of
Therapeutics and Materials