PROTAC® Protein Degraders: Past, Present, and Future

John G. Houston, PhD
President and Chief Executive Officer, Arvinas, Inc.

27 October 2021
Safe harbor and forward-looking statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the receipt of upfront, milestone and other payments under the Pfizer collaboration, the potential benefits of our arrangements with our collaborative partnerships, the development and regulatory status of our product candidates, such as statements with respect to our lead product candidates, ARV-110, ARV-471 and ARV-766 and other candidates in our pipeline, and the timing of clinical trials and data from those trials and plans for registration for our product candidates, and our discovery programs that may lead to our development of additional product candidates, the potential utility of our technology and therapeutic potential of our product candidates, the potential commercialization of any of our product candidates, and the sufficiency of our cash resources. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make as a result of various risks and uncertainties, including but not limited to: each party’s performance of its obligations under the Pfizer collaboration, whether we and Pfizer will be able to successfully conduct and complete clinical development for ARV-471, whether we will be able to successfully conduct Phase 1/2 clinical trials for ARV-110 and ARV-766, initiate and complete other clinical trials for our product candidates, and receive results from our clinical trials on our expected timelines, or at all, whether our cash resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, discussed in the “Risk Factors” section of the Company’s quarterly and annual reports on file with the Securities and Exchange Commission. The forward-looking statements contained in this presentation reflect our current views as of the date of this presentation with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law.

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This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.
We have come a long way since the first PROTAC® publication: 10+ bifunctional protein degraders in the clinic!

SELECT HETEROBIFUNCTIONAL DEGRADERS IN THE CLINIC

<table>
<thead>
<tr>
<th>Asset</th>
<th>Company</th>
<th>Target</th>
<th>Indication</th>
<th>Status</th>
<th>Therapeutic Focus</th>
<th>Market Capitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARV-110</td>
<td>Arvinas</td>
<td>AR</td>
<td>Prostate cancer</td>
<td>Phase 2</td>
<td>Oncology/Immuno-oncology, Neuroscience</td>
<td>~$4.4B (IPO 2018)</td>
</tr>
<tr>
<td>ARV-471</td>
<td></td>
<td>ER</td>
<td>Breast cancer</td>
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<td>ARV-766</td>
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</tr>
<tr>
<td>AR-LDD</td>
<td>Bristol-Myers Squibb</td>
<td>AR</td>
<td>Prostate cancer</td>
<td>Phase 1</td>
<td>Varied</td>
<td>Large Pharma</td>
</tr>
<tr>
<td>DT2216</td>
<td>Dialectic</td>
<td>BCL-XL</td>
<td>Liquid and solid tumors</td>
<td>Phase 1</td>
<td>Oncology</td>
<td>Private Company</td>
</tr>
<tr>
<td>GT20029</td>
<td>Kintor</td>
<td>AR</td>
<td>Acne and alopecia</td>
<td>Phase 1</td>
<td>Dermatology</td>
<td>~2.3B (IPO 2020)</td>
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<tr>
<td>KT-474</td>
<td>Kymera</td>
<td>IRAK4</td>
<td>AD, HS</td>
<td>Phase 1</td>
<td>Dermatology, Immunology, Oncology</td>
<td>~2.8B (IPO 2020)</td>
</tr>
<tr>
<td>NX-2127</td>
<td>Nurix</td>
<td>BTK</td>
<td>B-cell malignancies</td>
<td>Phase 1</td>
<td>Oncology</td>
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<tr>
<td>CFT7455</td>
<td>C4 Therapeutics</td>
<td>IKZF1/3</td>
<td>MM, NHL</td>
<td>Phase 1</td>
<td>Oncology</td>
<td>~$2.1B (IPO 2020)</td>
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<tr>
<td>FHD-609</td>
<td>FcGHorn Therapeutics</td>
<td>BRD9</td>
<td>Synovial sarcoma</td>
<td>Phase 1</td>
<td>Oncology</td>
<td>~$440M (IPO 2020)</td>
</tr>
</tbody>
</table>

AD, atopic dermatitis; HS, hidradenitis suppurativa; MM, multiple myeloma; NHL, non-Hodgkin’s lymphoma; AML, acute myeloid leukemia
1. Not a comprehensive list; 2. As of 10/20/21; 3. Kintor is listed on the Honk Kong Stock Exchange; market capitalization shown in USD
Source: ClinicalTrials.gov; company websites
We have come a long way since the first PROTAC® publication: 10+ bifunctional protein degraders in the clinic!

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### SELECT HETEROBIFUNCTIONAL DEGRADERS IN THE CLINIC

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**Source:** ClinicalTrials.gov; company websites
The success of Arvinas and others spurred a mini-industry around Targeted Protein Degradation

Select Arvinas Achievements and Companies Developing Protein Degraders†

<table>
<thead>
<tr>
<th>Year</th>
<th>Companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>Arvinas, GSK</td>
</tr>
<tr>
<td>2014</td>
<td>Nurix, BMS, Merck/Arvinas, Genentech/Arvinas</td>
</tr>
<tr>
<td>2015</td>
<td>Amphista, AstraZeneca, Biotheryx, Boehringer-Ingelheim, C4, HotSpot, Novartis</td>
</tr>
<tr>
<td>2016</td>
<td>Captor, Kymera, Navire, Peloton, Pfizer/Arvinas, Vividion</td>
</tr>
<tr>
<td>2017</td>
<td>Biogen, Cedilla, Culigen, Dialectic, J&amp;J, Kronos, PIN, Progenra, Sanofi, Sitryx</td>
</tr>
<tr>
<td>2018</td>
<td>Bayer/Arvinas, BridgeBio, Oncopia, Orum, Plexium, Proximity</td>
</tr>
<tr>
<td>2019</td>
<td>FogHorn, Hinova, Lycia, Mission, Monte-Rosa, Neomorph, Proxygen, Ranok, Xios</td>
</tr>
<tr>
<td>2020</td>
<td>Orionis, PAQ, Ubix</td>
</tr>
<tr>
<td>2021</td>
<td>Arvinas, Bayer/Arvinas, BridgeBio, Oncopia, Orum, Plexium, Proximity</td>
</tr>
</tbody>
</table>

† Not a comprehensive list; timeline lists the year in which the first targeted protein degradation program was disclosed for each company.
Source: company websites; press releases
Arvinas is a fast-growing company benefitting from the rapidly growing biotech community in Connecticut.

**Core Values**
- Pioneering, Excellence, Community, & Commitment

**People**
- 240+ highly experienced drug development professionals in New Haven, Connecticut
- 200+ FTEs at contract research organizations

**Bioscience in Connecticut**
- 40,000 employees across 2,500 companies
- Strong academic base for R&D partnerships
Arvinas 2025 Vision: A global organization delivering the benefits of PROTAC® degraders to patients

2013-2018
Built Arvinas’ Foundation as a Pioneer in Protein Degradation

2019-2021
Proved the Concept of Our PROTAC Discovery Engine

Integrated biotech building global footprint
- Extending the benefits of PROTAC protein degraders to patients worldwide and in new therapeutic areas
- Continuing build-out of global resources and capabilities
- PROTAC Discovery Engine sustainably delivering ≥1 clinical candidate per year
ARV-471 & ARV-110, our most advanced PROTACs: Proof-of-concept and opportunities to benefit patients in large areas of unmet need

ARV-471
Estrogen receptor- PROTAC®
*Breast Cancer Partnership*

- Potential best profile of any ER-targeting therapy:
  - Tolerability
  - ER degradation
  - Clinical benefit

- Phase 2 VERITAC trial ongoing

- Potential future endocrine therapy of choice in both adjuvant and metastatic settings

- >200k patients per year with high unmet need

ARV-110
Androgen receptor- PROTAC®
*Prostate Cancer*

- AR degradation and clear signals of efficacy observed in late-line mCRPC

- Extensive molecular profiling of tumors to understand drivers of resistance

- Phase 2 ARDENT trial ongoing; two potential paths to registration:
  1. 3L Molecularly Defined Patients
  2. Broader Patient Population 1L/2L

- >250k patients per year with high unmet need

Data as presented 12/14/2020

† US incidence data from SEER database
ARV-471: First-in-class ER-degrading PROTAC in advanced breast cancer

Resistance is the greatest challenge to current therapies

In 2021, there will be an estimated 192,134 new cases of ER+/HER2- breast cancer in the U.S.††

The unmet need in ER+/HER2- breast cancer represents a >$15b market opportunity†††


ARV-471

An investigational oral PROTAC® protein degrader for the treatment of ER+ metastatic breast cancer

• The injectable SERD fulvestrant established the importance of ER degradation for delivering benefit to patients with advanced breast cancer

• ARV-471 has the potential to degrade ER better than fulvestrant and become an oral, best-in-class ER-directed therapy
ARV-471 degraded ER up to 90% through the 120 mg dose level; average degradation of 62%

Baseline

68% Reduction in ER after treatment with 60 mg ARV-471

Data as presented 12/14/2020
Confirmed RECIST Partial Response in a patient with extensive prior therapy and an ESR1 mutation at 120 mg

Baseline

51% reduction in target lesions (RECIST partial response) after 4 cycles of ARV-471

Data as presented 12/14/2020
## ARV-471: Moving forward rapidly across the continuum of disease

### US ER+/HER2- Breast Cancer Treatment Paradigm (# of US patients†)

<table>
<thead>
<tr>
<th>LINE OF THERAPY</th>
<th>ENABLING TRIAL</th>
<th>REGIMEN</th>
</tr>
</thead>
</table>
| Adjuvant (Post-Surgical) Breast Cancer (~160K) | **Early Breast Cancer**  
Enabling trial in neoadjuvant setting | ARV-471 or ARV-471 + CDK4/6i (palbociclib) |
| **Metastatic Breast Cancer (~50K)** | **Phase 1b**  
Supportive study in 2/3L patients to enable 1L study | ARV-471 + CDK4/6i (palbociclib) |
| **First Line Metastatic Patients** | **VERITAC Phase 2**  
Expansion trial | ARV-471 |
| **Second Line Metastatic Patients** | | ARV-471 + everolimus |
| **Third Line Metastatic Patients** | | |

† SEER database; includes US patient population only

CDK, cyclin-dependent kinase
Our strategic collaboration with Pfizer accelerates global development and commercialization of ARV-471

**Collaboration Summary**

<table>
<thead>
<tr>
<th>Upfront Payment &amp; Equity Investment</th>
<th>$1B†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Development Expenses &amp; Commercial Costs</td>
<td>50% Arvinas / 50% Pfizer</td>
</tr>
<tr>
<td>Approval &amp; Commercial Milestones</td>
<td>Up to $1.4B</td>
</tr>
<tr>
<td>Profit Share</td>
<td>50% Arvinas / 50% Pfizer Worldwide</td>
</tr>
</tbody>
</table>

**Broad Impact to Arvinas**

- Accelerates and broadens global development and commercialization of ARV-471
- Leveraging of Pfizer’s breadth of expertise and experience successfully driving trials to approval
- Provides access to Pfizer’s global clinical, regulatory, medical, patient advocacy, and commercial footprint
- Accelerates Arvinas’ strategy to build a fully integrated biotech
- Shares development costs and risks while progressing ARV-471 as part of Arvinas’ pipeline
- Further enables the advancement of our deep pipeline in oncology, I-O, and neuroscience

† $650 million in cash and $350 million equity investment at $101.22 per share
ARV-110: AR-degrading PROTAC in metastatic prostate cancer

In 2021 alone, there will be an estimated 248,530 new cases of prostate cancer†††

34,130 deaths are attributed to the disease†††

High unmet need in prostate cancer treatment represents $8b market in the US alone††††

ARV-110 has shown clinical benefit in Phase 1 in a highly refractory patient population

A challenging patient population

- Median number of previous therapies: 5
- Patients were treated with both abiraterone and enzalutamide: 82%
- Patients were treated with prior chemotherapy: 76%
- Patients have non-AR mutations: 84%

Clinical benefit in Phase 1

- ARV-110 is well tolerated, allowing continued dose escalation up to 700 mg daily†, and potentially supporting use in earlier lines of therapy
- AR degradation and late-line activity suggest strong potential across multiple disease states
- AR molecular profiling identifies a molecularly defined, late line population that may offer a possible path to accelerated approval

† As of 12/14/2020
ARV-110 has shown encouraging efficacy signals in patients with extensive prior therapy and few to no treatment options.

- Up to 90% of early-stage prostate cancer patients treated with enzalutamide experience PSA reductions†
- PSA50 responses drop to 8-15% in patients with 3L mCRPC ‡

In the ARV-110 Phase 1 population, we expected <10% PSA50 response rate.

ARV-110 substantially exceeded expectations for PSA50 responses.

† Tombal, Lancet Oncology 2014; ‡ de Wit R, N Engl J Med. 2019; Hussain, ESMO 2019; ‡‡ Includes all patients with exposures above a threshold that predicted efficacy in preclinical models. mCRPC, metastatic castrate resistant prostate cancer; PSA50, prostate-specific antigen reduction >50%

Data as presented 12/14/2020
ARV-110: ARDENT is exploring potential paths forward in both molecularly defined and earlier-line patients with prostate cancer.

Anticipating Phase 1 dose escalation and interim ARDENT Phase 2 data at ASCO GU in February 2022

<table>
<thead>
<tr>
<th>STUDY SETTING</th>
<th>ENABLING TRIAL</th>
<th>REGISTRATIONAL TRIAL</th>
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</thead>
<tbody>
<tr>
<td>3L mCRPC Patients</td>
<td>ARDENT Phase 2</td>
<td>Pivotal Phase 2 for Accelerated Approval</td>
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<tr>
<td></td>
<td>AR T878/H875 subgroup</td>
<td>Molecularly defined patients</td>
</tr>
<tr>
<td>1L/2L mCRPC Patients</td>
<td>ARDENT Phase 2</td>
<td>Confirmatory Phase 3</td>
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<tr>
<td></td>
<td>“Less-pretreated” subgroup</td>
<td>Irrespective of AR profile</td>
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<tr>
<td>Castration-sensitive Prostate</td>
<td></td>
<td>Opportunity for further label expansion</td>
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<tr>
<td>Cancer Patients</td>
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</tbody>
</table>

mCRPC, metastatic castration-resistant prostate cancer
Arvinas’ breakthroughs are driven by our integrated PROTAC® Discovery Engine

Arvinas’ platform is built from nearly 20 years of experience, know-how, and IP

**PROTAC Discovery Engine**

1. **Ligase Selection and Ligand Identification**
   - E3 KnowledgeBase – matching the correct E3 ligase to correct target
   - Leveraging AI and structural understanding of ligases to identify and design ligands; deal with Insilico Medicine expands AI capabilities
   - Arvinas’ DNA-encoded libraries for advanced screening
   - Identification of new “warheads” for previously undruggable targets

2. **Rapid PROTAC Design**
   - Zone of Ubiquitination – we design PROTAC degraders to predict the precise location where a protein can be tagged
   - Predictive computational modeling
   - State-of-the-art proteomics capabilities

3. **Turning Degraders Into Drugs**
   - “Arvinas Rules” for drug-like properties, including blood-brain barrier penetration and oral bioavailability in humans
   - Deep knowledge of molecular features allow us to create PROTAC degraders with drug-like properties and activities
Broad pipeline across oncology / immuno-oncology and neuroscience for validated and “undruggable” targets

<table>
<thead>
<tr>
<th>ARVN Program</th>
<th>Indication</th>
<th>Exploratory</th>
<th>Research</th>
<th>IND Enabling</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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<tr>
<td>ARV-110</td>
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<td>mCRPC</td>
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<td>Solid Malignancies</td>
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<tr>
<td>Myc†</td>
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†Denotes historically undruggable proteins

Note: Pipeline is non-exhaustive and IND dates are anticipated. mCRPC, metastatic castration-resistant prostate cancer; ER+/HER2-, estrogen receptor+/human epidermal growth factor receptor 2-; NSCLC, non-small-cell lung carcinoma; CRC, colorectal cancer; FTLD-tau, frontotemporal lobar degeneration-tau; PSP, progressive supranuclear palsy; MSA, multiple systems atrophy
We anticipate a rapid pace of milestones in the coming year

**2021**
- Share completed Phase 1 data (*anticipated at SABCS*)
- Initiate Phase 1b combination study with everolimus
- Begin early breast cancer study (neoadjuvant setting)

**ARV-471 (ER PROTAC®)**
- Initiate Phase 3 studies in metastatic breast cancer (as monotherapy and in combination)
- VERITAC Phase 2 data
- Safety data from Phase 1b IBRANCE® (palbociclib) combination study data

**ARV-110 (AR PROTAC®)**
- Share complete Phase 1 dose escalation and interim ARDENT Phase 2 data (*anticipated at ASCO GU*)
- Share completed ARDENT Phase 2 data
- Share interim abiraterone combination data

**ARV-766 (AR PROTAC®)**
- Share Phase 1 data
- Initiate Phase 2

**INDs**
- Four additional INDs through 2023

**2022**
Strategic, target-based partnerships expand the impact of our PROTAC® Discovery Engine

- **Genentech**
  - **September 2015**
  - (expanded in November 2017)
  - Target discovery deal

- **Pfizer**
  - **December 2017**
  - Target discovery deal

- **Gerthbio**
  - **June 2019**
  - Target discovery deal and agriculture-focused joint-venture to fight crop disease and other challenges facing the global food supply

Partnerships to expand PROTAC® degraders beyond oncology and beyond human therapeutics
Oerth Bio exemplifies how Arvinas’ PROTAC® platform can enable novel solutions in other fields.

Partnerships to expand PROTAC® degraders beyond oncology and beyond human therapeutics.

- **September 2015** (expanded in November 2017)
  - Target discovery deal

- **December 2017**
  - Target discovery deal

- **June 2019**
  - Target discovery deal and agriculture-focused joint-venture to fight crop disease and other challenges facing the global food supply.
Our PROTAC® technology is being used to transform the future of farming with plant, fungi, and insect-specific degraders.

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</thead>
<tbody>
<tr>
<td><strong>BIOAVAILABLE</strong></td>
</tr>
<tr>
<td>Target site engagement validated, and phenotypes observed</td>
</tr>
<tr>
<td><strong>SELECTIVE</strong></td>
</tr>
<tr>
<td>By combining a fungi-exclusive ligase binder with a Bayer target previously shelved due to crossover plant phytotoxicity</td>
</tr>
<tr>
<td><strong>WEED CONTROL</strong></td>
</tr>
<tr>
<td>Effective as herbicides</td>
</tr>
<tr>
<td><strong>DISEASE CONTROL</strong></td>
</tr>
<tr>
<td>Active in multiple fungi</td>
</tr>
<tr>
<td><strong>INSECT CONTROL</strong></td>
</tr>
<tr>
<td>Effective in aphid assay</td>
</tr>
<tr>
<td><strong>INSECT UPTAKE</strong></td>
</tr>
<tr>
<td>Demonstrated ability to overcome uptake &amp; metabolism challenges</td>
</tr>
</tbody>
</table>
Arvinas aims to bring its expertise in proximity-inducing compounds beyond PROTACs

- Ubiquitin tagging and protein degradation is just one potential use of proximity induction
- Many other interactions could also be mediated by proximity-inducing compounds, potentially enabling additional novel therapeutic approaches

Source: Gerry et al. (2020)
Thank You

John G. Houston, PhD
President and Chief Executive Officer
Arvinas, Inc.