PROTAC® Protein Degraders: Past, Present, and Future

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President and Chief Executive Officer,
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27 October 2021

ARVINAS
The PROTAC® Company

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.

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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[1]

Asset	Company	Target	Indication	Status	Therapeutic Focus	Market Capitalization[2]
ARV-110	ARVINAS	AR	Prostate cancer	Phase 2	Oncology/Immuno-oncology, Neuroscience	~$4.4B (IPO 2018)
ARV-471		ER	Breast cancer	Phase 2		
ARV-766		AR	Prostate cancer	Phase 1		
AR-LDD	Bristol-Myers Squibb	AR	Prostate cancer	Phase 1	*Varied*	*Large Pharma*
DT2216	DIALECTIC THERAPEUTICS	BCL-XL	Liquid and solid tumors	Phase 1	Oncology	*Private Company*
GT20029	KINTOR	AR	Acne and alopecia	Phase 1	Dermatology	~2.3B[3] (IPO 2020)
KT-474	KYMERA	IRAK4	AD, HS	Phase 1	Dermatology, Immunology, Oncology	~2.8B (IPO 2020)
NX-2127	nurix	BTK	B-cell malignancies	Phase 1	Oncology	~1.3B (IPO 2021)
CFT7455	C4 Therapeutics	IKZF1/3	MM, NHL	Phase 1	Oncology	~$2.1B (IPO 2020)
FHD-609	FOGHORN THERAPEUTICS	BRD9	Synovial sarcoma	Phase 1	Oncology	~$440M (IPO 2020)

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

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SELECT HETEROBIFUNCTIONAL DEGRADERS IN THE CLINIC[1]

Clinical Trial Initiated in 2021

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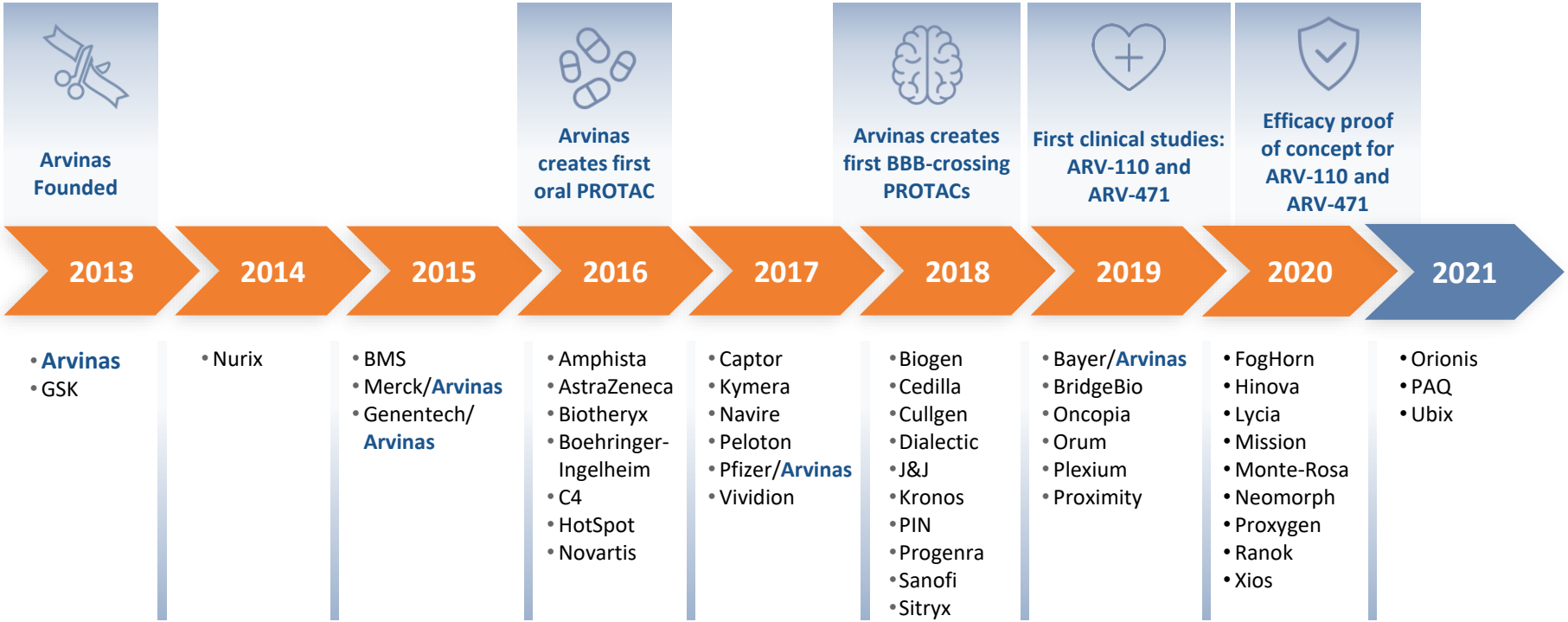
Source: ClinicalTrials.gov; company websites

The success of Arvinas and others spurred a mini-industry around Targeted Protein Degradation

Select Arvinas Achievements and Companies Developing Protein Degraders†



† 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

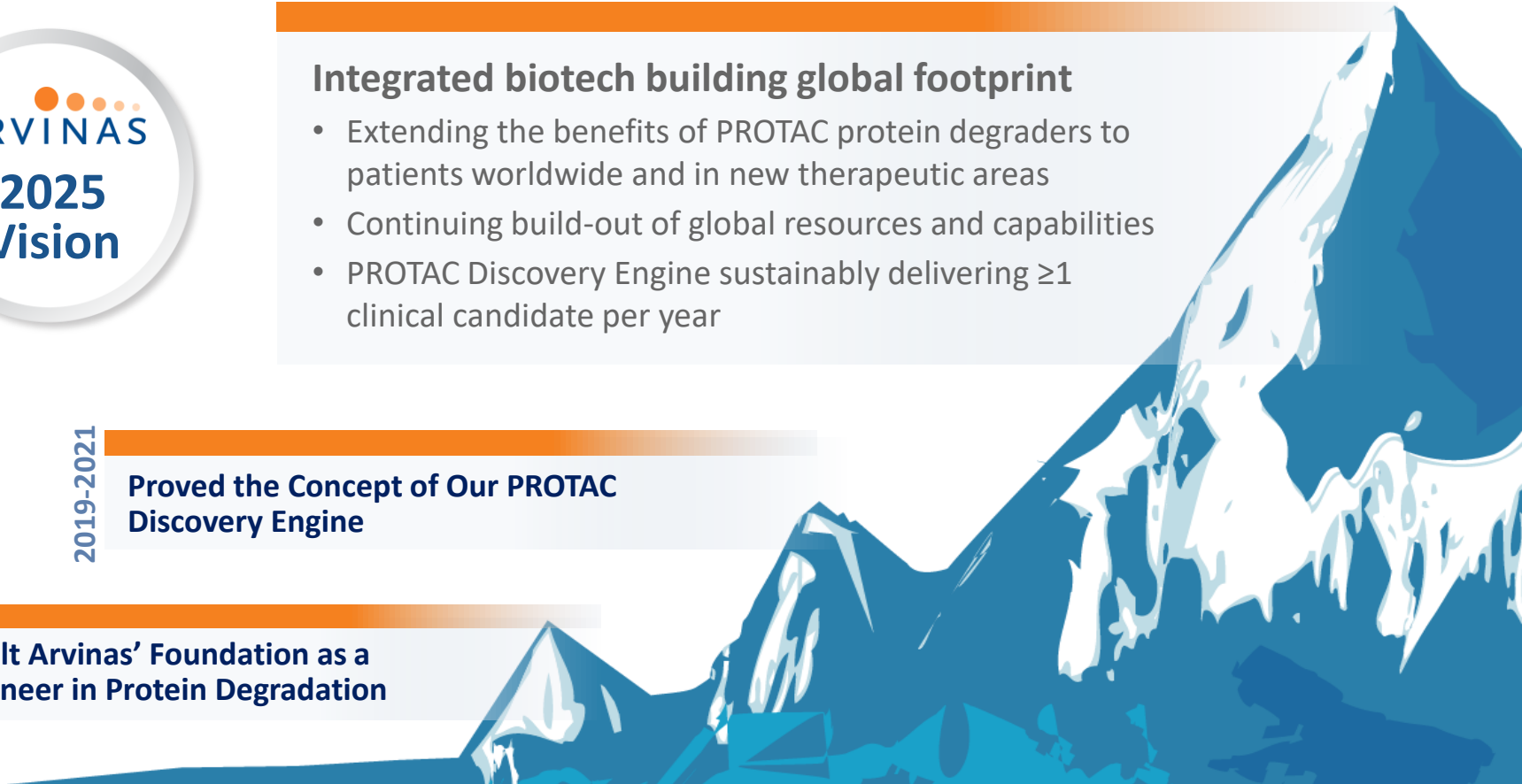
- 40,000 employees across 2,500 companies
- Strong academic base for R&D partnerships

Arvinas 2025 Vision: A global organization delivering the benefits of PROTAC® degraders to patients

ARVINAS
2025 Vision

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



2019-2021

Proved the Concept of Our PROTAC Discovery Engine

2013-2018

Built Arvinas' Foundation as a Pioneer in Protein Degradation

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

ARVINAS Pfizer

Potential best profile of any ER-targeting therapy:

- Tolerability
- ER degradation
- Clinical benefit

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

Phase 2 VERITAC trial ongoing

>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

Phase 2 ARDENT trial ongoing; two potential paths to registration:

1. **3L Molecularly Defined Patients**
2. **Broader Patient Population 1L/2L**

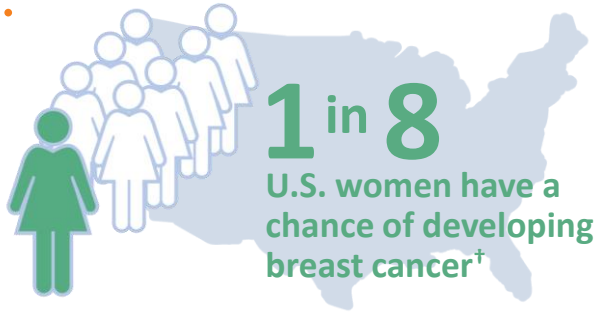
Extensive molecular profiling of tumors to understand drivers of resistance

>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



1 in 8
U.S. women have a chance of developing 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

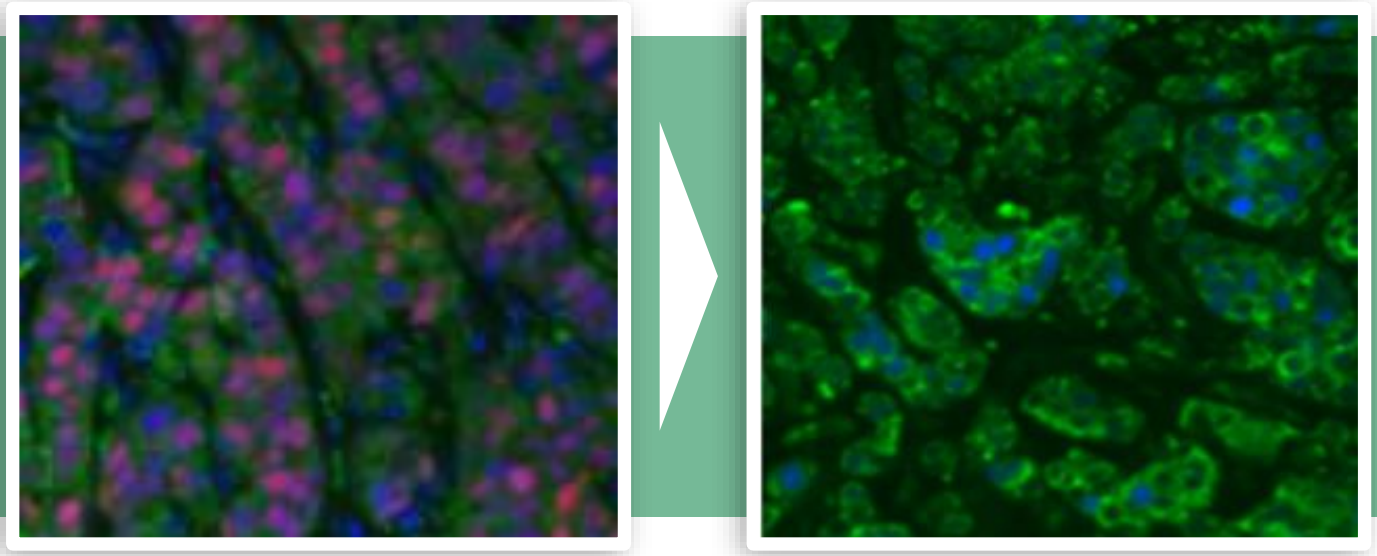
- **The injectable SERD fulvestrant established the importance of ER degradation for delivering benefit to patients with advanced breast cancer**
- **ARV-471 has the potential to degrade ER better than fulvestrant and become an oral, best-in-class ER-directed therapy**

† US CDC: https://www.cdc.gov/cancer/breast/young_women/bringyourbrave/breast_cancer_young_women/index.htm; accessed 5/25/21; †† US SEER database; †††Arvinas estimate. SERD, selective estrogen receptor degrader.

ARV-471 degraded ER up to 90% through the 120 mg dose level; average degradation of 62%

Data as presented 12/14/2020

ER Degradation in Tumor Biopsies



Baseline

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

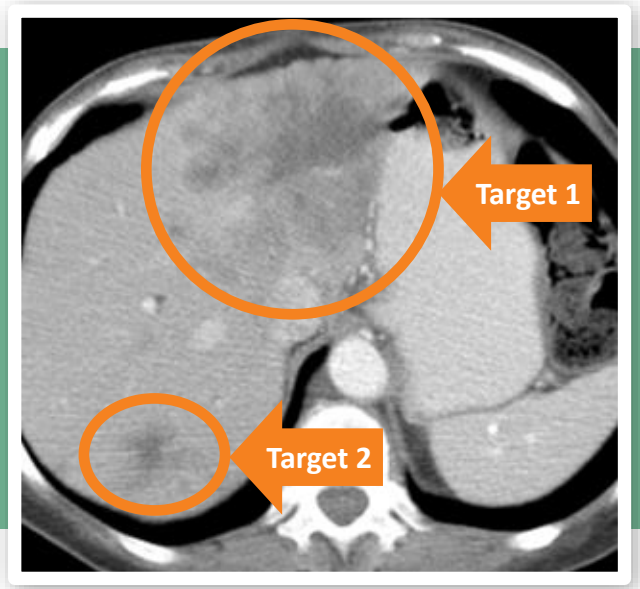
● *Estrogen receptor* ● *Nuclei* ● *Cytokeratin*

ARVINAS

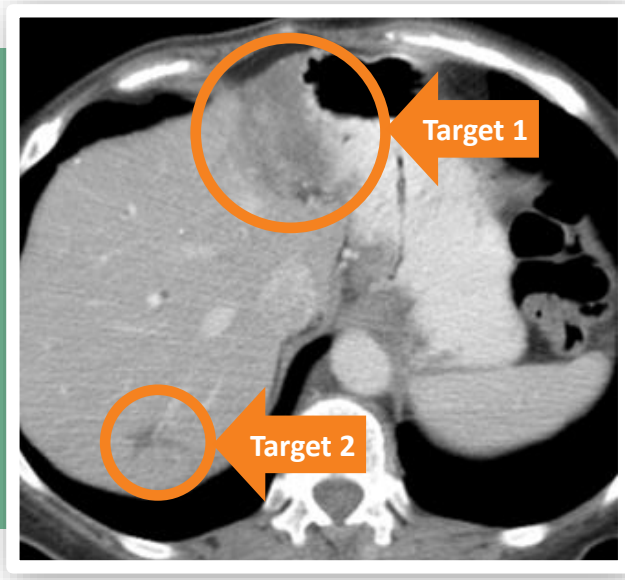
Confirmed RECIST Partial Response in a patient with extensive prior therapy and an ESR1 mutation at 120 mg

Data as presented 12/14/2020

Lesion Reduction



Baseline



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

ARV-471: Moving forward rapidly across the continuum of disease

US ER+/HER2- Breast Cancer Treatment Paradigm (# of US patients†)				
		Metastatic Breast Cancer (~50K)		
LINE OF THERAPY	**Adjuvant (Post-Surgical) Breast Cancer (~160K)**	**First Line Metastatic Patients**	**Second Line Metastatic Patients**	**Third Line Metastatic Patients**
ENABLING TRIAL	**Early Breast Cancer** *Enabling trial in neoadjuvant setting*	**Phase 1b** *Supportive study in 2/3L patients to enable 1L study*	**VERITAC Phase 2** *Expansion trial*	**Phase 1b**
REGIMEN	ARV-471 or ARV-471 + CDK4/6i (palbociclib)	ARV-471 + CDK4/6i (palbociclib)	ARV-471	ARV-471 + everolimus

† 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

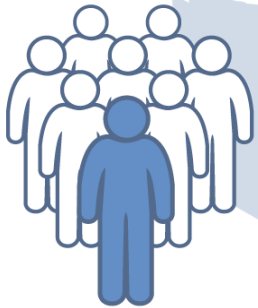
Upfront Payment & Equity Investment	$1B†
Development Expenses & Commercial Costs	50% Arvinas / 50% Pfizer
Approval & Commercial Milestones	Up to $1.4B
Profit Share	50% Arvinas / 50% Pfizer Worldwide

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



1 in 8

U.S. men will be diagnosed with prostate cancer during their lifetime†

Prostate cancer is the second leading cause of cancer death for men in the U.S.††

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

An investigational oral PROTAC® protein degrader that targets the androgen receptor (AR) for the treatment of prostate cancer

- **AR is a critical target in prostate cancer therapy**
- **Tumors develop resistance to standard-of-care AR inhibitors**
- **ARV-110 may overcome point mutations and other drivers of resistance**
- **Activity in late-line settings suggests potential for even stronger benefit in earlier-line, less-pretreated patients**

† CDC: https://www.cdc.gov/cancer/prostate/basic_info/risk_factors.htm; accessed 5/25/21; †† American Cancer Society; ††† US SEER database; †††† Arvinas estimate.

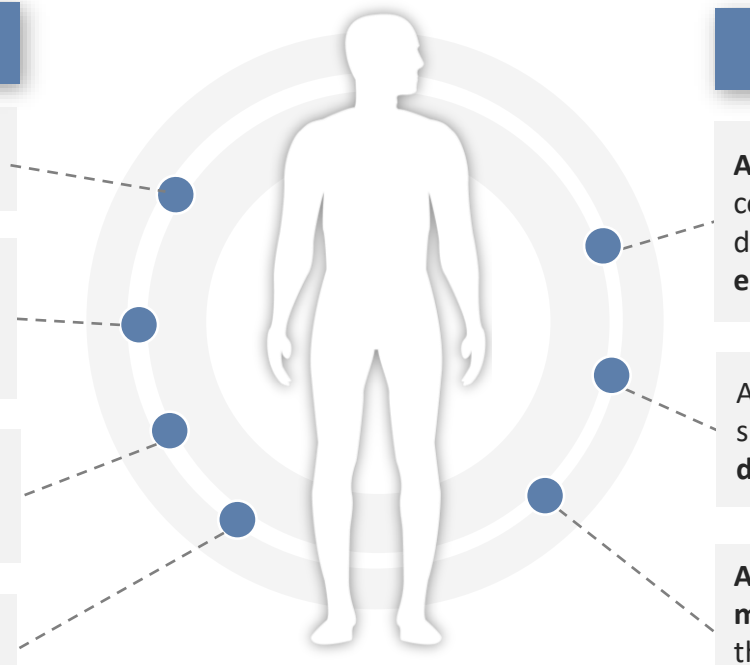
ARVINAS

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

Data as presented 12/14/2020

A challenging patient population

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



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

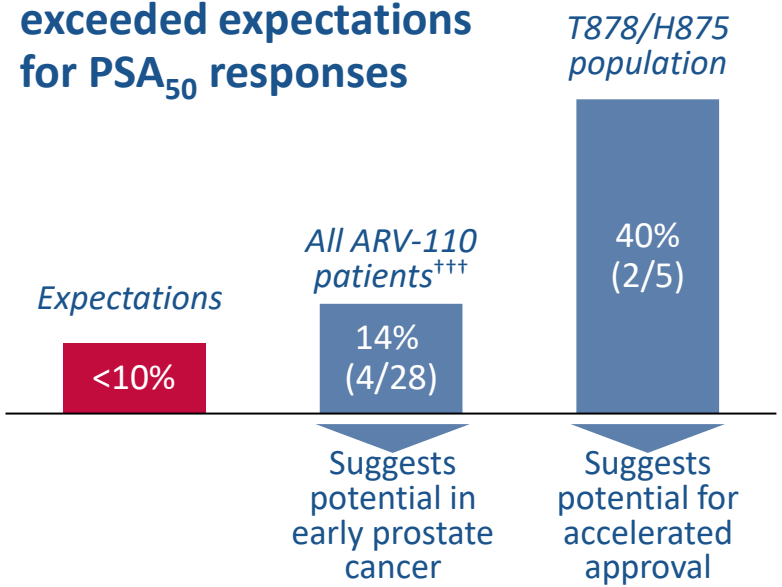
ARV-110 has shown encouraging efficacy signals in patients with extensive prior therapy and few to no treatment options

Data as presented 12/14/2020

- Up to 90% of early-stage prostate cancer patients treated with enzalutamide experience PSA reductions†
- PSA_{50} responses **drop to 8-15%** in patients with **3L** mCRPC††

In the ARV-110 Phase 1 population, we expected <10% PSA_{50} response rate

ARV-110 substantially exceeded expectations for PSA_{50} 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%

ARVINAS

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

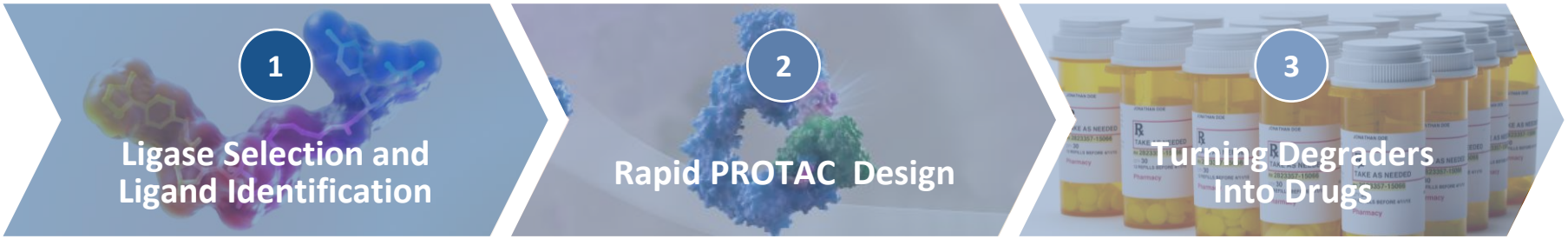
STUDY SETTING	ENABLING TRIAL	REGISTRATIONAL TRIAL
3L mCRPC Patients	**ARDENT Phase 2** *AR T878/H875 subgroup*	**Pivotal Phase 2 for Accelerated Approval** *Molecularly defined patients*
1L/2L mCRPC Patients	**ARDENT Phase 2** *"Less-pretreated" subgroup*	**Confirmatory Phase 3** *Irrespective of AR profile*
Castration-sensitive Prostate Cancer Patients	***Opportunity for further label expansion***	

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

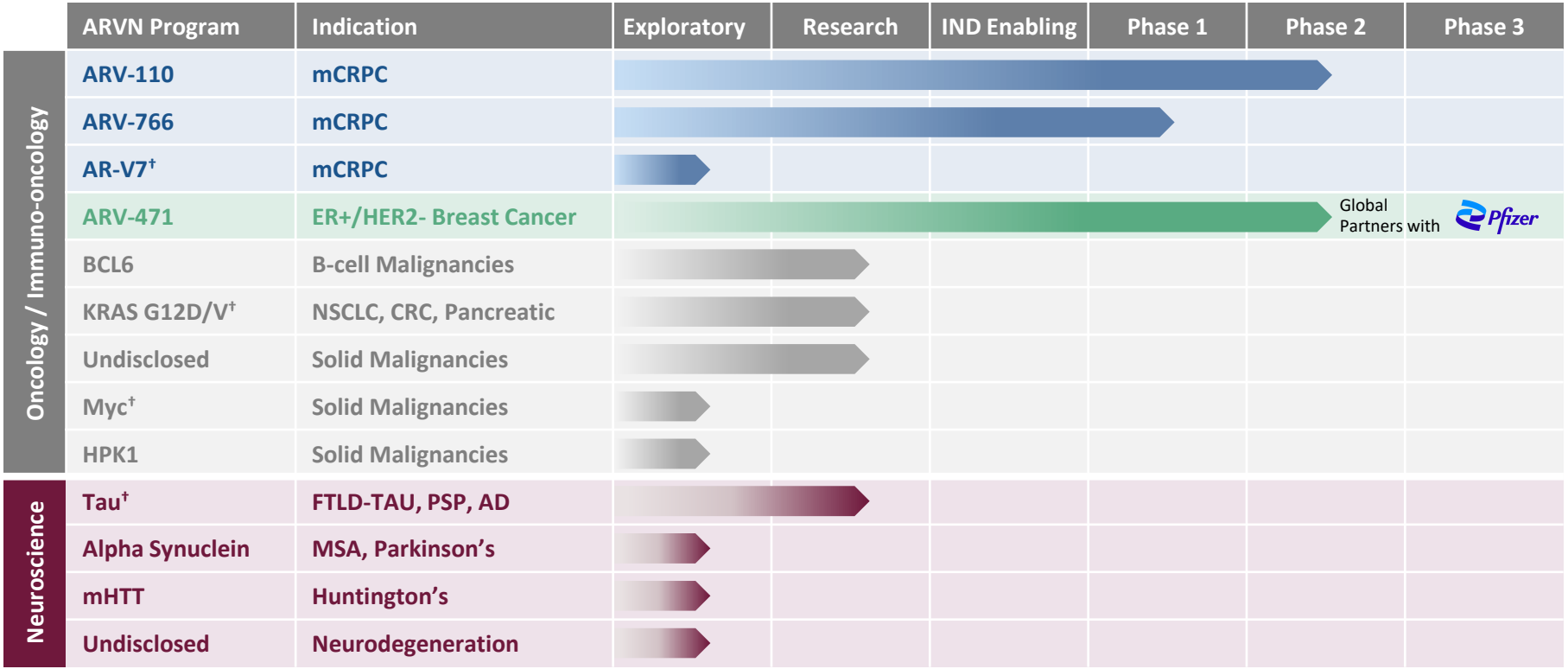


- E3 KnowledgeBase – matching the correct E3 ligase to correct target
- Leveraging AI and structural understanding of ligases to identify and design ligands; deal with Insilico Medicine expands AI capabilities
- Arvinas' DNA-encoded libraries for advanced screening
- Identification of new "warheads" for previously undruggable targets

- 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

- "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



†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	2022
ARV-471 (ER PROTAC®)	• Share completed Phase 1 data (*anticipated at SABCS*) • Initiate Phase 1b combination study with everolimus • Begin early breast cancer study (neoadjuvant setting)	• 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®)	• Initiate abiraterone combination study	• 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®)	• Initiate Phase 1	• Share Phase 1 data • Initiate Phase 2
INDs	• Four additional INDs through 2023	

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

ARVINAS

Genentech
A Member of the Roche Group

September 2015
(expanded in November 2017)
Target discovery deal

Pfizer

December 2017
Target discovery deal

Orthbio™ BAYER

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

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

Our PROTAC® technology is being used to transform the future of farming with plant, fungi, and insect-specific degraders

Oerthbio

BIOAVAILABLE AND SELECTIVE

WEED CONTROL
Effective as herbicides

BIOAVAILABLE
Target site engagement validated, and phenotypes observed

DISEASE CONTROL
Active in multiple fungi

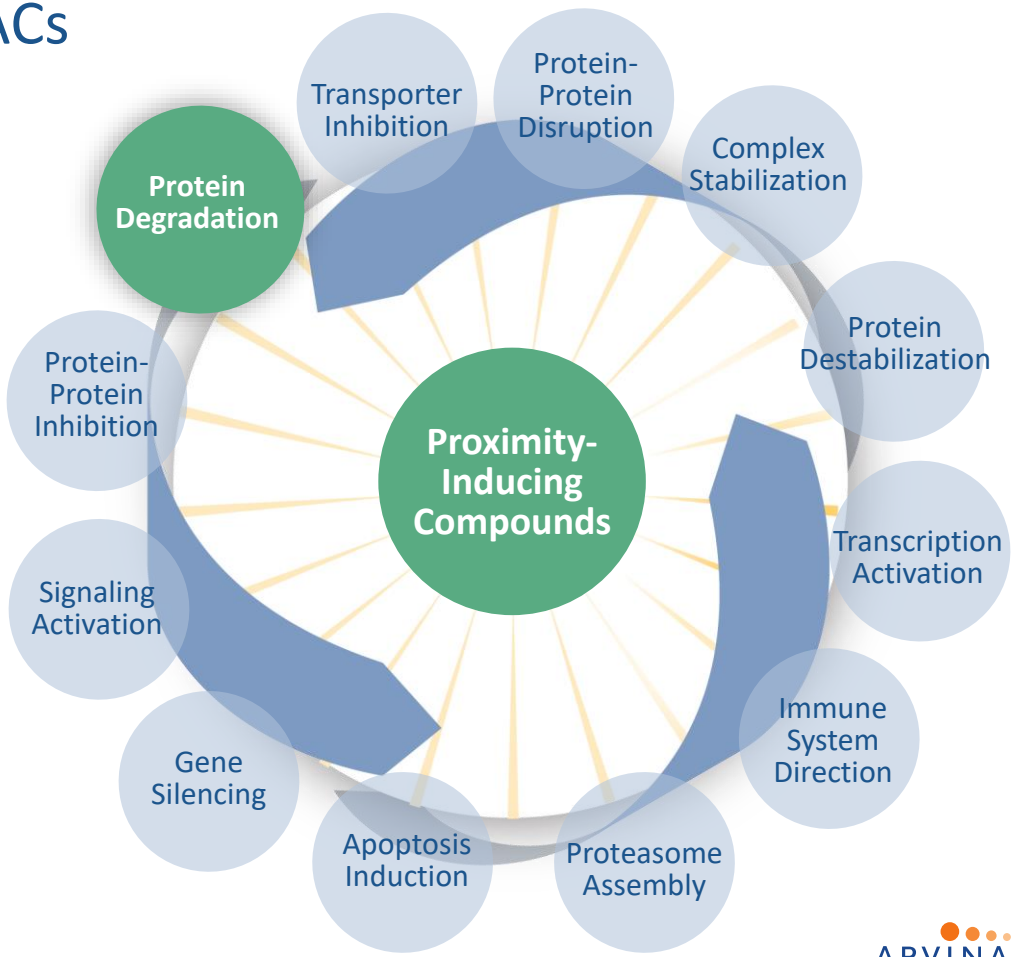
SELECTIVE
By combining a fungi-exclusive ligase binder with a Bayer target previously shelved due to crossover plant phytotoxicity

INSECT CONTROL
Effective in aphid assay

INSECT UPTAKE
Demonstrated ability to overcome uptake & metabolism challenges

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.

ARVINAS