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The PROTAC™ Company

PROTAC™ Targeted Protein Degraders

A New Therapeutic Modality

February 2019

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 development and regulatory status of our product candidates, such as statements with respect to our lead product candidates, ARV-110 and ARV-471, and the timing of IND submissions and clinical trials 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 product candidates, the potential commercialization of any of our product candidates, the potential benefits of our arrangements with Yale University and our collaborative partnerships, 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: whether we will be able to successfully initiate a Phase 1 clinical trial for ARV-110 or file an IND for ARV-471 on our expected timelines, or at all, whether our cash resources will be sufficient to fund design, initiation, and conduct of clinical trials, availability of data and results from clinical trials and other research and development activities, our scientific approach and general development progress, regulatory requirements, our foreseeable and unforeseeable operating expenses and capital expenditure requirements, our expected timeline 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 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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Arvinas: Leader in Protein Degradation, a Powerful New Modality

Novel PROTAC™ (proteolysis-targeting chimera) degrader platform

- Benefits of small molecule inhibitors and gene-based medicines
- Built with foundational technology and foremost experts from Yale University

Full worldwide development and commercialization rights for lead programs

- ARV-110 - Metastatic castration-resistant prostate cancer; Phase 1 expected in 1Q19
- ARV-471 - Estrogen receptor-positive metastatic breast cancer; Phase 1 expected mid-2019
- Brain-penetrant PROTAC programs targeting tauopathies and α-synucleinopathies

Strategic, discovery-stage partnerships with Pfizer and Genentech

- Up to $1.4B in potential milestones plus tiered royalties

Strong cash and IP positions

- First targeted protein degradation company to IPO (NASDAQ: ARVN; September 2018)
- ~$90M cash, cash equivalents, and marketable securities as of 9/30/18; additional $114M net IPO proceeds (Oct. 2018)[1]
- Broad platform IP, complemented by specific product IP
- Exclusive worldwide license to PROTAC degrader technology from Yale

Team built for success

- Strong leadership team with unparalleled protein degrader development experience
- World-class board and scientific advisors, including Craig Crews (PROTAC inventor)

1 Net of underwriter fees and discounts

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The Need for a New Approach

Our understanding of the proteins responsible for causing certain diseases has greatly outpaced innovation

Up to 80% of the human proteome is still considered “undruggable” and not addressable via small molecule inhibitors

Current treatment options for many diseases are suboptimal and/or suffer from rapid onset of resistance

Promising new approaches (siRNA, gene therapy) lack many of the drug-like properties of traditional small molecules

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A Strategic Approach to Proving and Delivering a Novel Technology Platform

Clinically validate the PROTAC™ protein degrader concept with well-defined targets

Prioritize additional targets where degradation has the potential to be superior to existing modalities

Treat patients with diseases inaccessible to current therapies by degrading "undruggable" targets

- Invest in our pipeline and our platform and grow our IP to expand our leadership in protein degradation
- Selectively collaborate with strong partners to enhance our capabilities and resources

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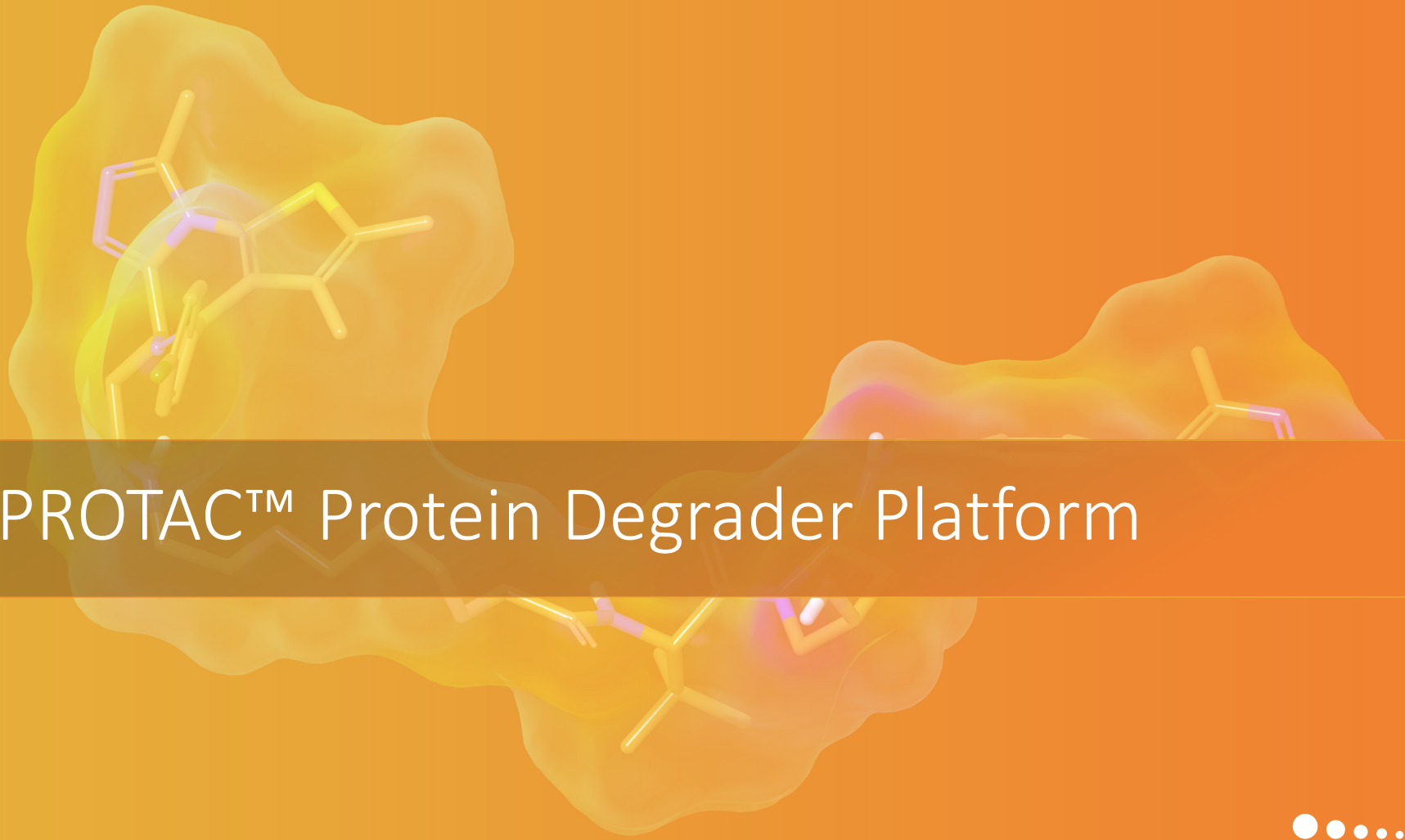

PROTAC™ Protein Degrader Platform

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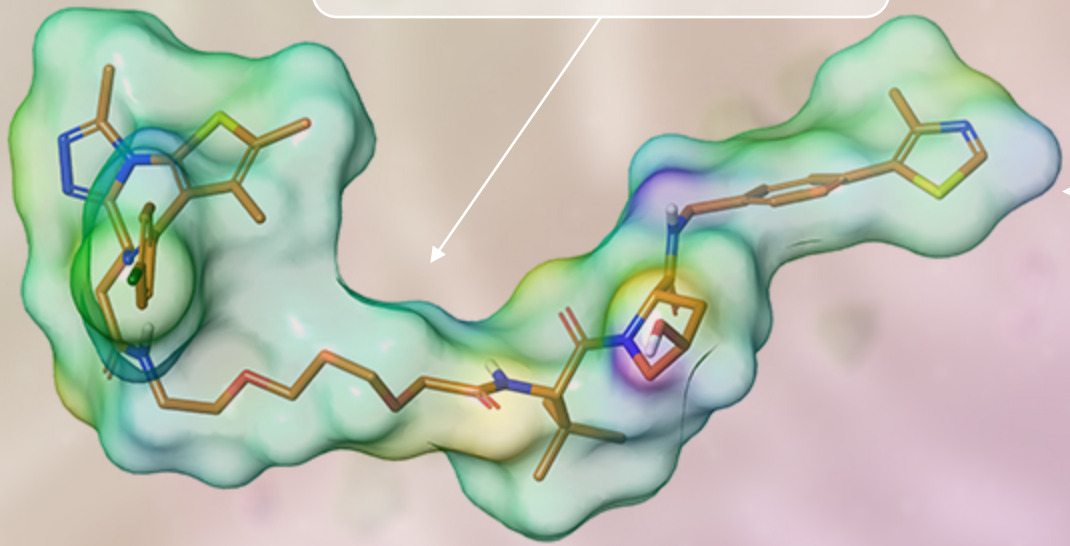
What is a PROTAC™ Protein Degrader?

A proteolysis-targeting chimera (PROTAC) degrader is a chimeric, modular small molecule engineered to induce the degradation of disease-causing proteins by the ubiquitin-proteasome system

A linker region orients the target protein and E3 ligase to enable activity

Protein ligand domain ("warhead") targets a specific protein



Ligase ligand recruits a specific E3 ubiquitin ligase

All three regions of the PROTAC degrader play a role in the specificity and potency of target degradation

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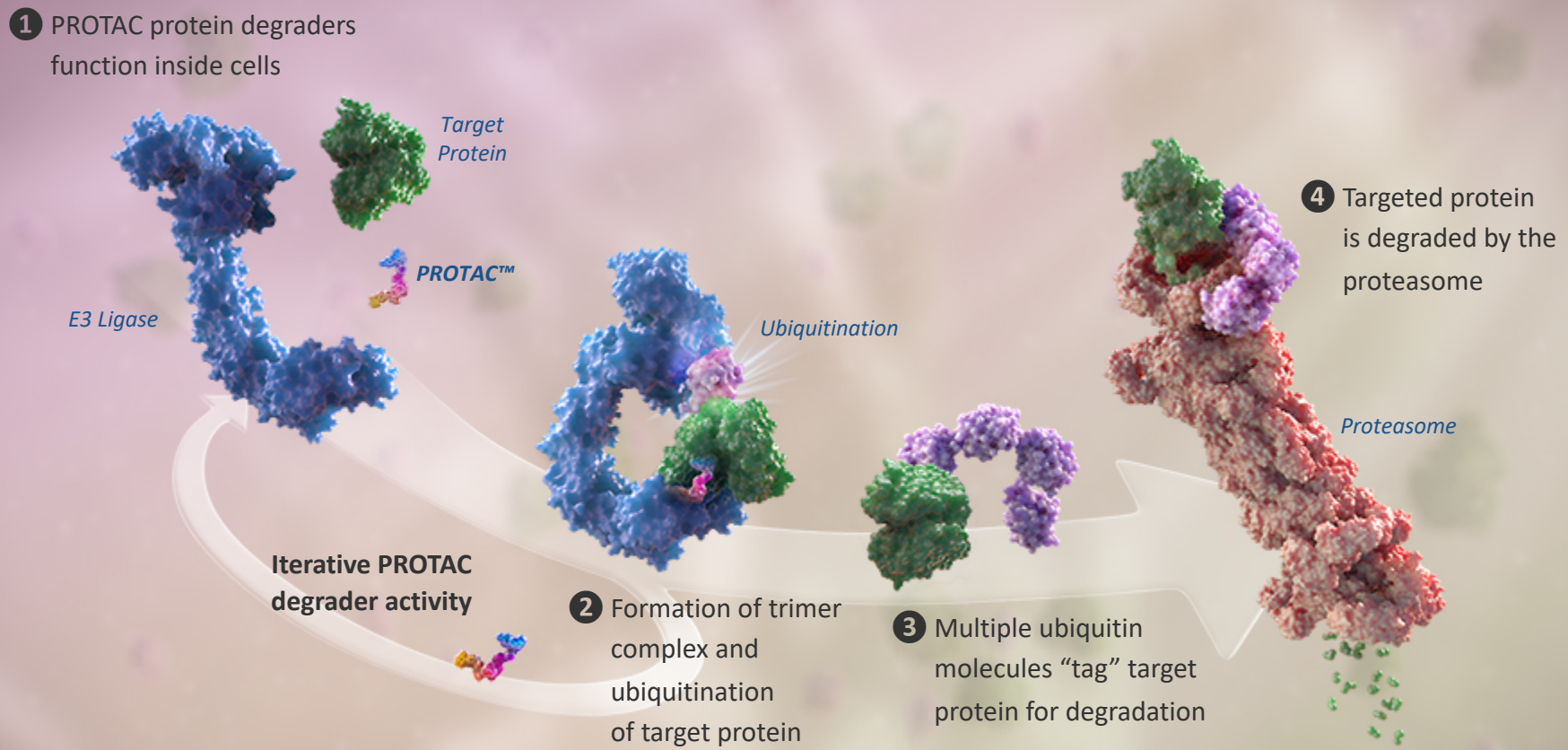
PROTAC™ Protein Degraders Harness the Ubiquitin-Proteasome System to Induce the Degradation of Disease-Causing Proteins



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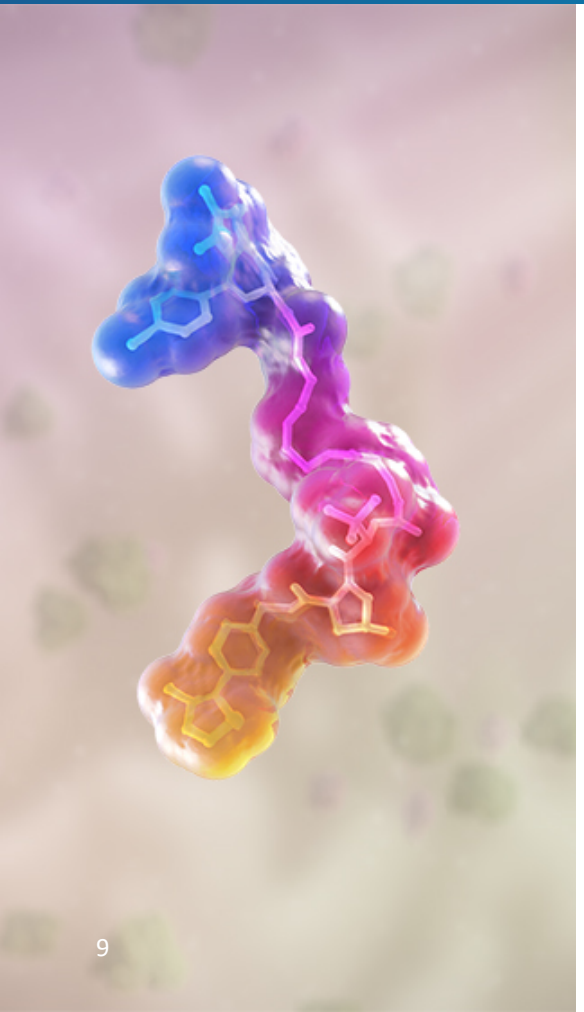
PROTAC™ Protein Degraders Combine the Advantages of Gene-based Medicines with the Benefits of Small Molecule Therapies



PROTAC protein degraders have distinct advantages over both small molecule inhibitors and gene-based medicines	PROTAC™ Protein Degraders	Small Molecule Inhibitors	Gene-Based Medicines
Eliminate pathogenic proteins	✓	✗	
Target scaffolding function	✓	✗	
Potential to treat “undruggable” proteins	✓	✗	
Iterative mechanism of action	✓	✗	✗
Broad tissue penetration	✓		✗
Orally bioavailable	✓		✗
Ease of manufacturing	✓		✗

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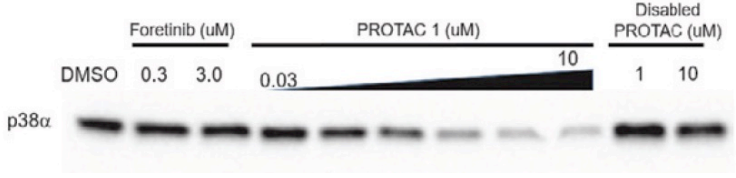
Weak or Promiscuous Ligands Can Be Converted into Potent and Selective PROTAC™ Degraders

When developed into PROTAC degraders, weak binders can become potent degraders

- Foretinib is a relatively weak binder to p38α
- PROTAC 1 is a foretinib-based PROTAC degrader with a p38α binding affinity of 11 μM
- Despite its 11 μM binding affinity, PROTAC 1 has a DC_{50} of 210 nM[1]
  - Based on experience, optimization of potency better than 210 nM is likely

A PROTAC degrader based on foretinib has a nanomolar DC_{50} despite a 11 μM binding affinity

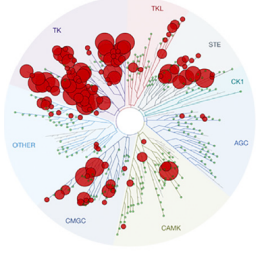


DC_{50} = 210 nM[1]

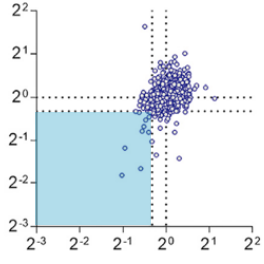
When developed into PROTAC degraders, promiscuous ligands can become selective degraders

- Foretinib binds to 133 protein kinases (*left panel*)
- In cells treated with a foretinib-based PROTAC degrader, only a small subset of cellular proteins are degraded (*blue-shaded quadrant of the right panel*)

Binds 133 Kinases



Degrades <10 Proteins



Source: Bondeson et al., 2018, Cell Chemical Biology
1 DC_{50} = Half-maximal degradation concentration

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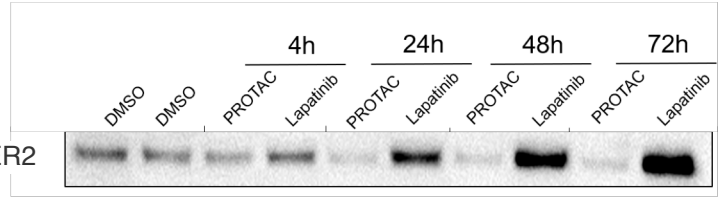
Potential Additional Advantages of PROTAC™ Protein Degraders Over Inhibitors

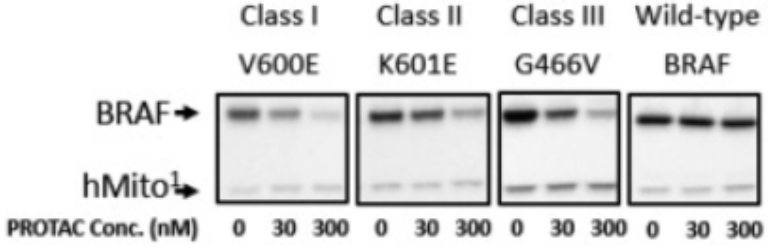
Overcome Target Protein Overexpression

PROTAC degraders can disable this common tumor resistance mechanism



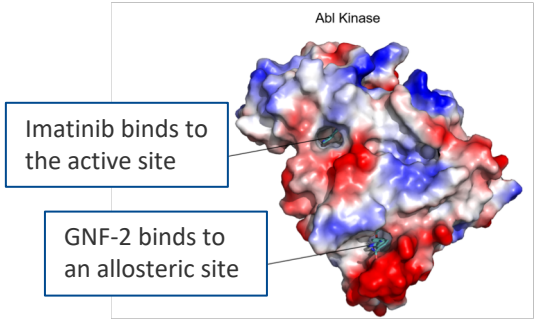
Selectively Eliminate Mutated Proteins

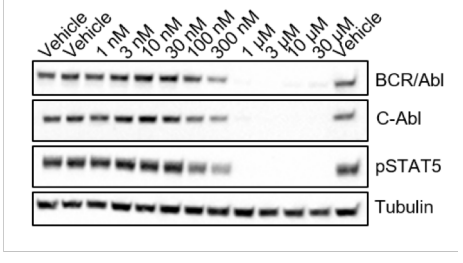
PROTAC degraders can specifically target mutant proteins but spare the wild type



Use of Allosteric Sites to Degrade Undruggable Targets

PROTAC degraders do not require strong binding to their targets, which may allow them to degrade undruggable targets





1 hMito is a protein this particular PROTAC degrader is not targeted to degrade, and is included as a loading control

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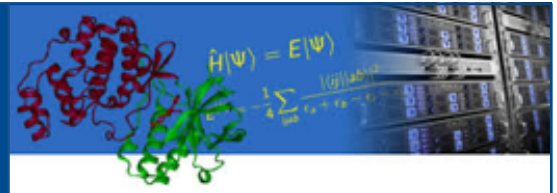
Arvinas' Technology and Expertise Enable Effective Hit ID and Optimized Development Candidates

Capabilities



Computational Chemistry
- Molecular Dynamics Simulations
- Site Directed Mutagenesis
- GPU-enabled

Structural Information
- X-Ray, SAR
- Ligand Optimization

Medicinal Chemistry
- Fit-for-Purpose PROTAC™ Matrix
- Rapid Synthesis
- Diversity

Discovery Process

Target Selection
- Differential Biology/Profile
- Chemical Equity
- Biophysics

Hit Identification
- >90% Success Rate
- Efficient, Rapid Process
- Linker SAR Generated

Clinical Candidate Optimization
- PROTAC-Specific Design Metrics
- Holistic Optimization Strategy
- Advanced bRo5 Profiles (oral)

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Research and Development Programs

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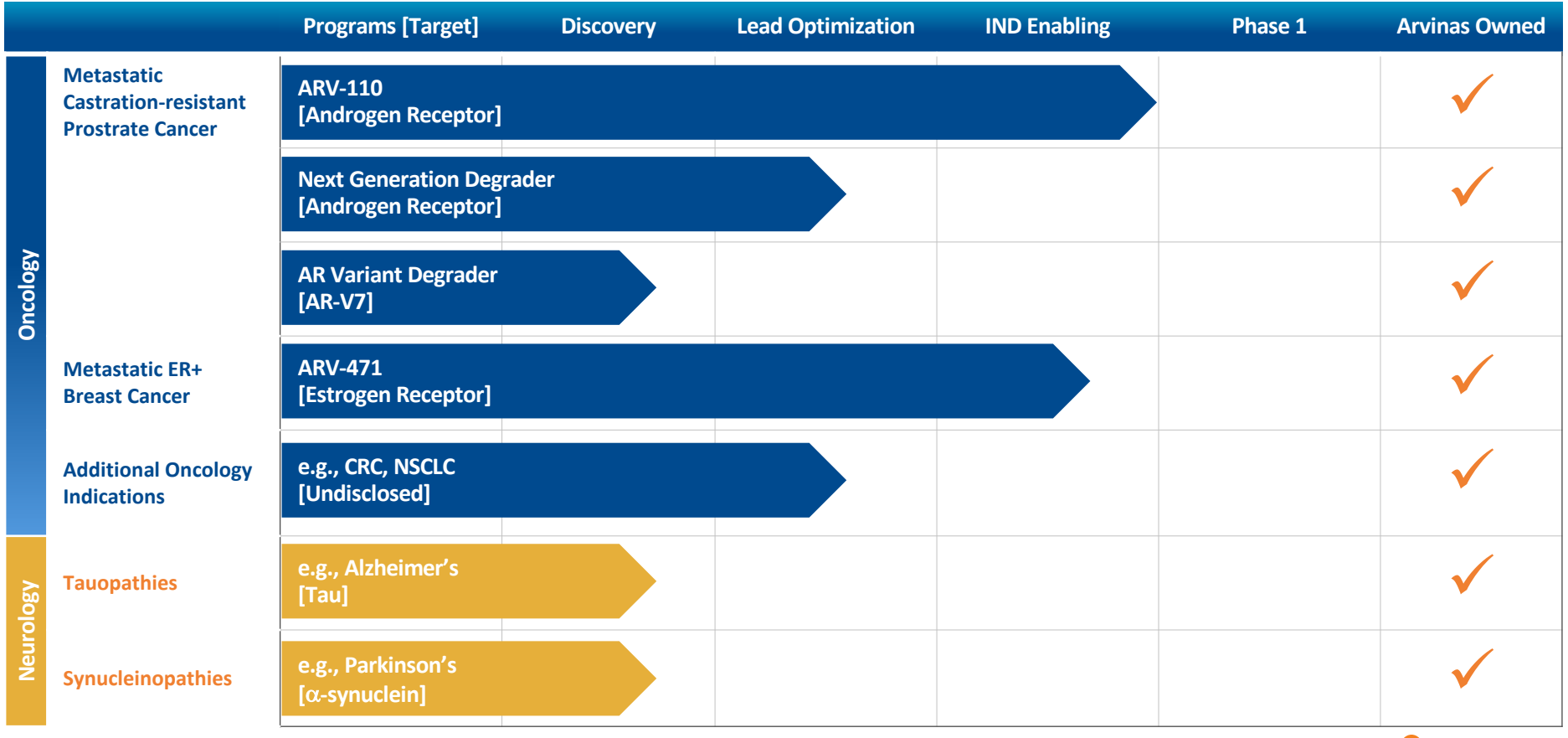
High Potential PROTAC™ Pipeline, Focused on Cancer and Neurology



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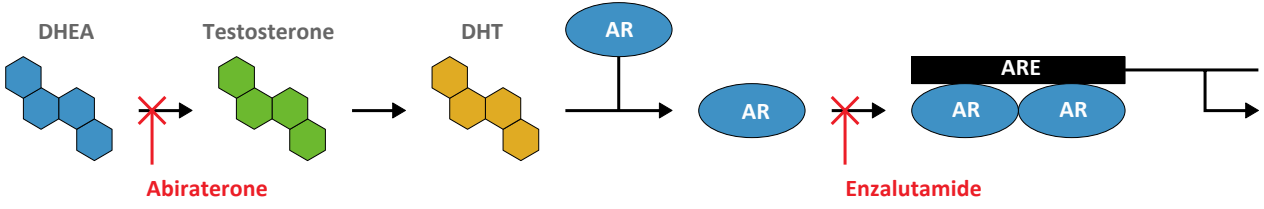
Androgen Receptor and Metastatic Castration Resistant Prostate Cancer (mCRPC)

Prostate cancer is the second leading cause of cancer death in men in the U.S. (~160k diagnosed/yr[1]); 35-45k new incidences of mCRPC in the U.S. each year



- Downstream PSA production
- Disease progression

Androgen Receptor (AR) Activity Drives Prostate Cancer[2]

- Current agents work by decreasing androgen levels (abiraterone) or blocking androgen binding to AR (enzalutamide)
- 15-25% of patients do not respond to abiraterone or enzalutamide (intrinsic resistance)

Acquired Resistance Mechanisms to Abiraterone and Enzalutamide

- AR gene amplification (40-60% of patients)
- AR gene enhancer amplification (>70% of patients)
- AR point mutations (~15% of patients)
- Intra-tumoral androgen production

In resistant patients, PSA levels rise, suggesting that AR remains the principal driver of disease

1. American Cancer Society
2. DHEA, dehydroepiandrosterone; DHT, dihydrotestosterone; AR, androgen receptor; ARE, androgen response element

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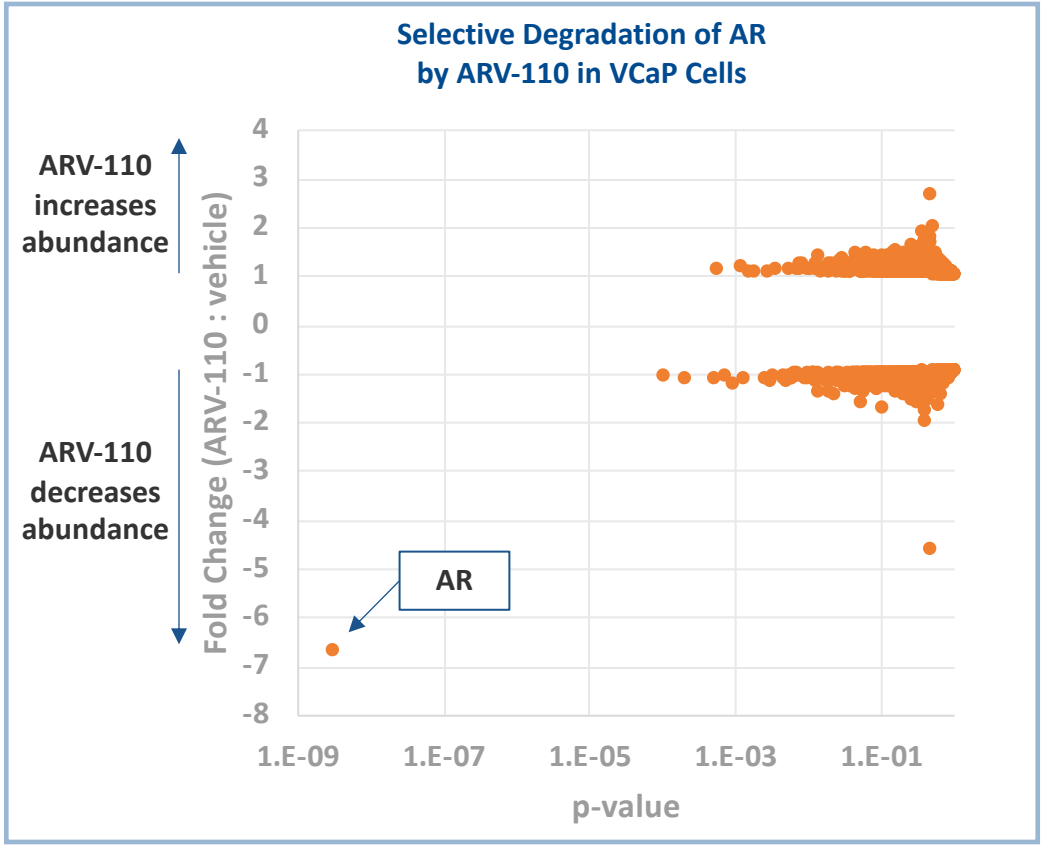
Our Androgen Receptor-Targeting PROTAC™ Degrader: ARV-110

Orally bioavailable androgen receptor-targeted PROTAC protein degrader

- ARV-110 is in development for the treatment of men with mCRPC who have progressed on abiraterone and/or enzalutamide
- Appears to overcome mechanisms of resistance to current standards of care
- **DC_{50} = 1 nM** in VCaP cells[1]

ARV-110 Selectively Degrades AR

- After 8 hours of treatment of VCaP cells with 10 nM ARV-110 *in vitro*, AR was the only degraded protein among the nearly 4,000 proteins measured
  - 85% D_{max}[2]
  - p-value: $3x10^{-9}$



1 VCaP, Vertebral Cancer of the Prostate
2 D_{max}, maximal degradation

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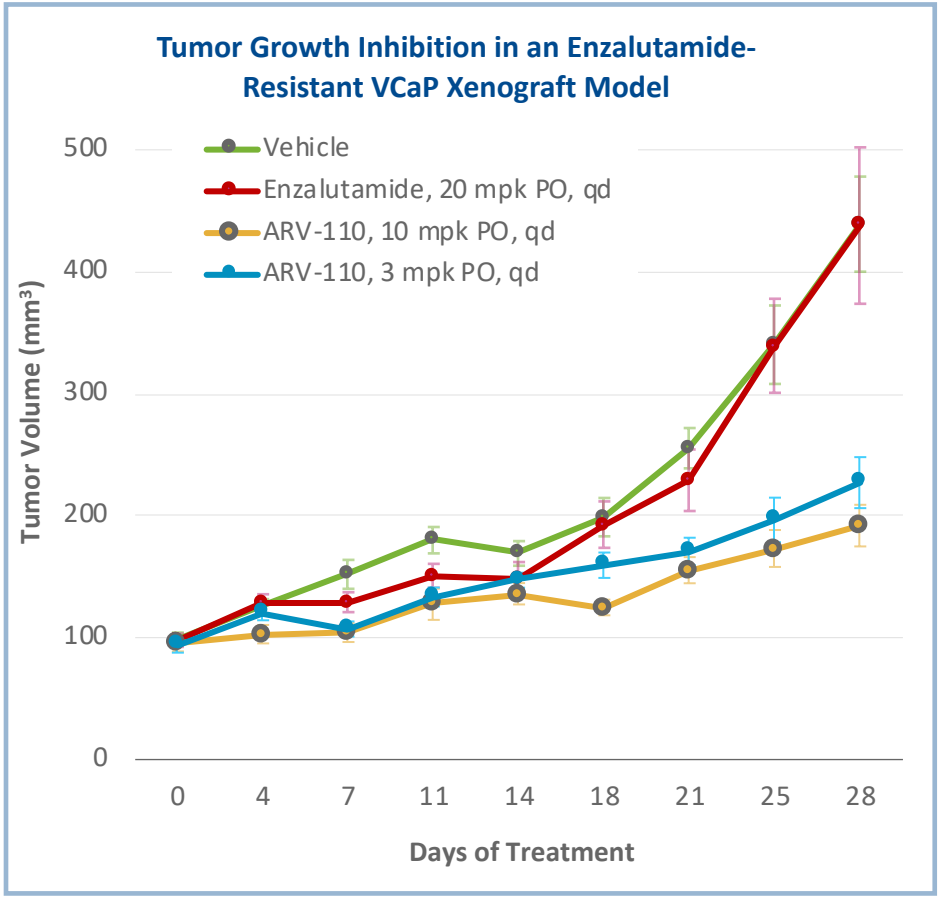
ARV-110 Inhibits Tumor Growth in an *In Vivo* Model of Acquired Enzalutamide Resistance

- *In vivo* mouse xenograft model of acquired enzalutamide resistance developed at Arvinas
- In this model, VCaP tumors acquired resistance to enzalutamide after being continuously propagated in castrated, enzalutamide treated mice for ~3 years
- Daily and orally delivered ARV-110 significantly inhibited tumor growth (*at right*)
  - 10 mpk ARV-110: 70% tumor growth inhibition



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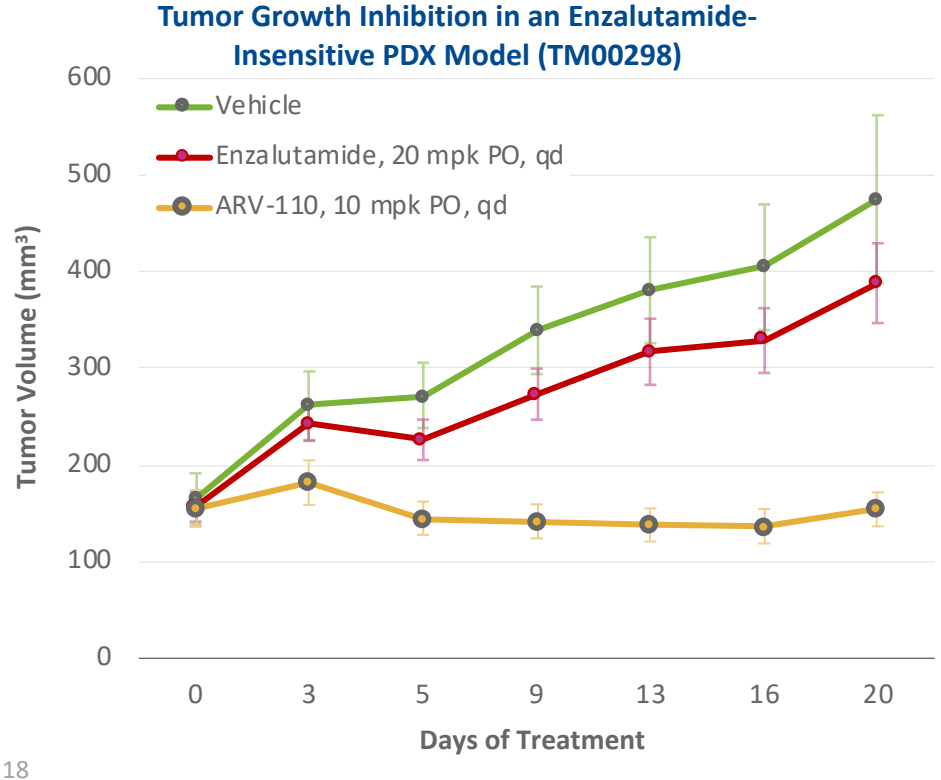
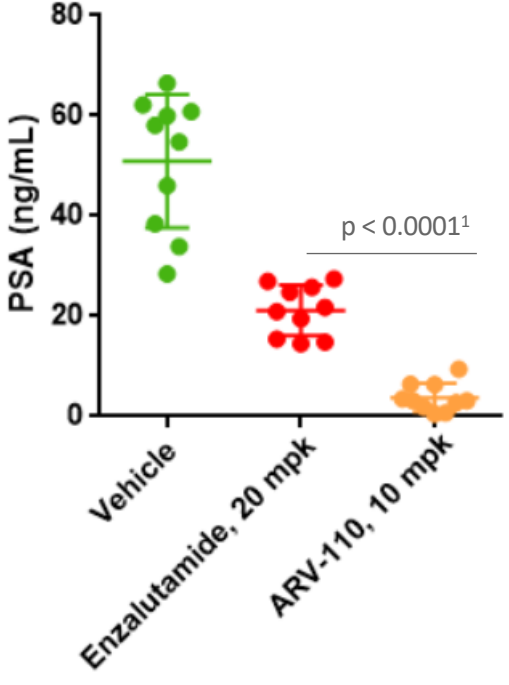
ARV-110 Demonstrates Efficacy and Plasma PSA Reduction in an Enzalutamide-Insensitive Patient Derived Xenograft Model

- Orally delivered ARV-110 significantly inhibited tumor growth in these enza-insensitive tumors (TGI: 100%)



- Plasma PSA levels following ARV-110 treatment significantly decreased vs. mice treated with vehicle or enzalutamide



1 p value refers to ARV-110 vs. enzalutamide

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ARV-110: Development Status

ARV-110 clinical trial planned for 1Q19

- Potential to be the first-in-class AR degrader
- Good laboratory practice (GLP) toxicity studies support planned clinical development
- Received FDA clearance of IND for Phase 1 trial in December 2018
- Initiation of phase 1 trial expected in 1Q19
- Program wholly owned by Arvinas

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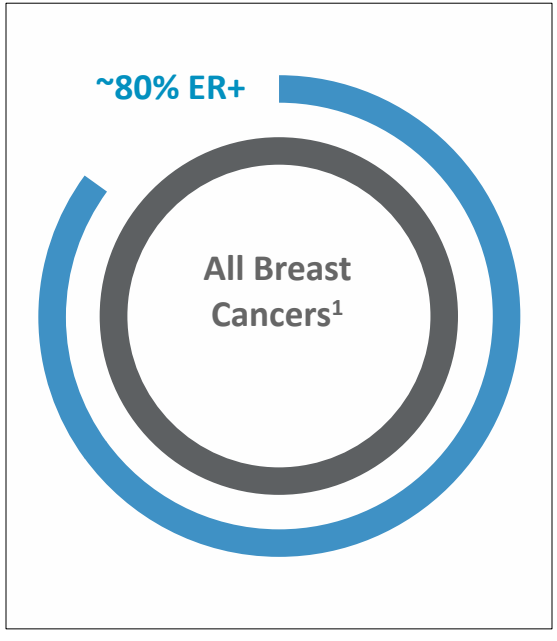
Estrogen Receptor and Breast Cancer

Breast cancer is the **second leading cause** of **cancer death in women**



Types of Breast Cancer

- Breast cancer is the second most common cancer in women
- ~266,000 women are expected to be diagnosed with invasive breast cancer in the US in 2018[2]
- Metastatic breast cancer accounts for ~6% of newly diagnosed cases[3]

Targeted Approaches to Treat ER+ Breast Cancer

- Fulvestrant has validated the value of ER degradation
- After 6 months of fulvestrant treatment, up to 50% of ER baseline levels remain[4]

A superior ER degrader is needed

1 National Cancer Institute, Hormone Therapy for Breast Cancer 2. American Cancer Society; 3 Malmgren, J.A., Breast Cancer Res Treat (2018) 167:579–590; 4 Gutteridge et. Al., Breast Cancer Res Treat 2004;**88** suppl 1:S177;

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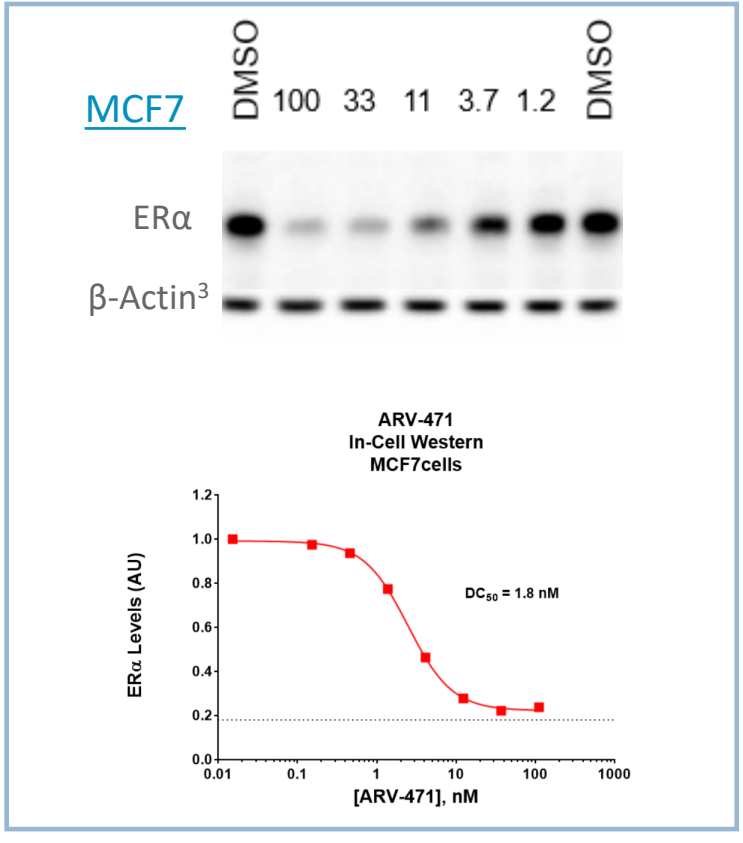
Our Estrogen Receptor-Targeting PROTAC™ degrader: ARV-471

Orally bioavailable estrogen receptor-targeted PROTAC protein degrader

- ARV-471 is in development for the treatment of women with ER+ locally advanced or metastatic breast cancer
- Potential as both a single agent and in combination with CDK4/6 inhibitors

ARV-471 Degrades ER in ER+ Breast Cancer Cell Lines

- ARV-471 induces ER degradation in multiple ER+ breast cancer cell lines, including MCF-7 cells and ESR1-mutant lines[1]
- **DC_{50} = 1.8 nM** in MCF7 cells[2]



1 Also tested: MB-134-VI, T47D, D538G, Y537S, ZR-75-1, BT474, CAMA-1
2 DC_{50} = Half-maximal degradation concentration
3 Beta-actin is a protein ARV-471 and fulvestrant are not targeted to degrade, and is included as a loading control

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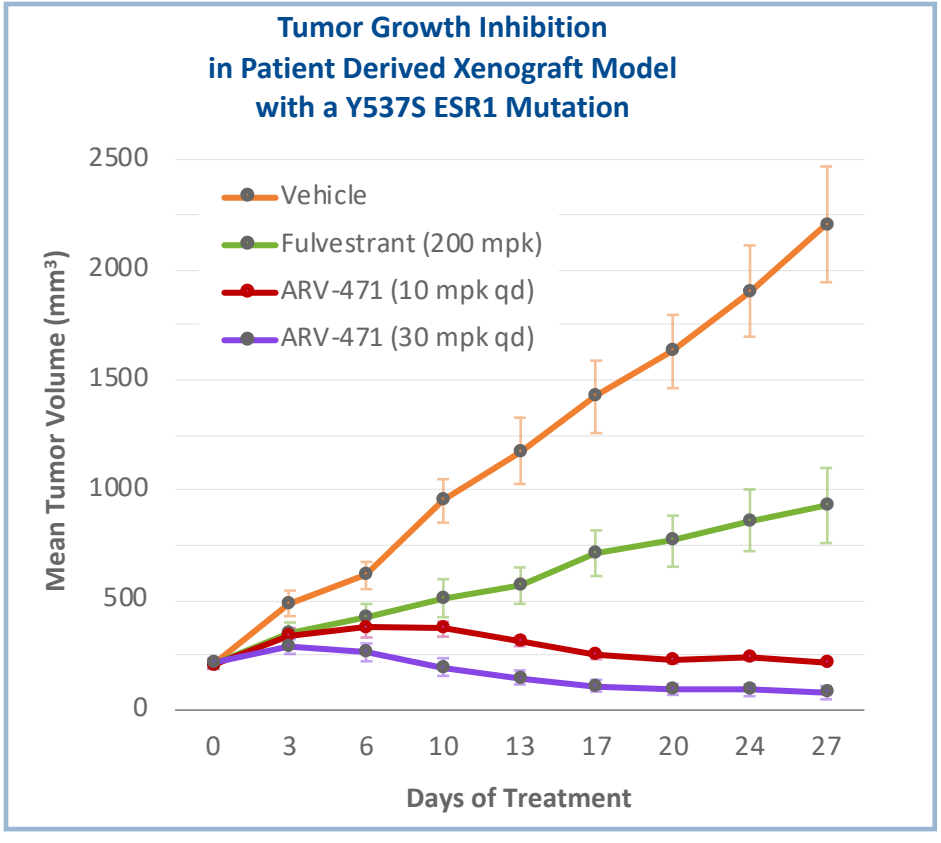
ARV-471: Superior Tumor Growth Inhibition Versus Fulvestrant in a Y537S (ER Gene Mutation) PDX Model

ARV-471 *In Vivo* Preclinical Development

- Oral, daily dose of ARV-471 inhibited tumor growth by 99% at 10 mpk and 106% at 30 mpk in an ESR1 mutant PDX model (*at right*)
- Superior inhibitor of tumor growth compared to fulvestrant[1]
- In corresponding quantitative western blots, ER is reduced by 79% and 88% in the 10 mpk and 30 mpk arms, respectively, vs. 63% for fulvestrant



1 Fulvestrant schedule: 2x weekly x2 / q7dx2

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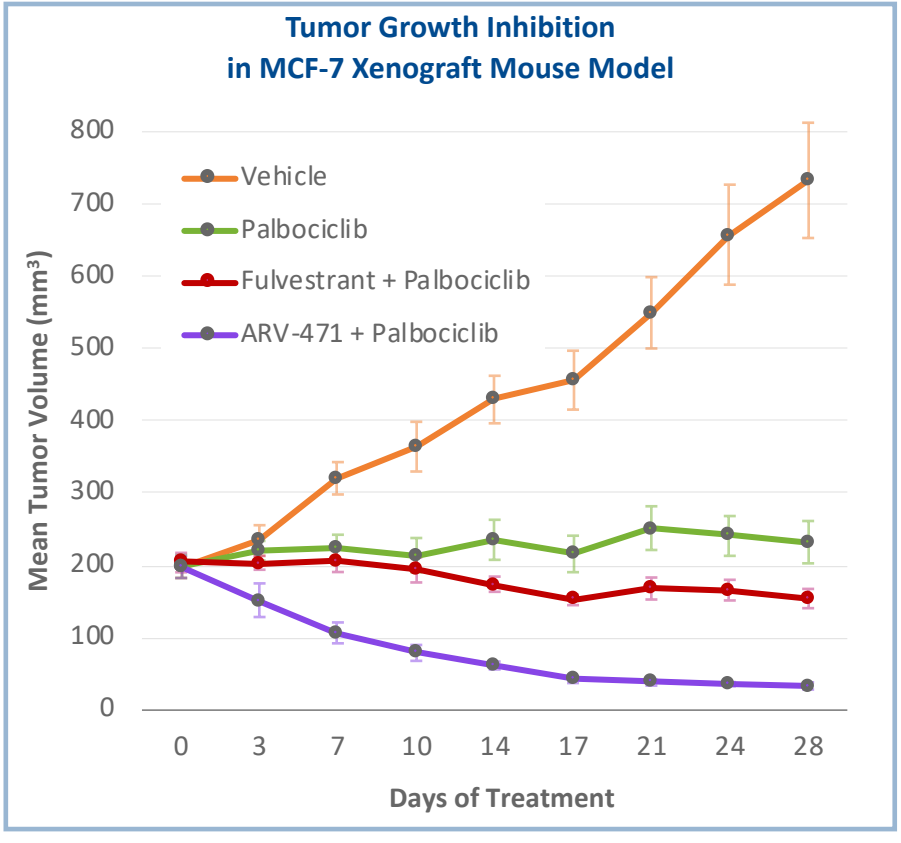
In Combination with Palbociclib, ARV-471 Exhibits Superior Tumor Shrinkage Versus Fulvestrant

ARV-471 *In Vivo* Preclinical Development

- Achieved significant tumor shrinkage in combination with palbociclib (131% TGI)
  - In all 10 mice in experiment, tumors reduced by >80%
- Superior tumor shrinkage (in combination with palbociclib) compared to fulvestrant (108% TGI)



Palbociclib arm: 60 mpk po qd; 94% TGI.
Fulvestrant + Palbociclib arm: Fulvestrant 200 mpk sc biwx 2, qwx 3 + palbociclib 60 mpk po qd; 108% TGI
ARV-471 + Palbociclib arm: ARV-471 30 mpk po qd + palbociclib 60 mpk po qd; 131% TGI

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ARV-471: Development Status

ARV-471 clinical trial planned for mid-2019

- IND-enabling GLP toxicology studies are in the reporting phase
- IND expected in 1H19, and initiation of Phase 1 clinical trial expected in mid-2019
- After Phase 1, a Phase 1b trial in combination with CDK4/6 inhibitor is planned
- Program wholly owned by Arvinas

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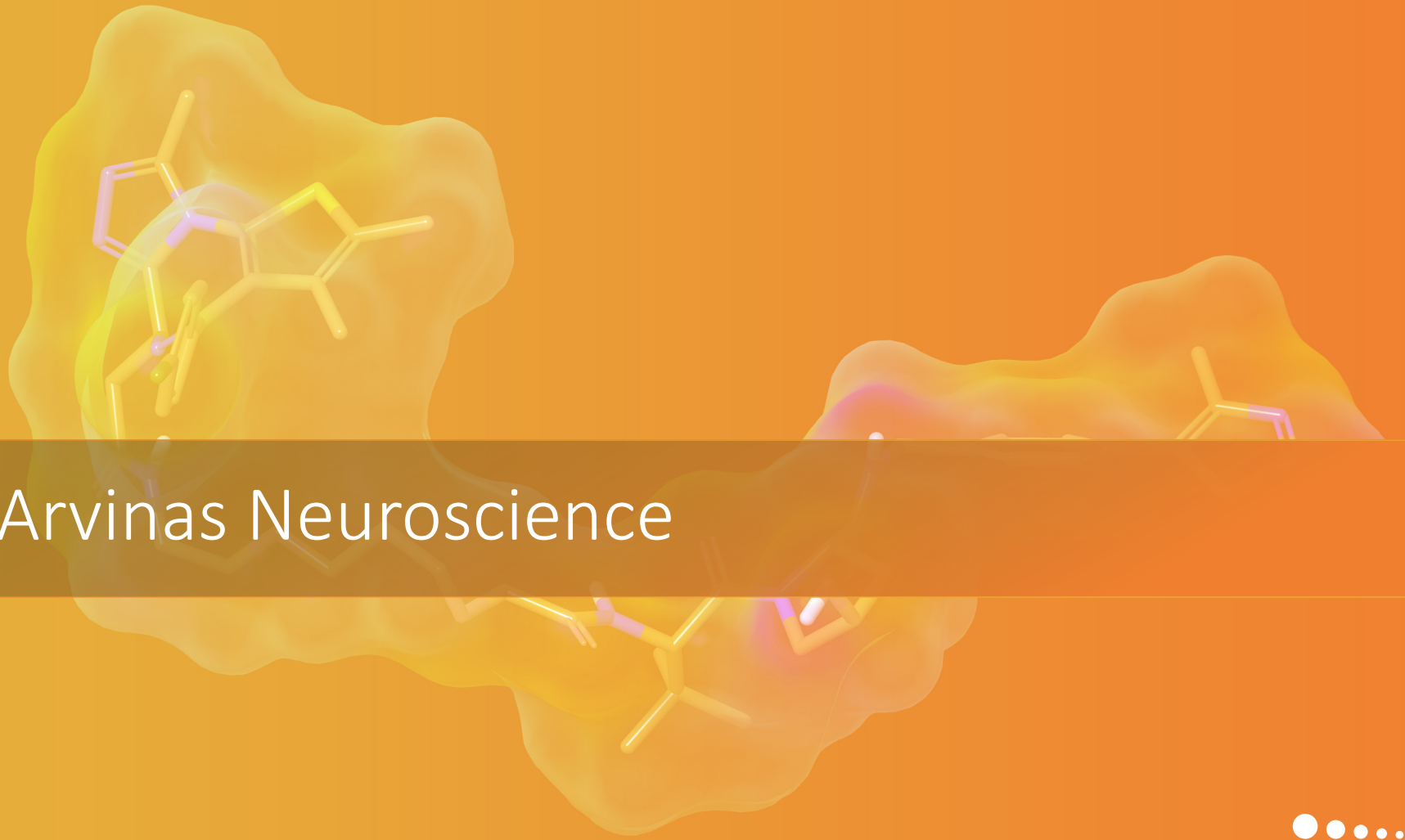

Arvinas Neuroscience

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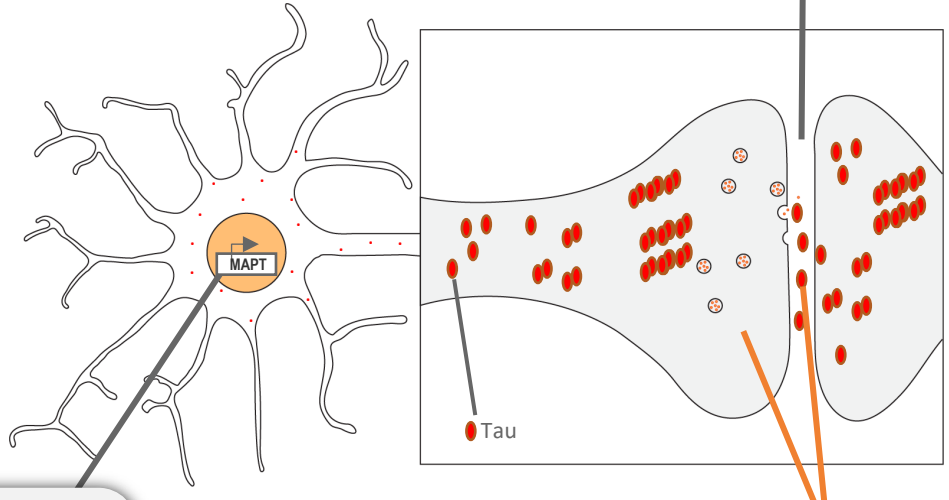
Why Are We Excited about the Opportunity for PROTAC Degraders in Neurological Diseases?

- PROTAC degraders may overcome the limitations of other platforms, including antisense oligonucleotides (ASO) and monoclonal antibodies (Ab)

Ab
- Blocks only extracellular pathologic tau
- IV dosing results in only 0.1% in CSF



ASO
- Degrades mRNA, impacting intra- and extracellular tau
- Does not discriminate between wild type and pathologic tau
- Requires intrathecal dosing

PROTAC™ *Potential*
- Reduce intra- and extracellular pathologic tau
- Discriminate between wild type and pathologic tau
- Oral administration with BBB biodistribution

ASO, antisense oligonucleotide; Ab, antibody; CSF, cerebrospinal fluid; BBB, blood-brain barrier

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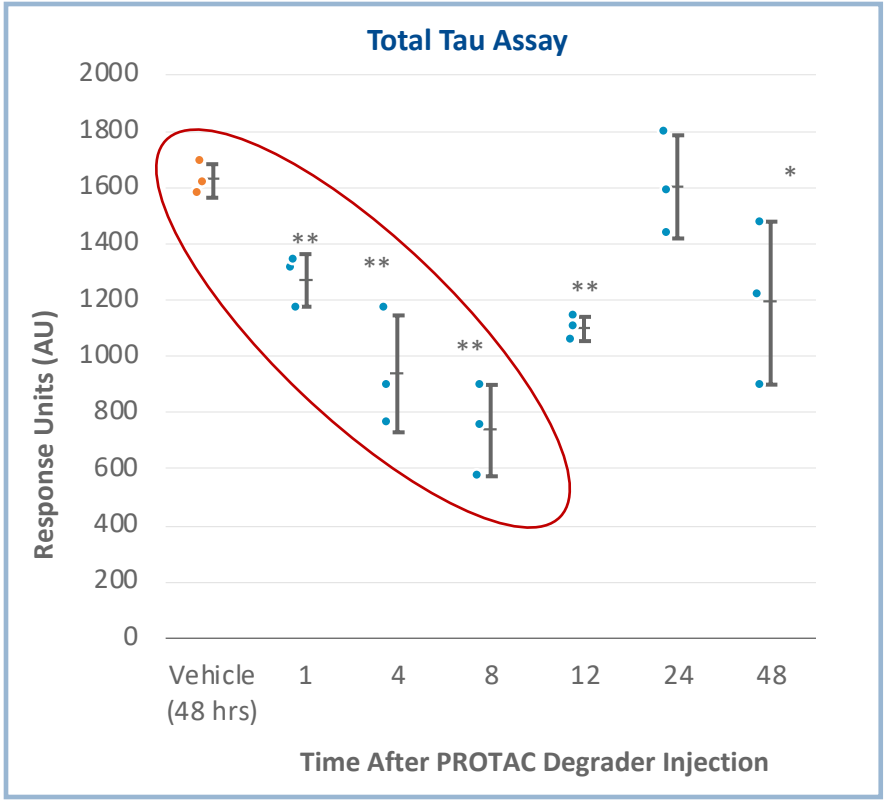
In the Brain, Our PROTAC Degraders Have Degraded Tau

Arvinas' Early Work in Neurodegeneration

- Neurological diseases have high unmet need, especially in neurodegeneration (no approved disease-modifying therapies)
  - Alzheimer's and Parkinson's diseases encompass the largest patient populations (US prevalence of ~6M and ~1M, respectively)[1,2]
- Direct (hippocampus) injection of tau-directed PROTAC™ degrader reduced tau levels by ~50% (*at right*)
- Tau- and α-synuclein-targeted PROTAC protein degraders have penetrated the BBB in rodents (*next page*)



1 Alzheimer's Association; "2018 Alzheimer's Disease Facts and Figures." Alzheimer's and Dementia; V.14; No.3; 2018; p367)
2 Parkinson's Foundation: http://parkinson.org/Understanding-Parkinsons/Causes-and-Statistics/Statistics
**p<0.01, *p<0.05

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Our PROTAC Degraders Have Crossed the Blood-Brain Barrier (BBB)

- Micromolar rodent brain exposure achieved after peripheral (IV) administration
- Brain to Plasma ratio >0.5 achievable with PROTAC degraders

PROTAC	Species	Dose (mg/kg)	[Plasma 1h] (ng/ml)	[Brain 1h] (ng/g)	B/P ratio
1	mouse	10	309	227	0.8
2	mouse	10	843	3920	4.7
3	mouse	10	285	1425	5.0

- Over a 4-hour time course, PROTAC degraders are more durable in the brain than in plasma
- Next step: Test BBB-penetrant, active PROTACs for tau degradation in tauopathy rodent brain

Time (hours)	1	2	4
B/P Ratio	4.7	6.8	8.9

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Arvinas' Approach in Neurodegeneration

Approach: Prove the concept with PROTAC degraders in defined populations while pursuing larger, multifactorial indications

Conceptual

Tau	FTDP (~3K)	Progressive supranuclear palsy (~20K)	ApoE4 AD risk allele carriers (600-900K)	Alzheimer's (~6M)[1]
α-synuclein	Synuclein mutations, e.g., duplication/ triplication (~4K)[2]	Multiple systems atrophy (~50K)[3]	GBA PD risk allele carriers (~500K)	Parkinson's (~1M)[4]

FTDP, frontotemporal dementia and parkinsonism; GBA, glucocerebrosidase gene; AD, Alzheimer's disease; PD, Parkinson's disease

1 Alzheimer's Association; "2018 Alzheimer's Disease Facts and Figures." Alzheimer's and Dementia; V.14; No.3; 2018; p36

2 Kowal. Movement Disorders 2013, 28: 311-319; Nishioka. Intechopen 2011

3 NINDS; https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Multiple-System-Atrophy

4 Parkinson's Foundation: http://parkinson.org/Understanding-Parkinsons/Causes-and-Statistics/Statistics

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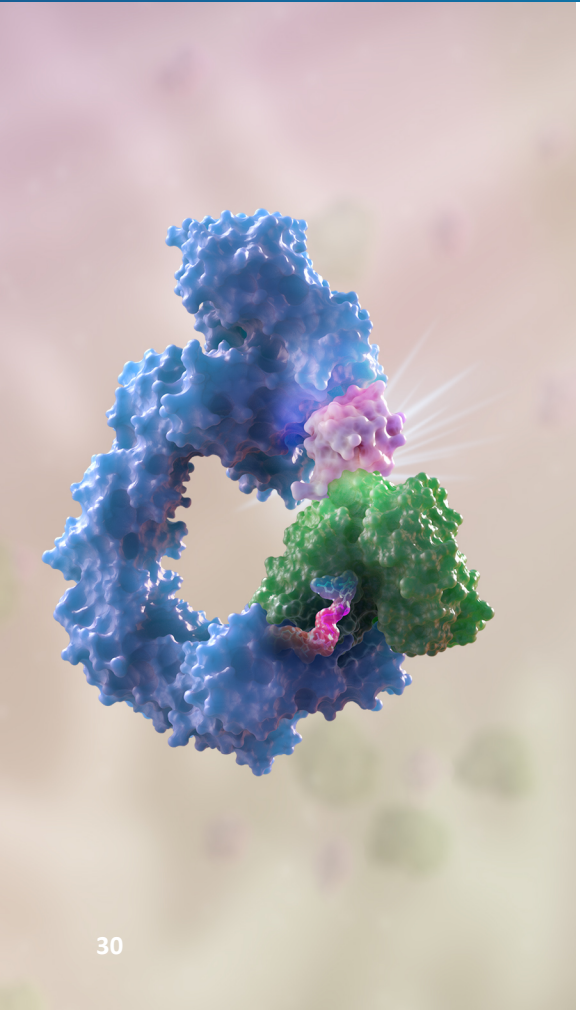
Future Targets and Platform Expansion



“Undruggable” Targets

- The ~80% of proteins not addressable by small-molecule inhibition may be degradable by PROTAC™ protein degraders

Platform Expansion

- Identifying and leveraging tissue and disease-specific E3 ligases
- Enhanced prediction of degradation selectivity

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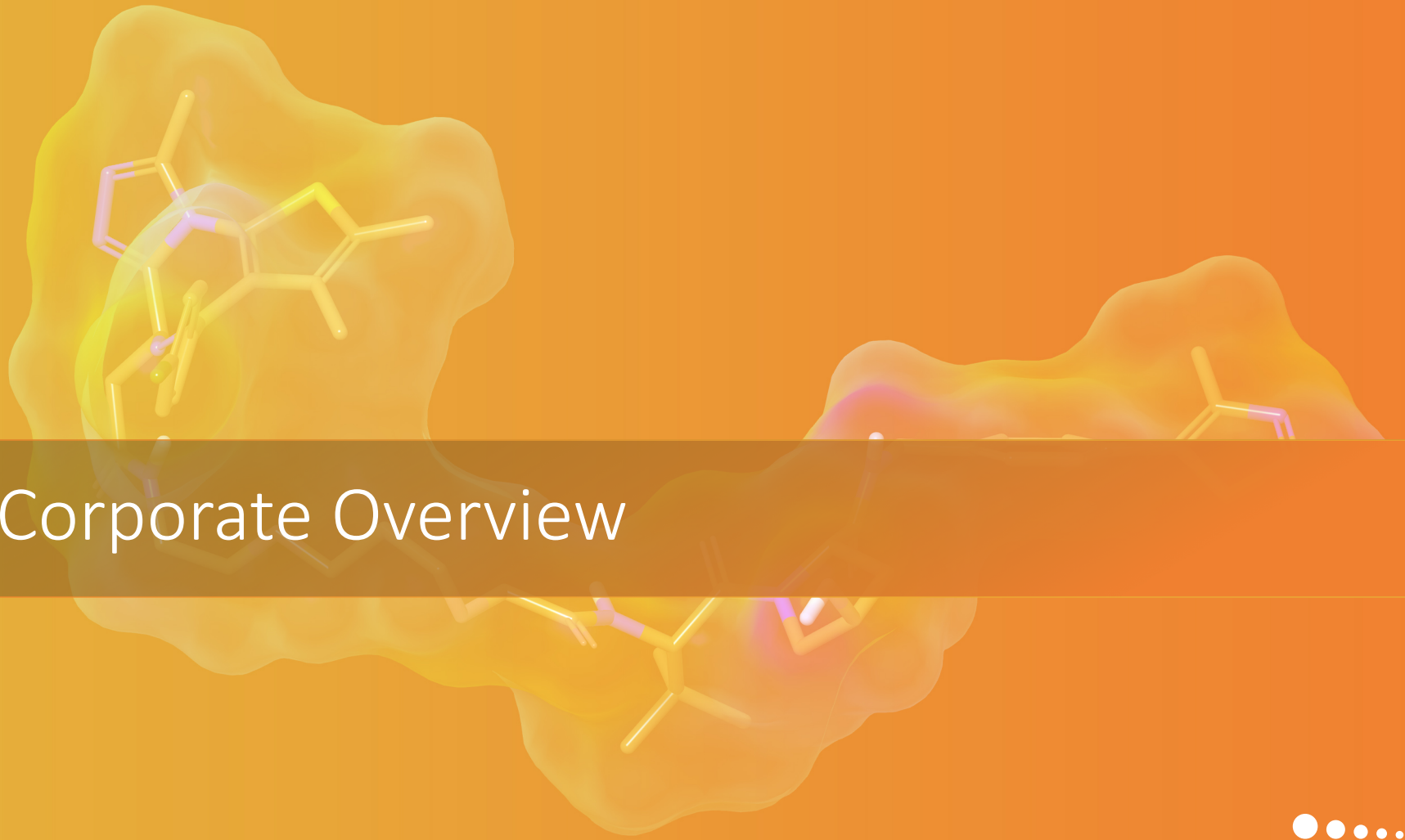

Corporate Overview

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Financial Snapshot

$114 Million

Net Proceeds from IPO (closed October 2018)[1]

~$90 Million

Cash, cash equivalents, and marketable securities as of September 30, 2018

~31 Million

Common shares outstanding post-IPO

Analyst Coverage

Citibank, Goldman Sachs, Piper Jaffray[2]

1 Net of underwriter fees and discounts

2 The foregoing list includes the names of all brokerage firms known by the company as of 1/4/19 to have analysts covering the company. This list may not be complete and is subject to change as firms add or delete coverage. Please note that any opinions, estimates or forecasts regarding the company made by these analysts are theirs alone and may not represent the opinions, estimates or forecasts of the company.

ARVINAS

Seasoned Leadership with Expertise in Advancing Novel Technologies

Leadership Team

John G. Houston, Ph.D.
President & CEO
Bristol-Myers Squibb · gsk

Sean Cassidy, C.P.A., M.B.A.
CFO
CuraGen Corporation · Deloitte.

Andy Crew, Ph.D.
SVP Chemistry
astellas · Tularik

Ian Taylor, Ph.D.
SVP Biology
Pfizer · Bayer

Angela Cacace, Ph.D.
VP Neuro and Platform Biology
Fulcrum Therapeutics · Bristol-Myers Squibb

John A. Grosso, Ph.D.
VP Chemistry, Mfg. & Controls
Bristol-Myers Squibb · vitae Pharmaceuticals

Marcia Dougan Moore, M.P.H.
VP Development Operations
ALEXION · Bristol-Myers Squibb

Randy Teel, Ph.D.
VP Corporate Development
ALEXION · McKinsey&Company

Steve Weiss
VP Human Resources
ALEXION · GE

Matthew Batters, J.D.
ED Bus. Dev., Trans. & Counsel
ALEXION · Skadden

Board of Directors

Timothy Shannon, M.D. *Chairman* — Canaan
John G. Houston, Ph.D. — ARVINAS
Ted Kennedy, Jr., J.D. — EPSTEIN BECKER GREEN
Jakob Loven, Ph.D. — nextechinvest
Brad Margus — cerevance
Briggs Morrison, M.D. — Syndax
Kush M. Parmar, M.D., Ph.D. — 5AM VENTURES
Liam Ratcliffe, M.D., Ph.D. — NEW LEAF VENTURE PARTNERS

ARVINAS

Strategic Partnerships are Validating our PROTAC™ Protein Degrader Technology

Genentech
A Member of the Roche Group

September 2015

(expanded in November 2017)

- Target discovery deal
- Upfront, development, and commercial milestone aggregate payments in excess of $650M
- Tiered royalties

Pfizer

December 2017

- Target discovery deal
- Upfront, development, and commercial milestone aggregate payments up to $830M
- Tiered royalties

Aggregate payments of up to $1.4B in potential milestones

ARVINAS

The PROTAC™ Company: Leading in Protein Degradation Therapeutics

- Expecting to be the first PROTAC degrader in the clinic
- Leading platform and product IP, driven by nearly two decades of PROTAC protein degradation research
- First to publish data on orally available PROTAC protein degraders
- Leadership team with experience getting drugs to market
- Strong financial position to advance the platform and product candidates

ARVINAS

For more information

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Business Development

bd@arvinas.com

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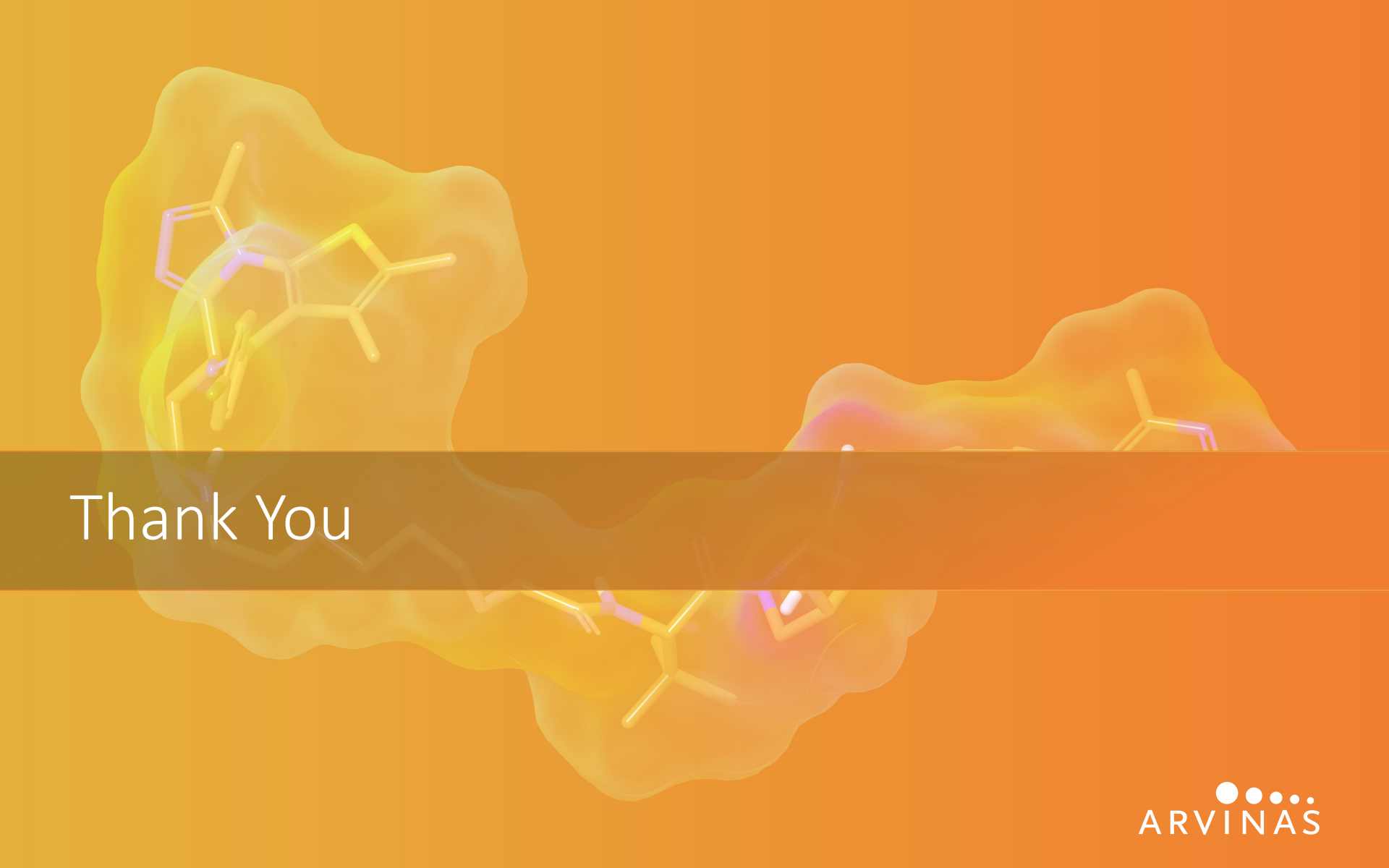

Thank You

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