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The PROTAC® Company

Moving PROTAC® Protein Degraders from the Laboratory to the Clinic

IAN TAYLOR, PHD

2nd Annual Targeted Protein Degradation Summit

OCTOBER 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 clinical trials and data from those 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 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: whether we will be able to successfully conduct Phase 1 clinical trials for ARV-110 and ARV-471, 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 on 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 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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Arvinas: Company Overview

HISTORY

- Founded July 2013; New Haven, CT
- ~125 employees
- September 2018 IPO

PIPELINE

- **ARV-110** - Metastatic castration-resistant prostate cancer; **Phase 1 initiated 1Q19**, and received "Fast Track" designation from FDA in May 2019
- **ARV-471** - Estrogen receptor-positive / HER2-negative locally advanced or metastatic breast cancer; **Phase 1 initiated 3Q19**
- Brain-penetrant PROTAC® programs targeting tauopathies and α-synucleinopathies

COLLABORATORS

- Exclusive worldwide license to PROTAC® degrader technology with Yale University
- Strategic, discovery-stage partnerships with Pfizer, Genentech and Bayer
- Partnerships across broad set of therapeutic areas and a JV for agricultural applications

OUTSTANDING TEAM

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

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High Potential PROTAC® Pipeline, Focused on Cancer and Neurology[1]

1 Pipeline as of October 23, 2019

2 PSP, progressive supranuclear palsy

3 MSA, multiple systems atrophy

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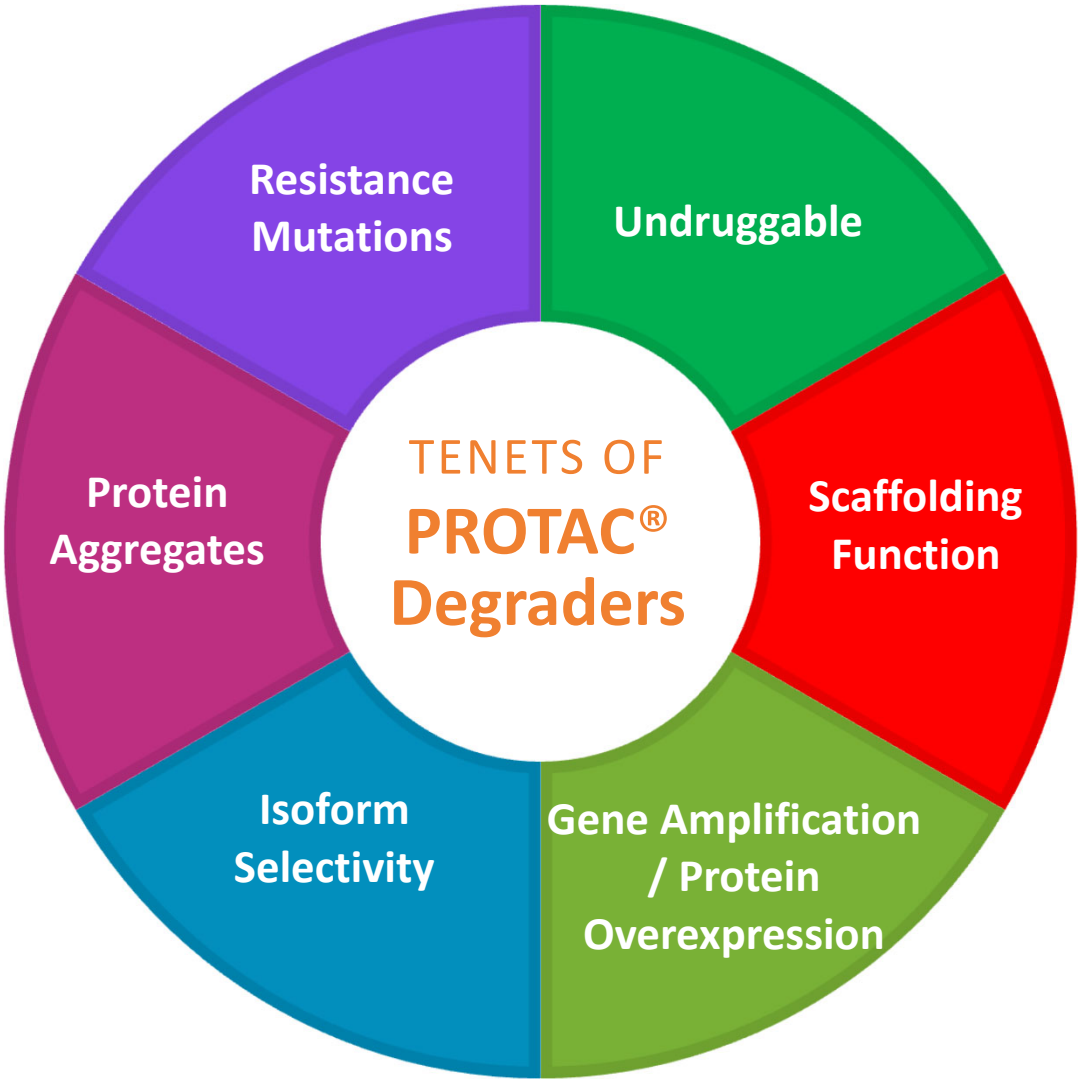
The "Tenets of PROTAC® Degraders"

Areas where the PROTAC® mechanism of action may be particularly well-suited



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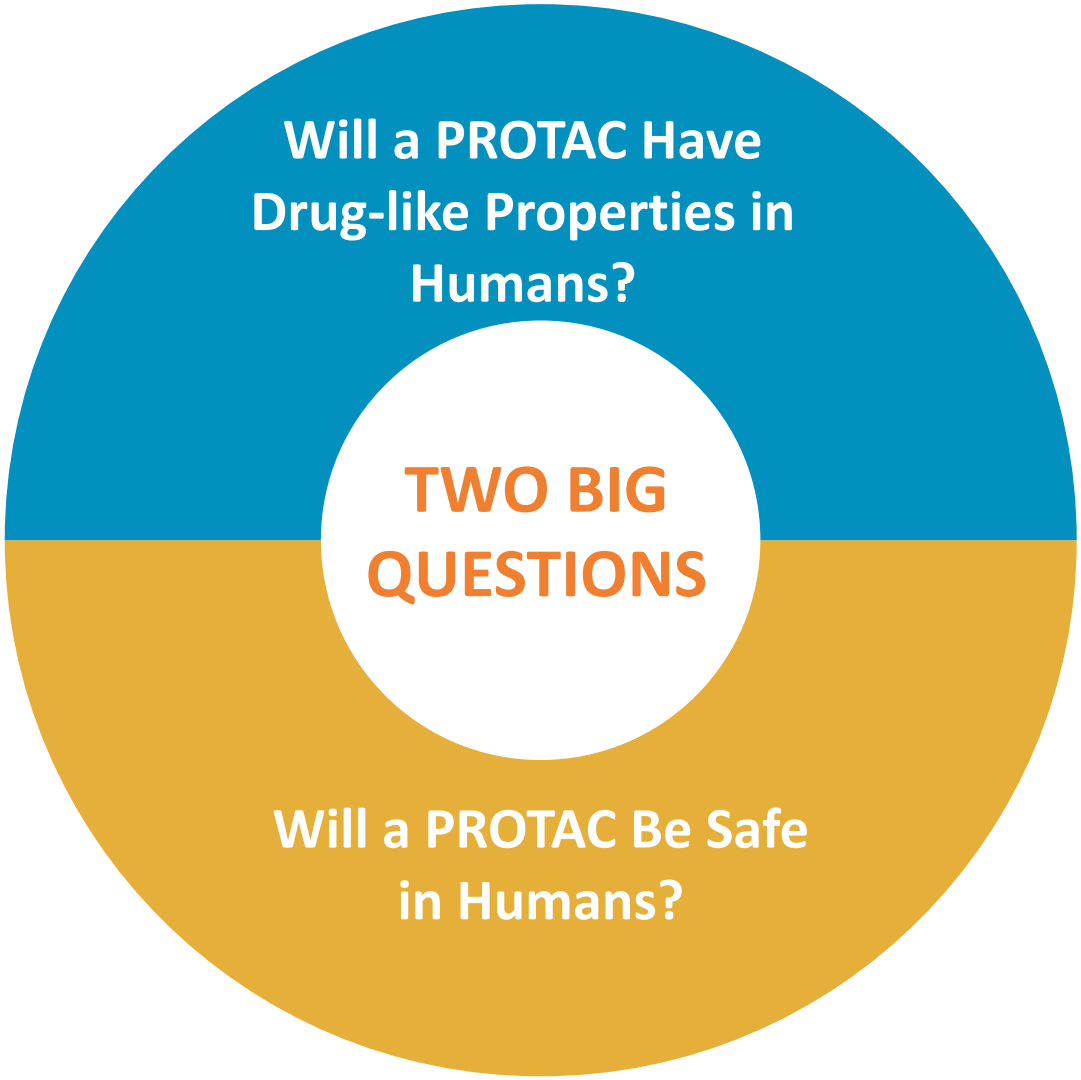
Two Big Questions of the PROTAC® Platform As It Moves From Laboratory to the Clinic



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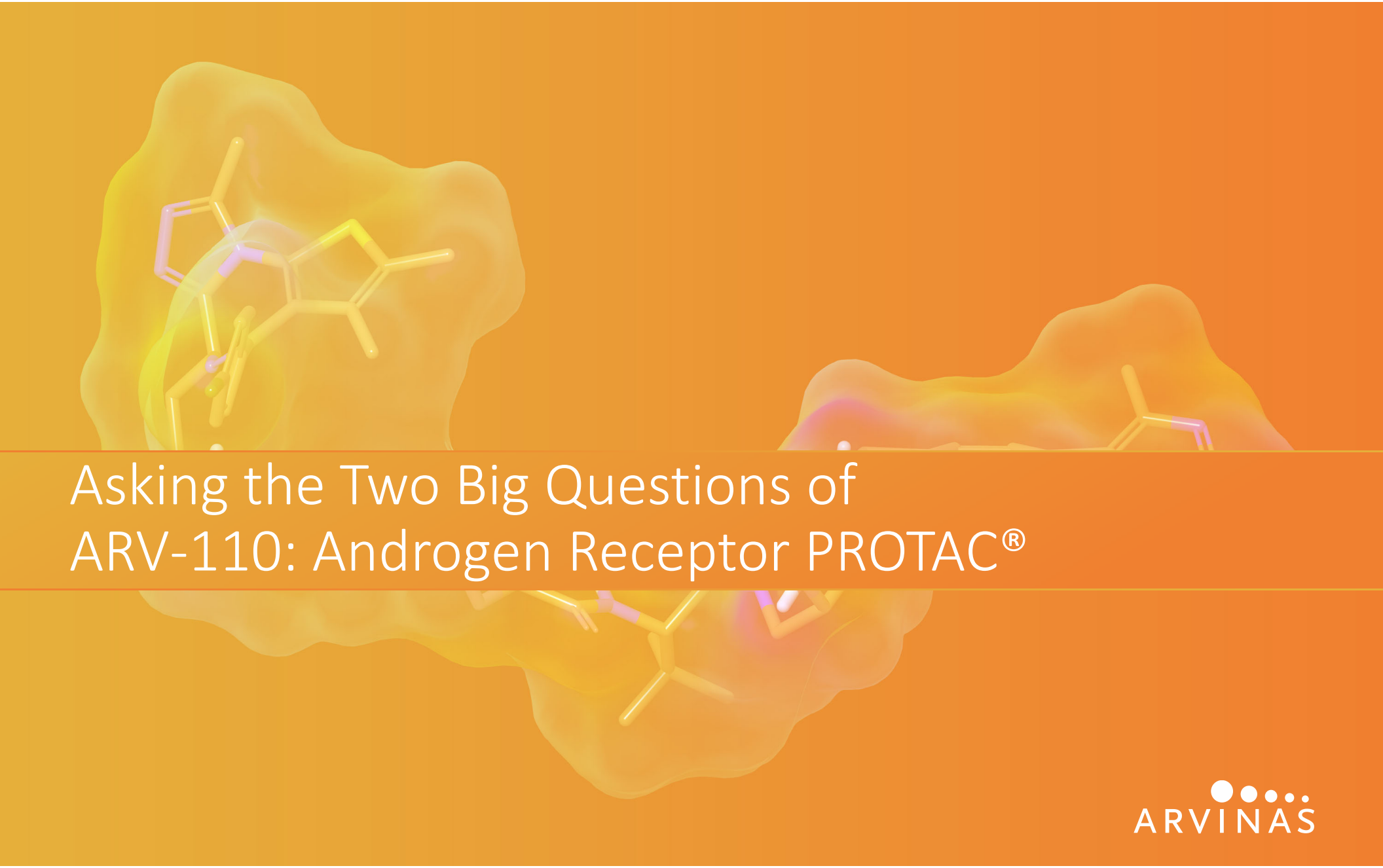

Asking the Two Big Questions of ARV-110: Androgen Receptor PROTAC®

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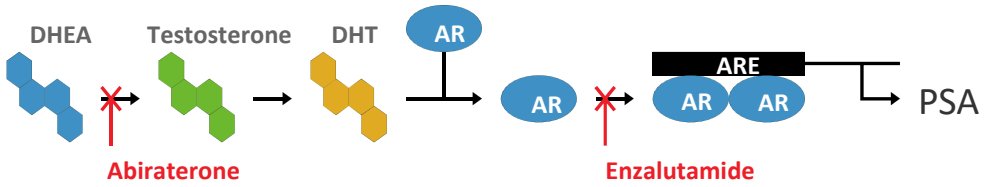
ARV-110: AR Degrader for Men with Metastatic Castration-Resistant Prostate Cancer (mCRPC)[1]

Androgen Receptor (AR) Activity Drives Prostate Cancer

- Current agents work by decreasing androgen levels (abiraterone) or blocking androgen binding to AR (enzalutamide)
- **15-25%** of patients never respond to abiraterone or enzalutamide (**intrinsic resistance**)
- **Resistance mechanisms** to abiraterone and enzalutamide include:
  - **AR gene amplification** (40-60% of patients)
  - **AR gene enhancer amplification** (>70% of patients)
  - **AR point mutations** (~15% of patients)
  - **Intra-tumoral androgen production**

PROTAC® Degrader ARV-110

- Highly selective degrader of AR; DC_{50} = 1 nM
- In preclinical models, overcomes resistance mechanisms to enzalutamide and abiraterone
- Not brain penetrant
- First-in-class AR degrader being tested in men with metastatic castration-resistant prostate cancer who have progressed on standards of care (enzalutamide, abiraterone)
- **Phase 1 clinical trial initiated 1Q19**
- **Received FDA "Fast Track" designation in May 2019**



1. According to the American Cancer Society, prostate cancer is the second leading cause of cancer death in men in the U.S. (~174k diagnosed/yr1); 35-45k new incidences of mCRPC in the U.S. each year

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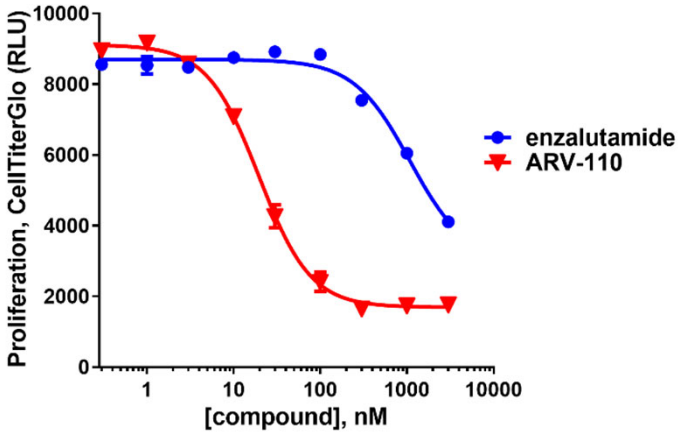
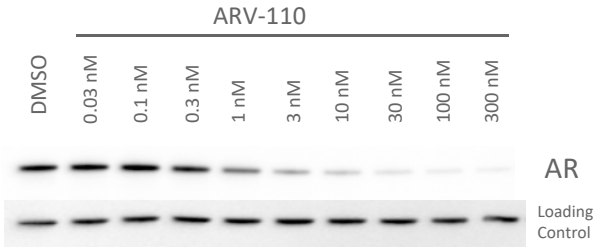
ARV-110 Potently and Rapidly Degrades AR and Inhibits Proliferation Better than Enzalutamide in Preclinical Models

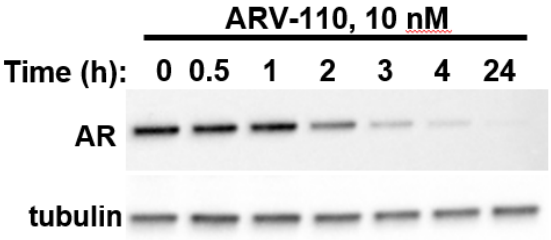
In vitro studies

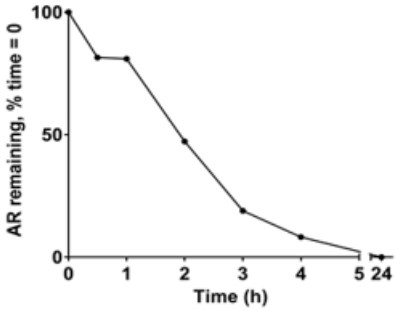
- ARV-110 degraded 95% to 98% of AR in multiple cell lines typically used in prostate cancer research, including VCaP cells
  - DC_{50} in VCaP = 1 nM
  - Near-maximal degradation within 4 hours of administration
  - ARV-110 inhibits VCaP proliferation ~60x more potently than enzalutamide



VCaP Cells:







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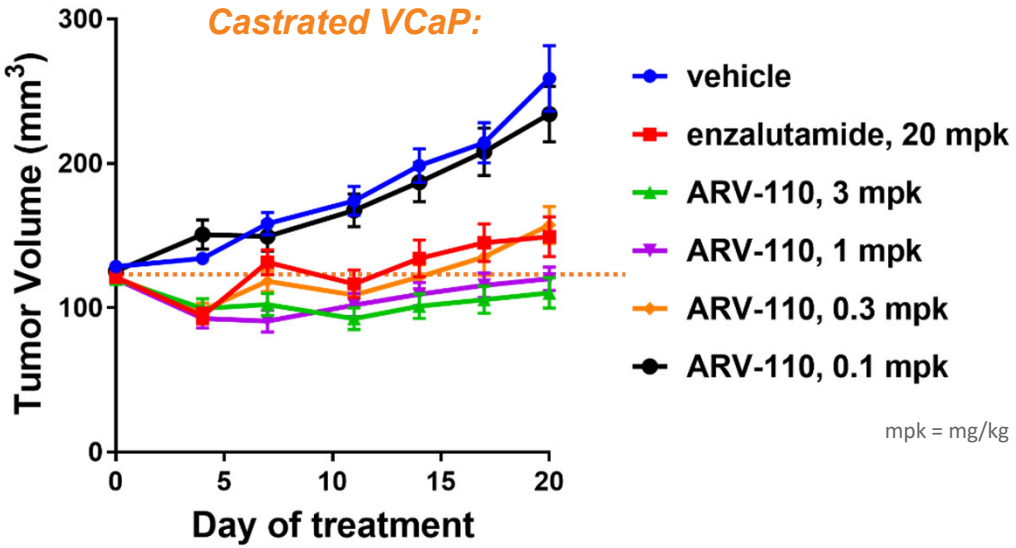
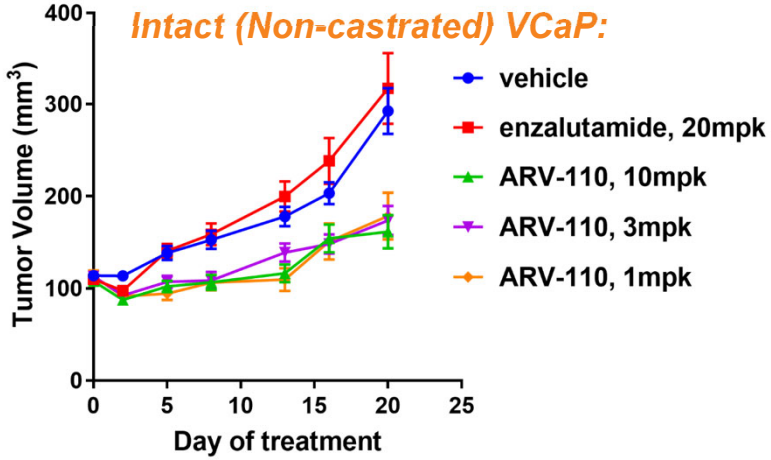
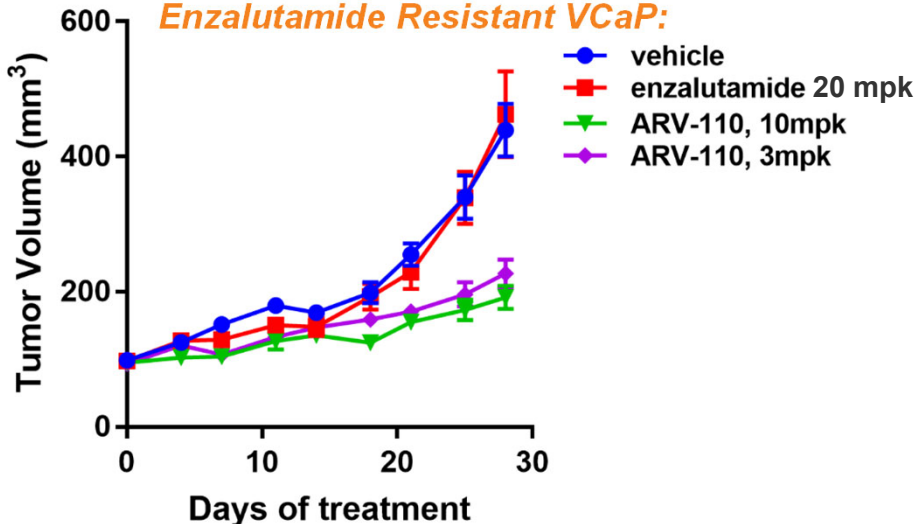
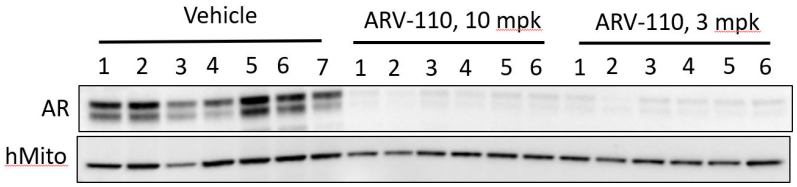
ARV-110 Inhibits AR-Dependent Tumor Growth in Xenograft Models with Oral, Daily Dosing



mpk = mg/kg







Dose po, qd	Mean AUC_{0-24} ng*hr/ml†	Mean C_{max} ng/ml‡
1 mpk	3628	224
3 mpk	8106	507

Values represent total drug concentrations

† AUC_{0-24} or Area Under the Curve is a measurement of total exposure from 0-24 hours after last dose

‡ C_{max} is a measurement of peak concentration

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ARV-110: GLP Toxicology Studies Supported Moving into Clinical Development

Design:

Animals dosed daily, orally for 28 days; 14-day recovery for high-dose animals

Dog Study:

- 3, 10, or 30 mpk;
- 30 mpk exceeded MTD;

  NOAEL = 10 mpk
- **DLT: Gastrointestinal alteration** (e.g., loose/discolored stools) at all dose levels, including with vehicle alone

  Dog is most sensitive species
- Reversible liver function enzyme elevation in some mid- and high-dose animals; considered non-adverse
- **Decreased prostate weights** in all male animals; believed attributable to ARV-110 pharmacology

Rat Study:

- Male animals, 20, 60, or 120 mpk per day; Female animals, 20, 40, or 80 mpk per day
- Overall, ARV-110 was well tolerated at all doses

  Exception: 80 mpk in females; decreased body weight and food consumption; **NOAEL = 40 mpk**

  All findings in male high-dose animals (liver hypertrophy, femur physis thickening) fully reversible; **NOAEL = 120 mpk**
- **Decreased prostate weights** noted in all male animals; believed attributable to ARV-110 pharmacology

MTD, maximum tolerated dose. NOAEL, no observed adverse effect level; mpk = mg/kg

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ARV-110: Phase 1 Study

First patient dosed March 2019

Design:

- "3 + 3" dose escalation; starting dose = 35 mg, orally, once daily (po, qd) with food
- Dose increases dependent on toxicities: range 25% (if 1 DLT in 6 pts) to 100% (≤Grade 1 Adverse Events)

Key Entry Criteria:

- Men with mCRPC
- At least two prior systemic therapies, at least one of which was abiraterone or enzalutamide
- Disease progression on most recent therapy
  - Rising PSA or 2+ new lesions upon bone scan

Key Objectives:

- Maximum Tolerated Dose/ Recommended Phase 2 Dose/ Safety
- Pharmacokinetics
- Anti-Tumor Activity (PSA, RECIST)
- Biomarkers

Biomarkers:

- AR degradation in circulating tumor cells (CTCs) and pre- vs post-treatment biopsies (when available)
- AR (and other) gene mutations, amplifications in circulating tumor DNA (ctDNA)
- AR-V7 in CTCs

PSA, Prostate specific antigen. RECIST, Response evaluation criteria in solid tumors

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ARV-110 Phase 1 Dose Escalation— Pharmacokinetics is Dose Proportional

Preclinical Efficacious Exposure Range

Dose (po, qd)	AUC_{0-24} (ng*hr/ml)	C_{max} (ng/ml)
1 mpk	3628	224
3 mpk	8106	507

Phase 1 Data

Dose po, qd	Day 1 AUC_{0-24} (ng*h/mL) Mean	Day 1 C_{max} (ng/ml) Mean	Day 15 AUC_{0-24} (ng*h/mL) Mean[a]	Day 15 C_{max} (ng/ml) Mean
35 mg	160.5	11.1	1701	83
70 mg	300	19.6	2538	141
140 mg	865	54	5023	353

[a] Day 15 AUCs calculated using imputed 24 hour values

- Accumulation occurs between Day 1 and Day 15

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ARV-110 Phase 1 Dose Escalation— Pharmacokinetics is Dose Proportional

Preclinical Efficacious Exposure Range

Dose (po, qd)	AUC_{0-24} (ng*hr/ml)	C_{max} (ng/ml)
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Phase 1 Data

Dose po, qd	Day 1 AUC_{0-24} (ng*h/mL) Mean	Day 1 C_{max} (ng/ml) Mean	Day 15 AUC_{0-24} (ng*h/mL) Mean[a]	Day 15 C_{max} (ng/ml) Mean
35 mg	160.5	11.1	1701	83
70 mg	300	19.6	2538	141
140 mg	865	54	**5023**	**353**

[a] Day 15 AUCs calculated using imputed 24 hour values

- Accumulation occurs between Day 1 and Day 15
- Exposure at 140 mg has entered the preclinical efficacious range associated with tumor growth inhibition

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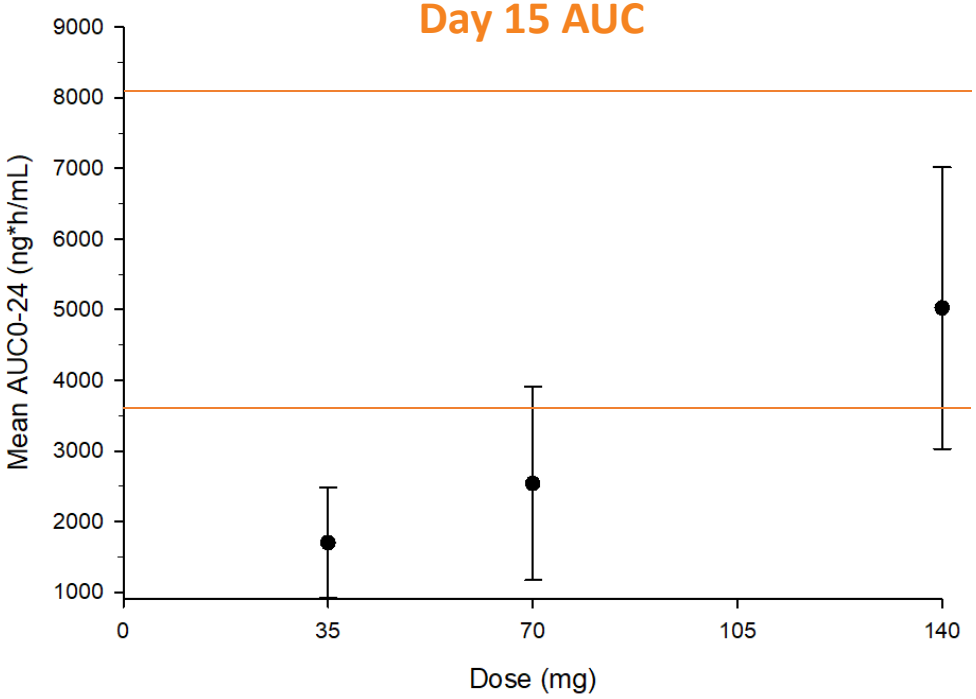
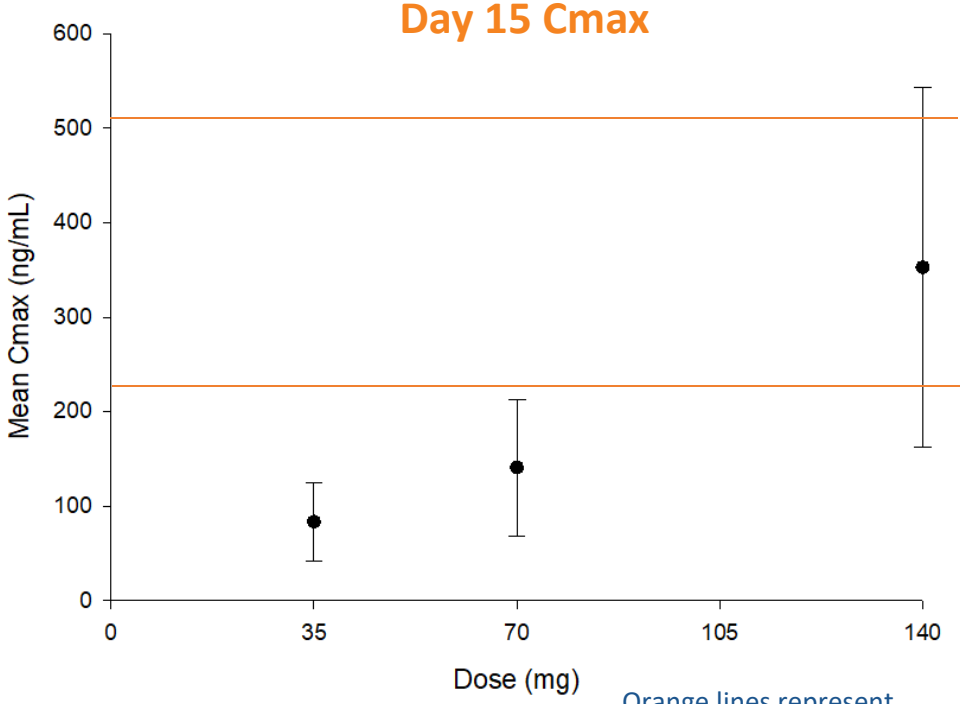
ARV-110 Phase 1 Dose Escalation— Pharmacokinetics is Dose Proportional

Day 15 AUC



Day 15 Cmax



Dose po, qd	Day 15 AUC_{0-24} (ng*h/mL) Mean[a]	Day 15 C_{max} (ng/ml) Mean
35 mg	1701	83
70 mg	2538	141
140 mg	5023	353

Orange lines represent AUC and C_{max} associated with tumor growth inhibition at 1 mpk and 3 mpk in preclinical models

[a] Day 15 AUCs calculated using imputed 24 hour values

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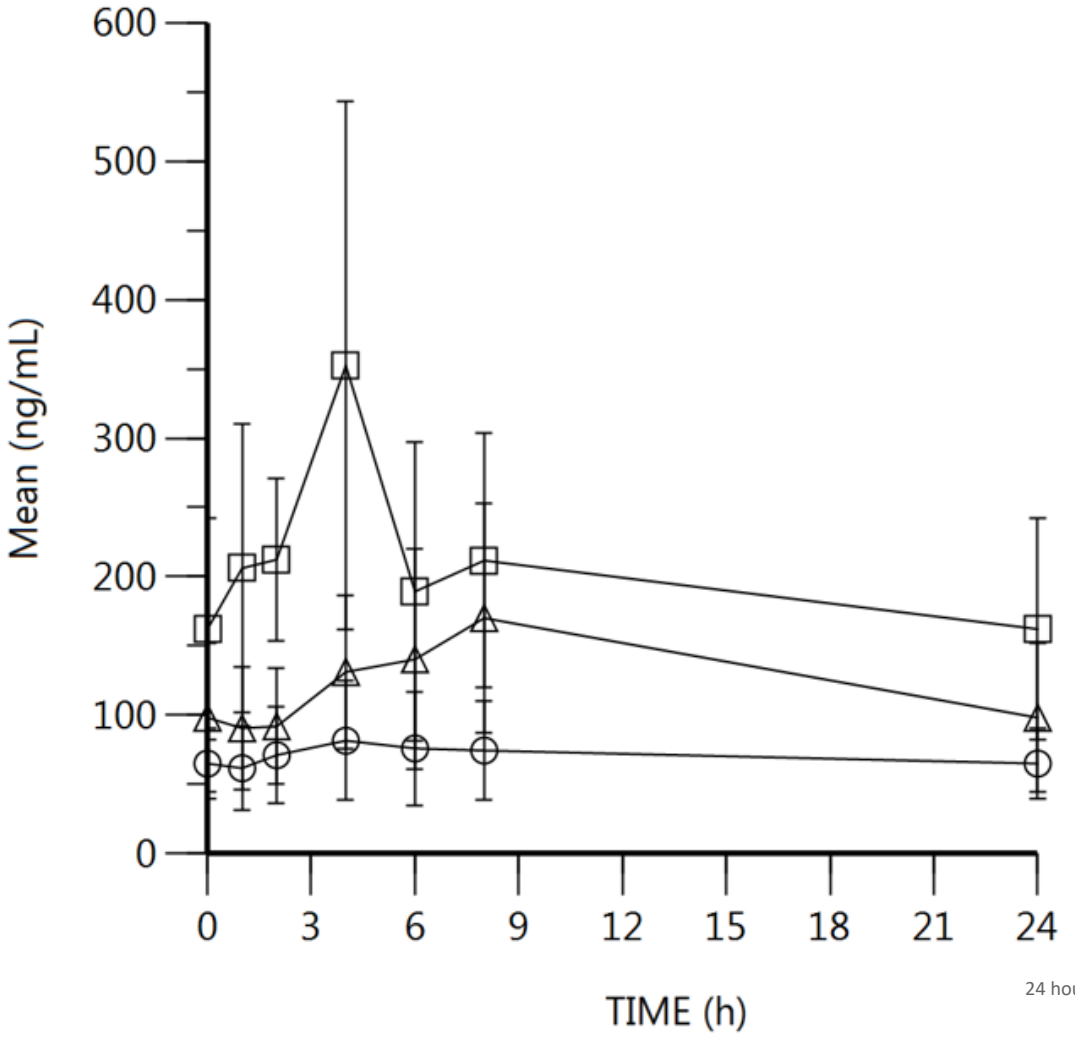
ARV-110 Phase 1 Dose Escalation—Day 15 Pharmacokinetics



$T_{max†}$ = 4 - 8 hours

$t_{1/2‡}$ = estimated 3 - 7 days

† Time of to reach maximum concentration (Cmax)

‡ Effective half-life: rate of accumulation or elimination of a pharmacologic substance

Cohort 3 (140 mg)

Cohort 2 (70 mg)

Cohort 1 (35 mg)

24 hour values are imputed from time zero

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ARV-110 Phase 1 Dose Escalation Safety/Tolerability: Overall Favorable Profile Observed to Date

- Three cohorts through 28 day dose limiting toxicity evaluation period; fourth cohort enrolling

Dose Level[a]	N	Key Safety Findings
35 mg	3	• No Dose Limiting Toxicities (DLTs) • No Treatment Related Adverse Events (AEs)
70 mg	4	• No DLTs • No Grade 2/3/4 Treatment Related AEs
140 mg[b]	3[c]	• No DLTs • No Grade 2/3/4 Treatment Related AEs
280 mg	3	• TBD

[a] Orally, once daily

[b] Data not yet 100% source data verified

[c] Not including 1 non-evaluable patient (discontinued on day 1; patient's condition had worsened in the interval from screening to the morning of treatment initiation consistent with rapid progression of his cancer.)

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First-in-Human Androgen Receptor PROTAC®
ARV-110 Proceeding Through Dose Escalation

- 10 patients with mCRPC treated across three dose levels
- At doses thus far tested, ARV-110 demonstrating an acceptable safety profile
- Pharmacokinetics show dose-proportional increase in exposure
- Dose escalation continues into higher dose level(s)
- Topline data including PSA and RECIST responses from completed dose escalation – and pharmacodynamic/molecular data--planned in 1st half 2020 at major medical conference

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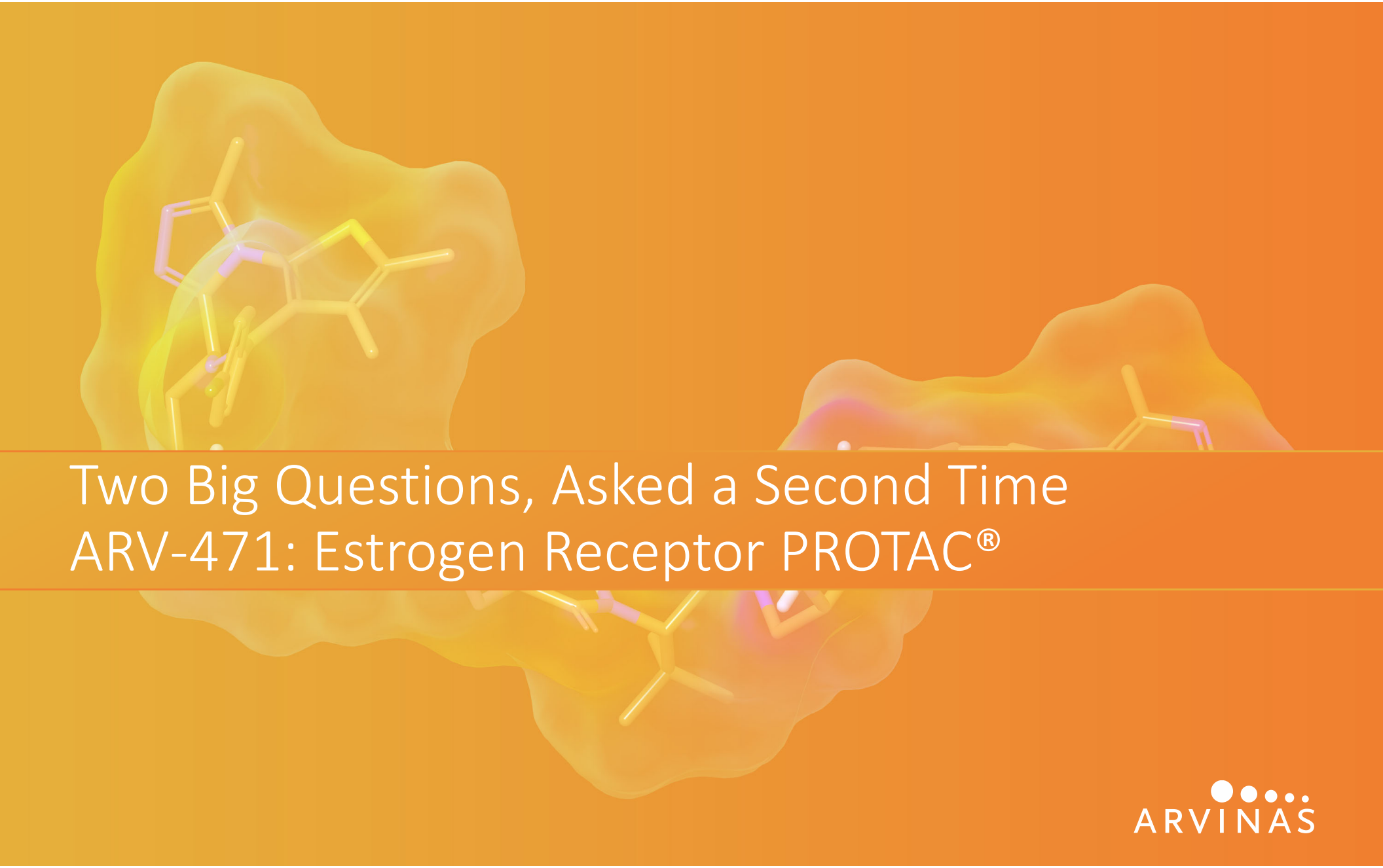

Two Big Questions, Asked a Second Time
ARV-471: Estrogen Receptor PROTAC®

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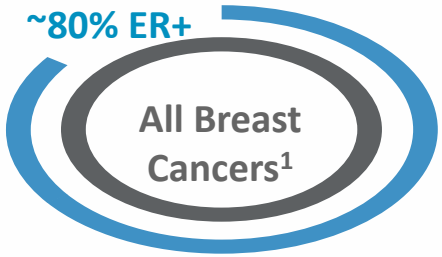
ARV-471: ER Degrader for Patients with Locally Advanced or Metastatic Breast Cancer

Breast cancer is the second most common cancer in women[1]

- ~268,000 women are expected to be diagnosed with invasive breast cancer in the US in 2019[1]
- Metastatic breast cancer accounts for ~6% of newly diagnosed cases[2]
- 80% of newly diagnosed breast cancers are estrogen receptor (ER) positive[3]
- Fulvestrant has validated the relevance of ER degradation in breast cancer
- After 6 months of fulvestrant treatment, up to 50% of ER baseline levels remain[4]

PROTAC® Degrader ARV-471

- ARV-471 is a potent degrader (DC_{50} = 1.8 nM) of the estrogen receptor, which is in development for the treatment of patients with ER+ locally advanced or metastatic breast cancer
- **Phase 1 clinical trial initiated 3Q2019**
- After Phase 1 dose escalation, a Phase 1b trial in combination with CDK4/6 inhibitor is planned



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

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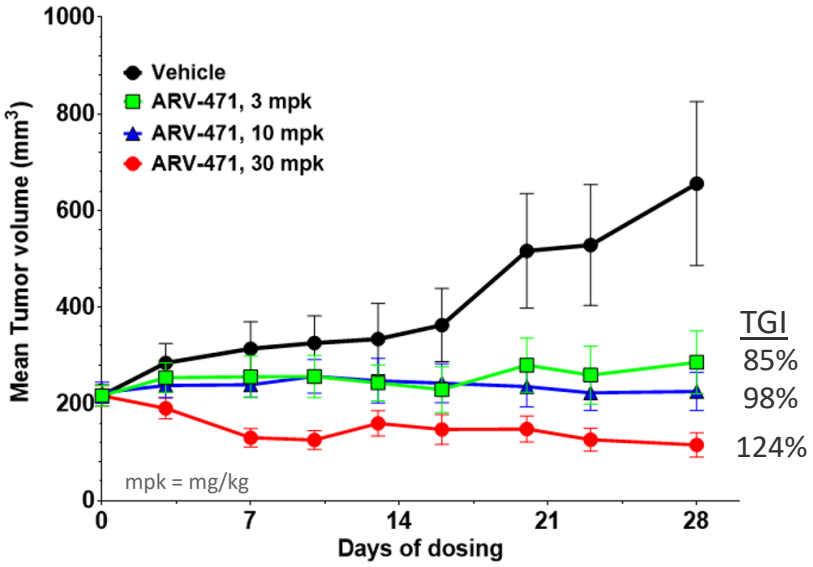
Orally Dosed ARV-471 Shrinks Tumors and Robustly Degrades ER in MCF7 Xenografts

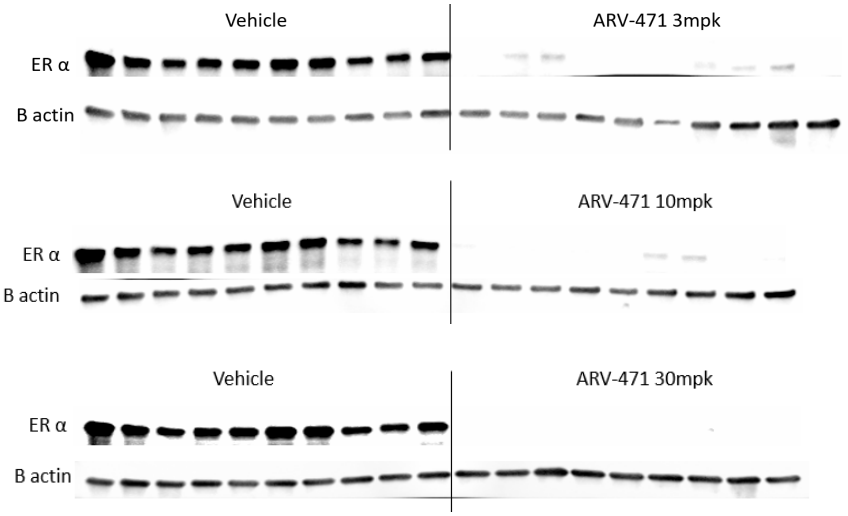


Dose po, qd	Mean AUC_{0-24} ng*hr/ml	Mean C_{max} ng/ml
3 mpk	658	84
10 mpk	2538	312
30 mpk[a]	5717	962

[a] Single dose

Values represent total drug concentrations

WESTERN BLOT PD (18 hours post last dose)	% ER REDUCTION
3 mpk	95
10 mpk	97
30 mpk	94



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ARV-471: GLP Toxicology Studies Supported Moving into Clinical Development

Design:
Animals dosed once daily, orally, for 28 days; 28-day recovery period for high-dose animals.

Dog Study:

- Doses of 15, 45, or 90 mpk administered to all animals; **NOAEL = 90 mpk**

Rat Study:

- Doses of 3, 10, 30 or 100 mpk administered to all animals; **NOAEL = 100 mpk**

The studies have shown **no clinical signs of toxicity** following daily oral doses of ARV-471 up to 100 mg/kg/day in rats and 90 mg/kg/day in dogs, **nor effects on overall animal health and well-being**.

NOAEL, no observed adverse effect level

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ARV-471: Phase 1 Study

First patient dosed August 2019

Design:

- "3 + 3" dose escalation; starting dose = 30 mg orally, once daily (po, qd) with food
- Dose increases dependent on toxicities: range 25% (if 1 DLT in 6 pts) to 100% (≤Grade 1 Adverse Events)

Key Entry Criteria:

- ER+/HER2- advanced breast cancer
- At least two prior endocrine therapies in any setting, and a CDK4/6 inhibitor
- Up to three prior cytotoxic chemotherapy regimens

Key Objectives:

- Maximum Tolerated Dose/ Recommended Phase 2 Dose/Safety
- Pharmacokinetics
- Anti-tumor activity (RECIST, CBR)
- Biomarkers

Biomarkers:

- ER gene (ESR1) mutational status in ctDNA and/or tumor tissue
- ER, Progesterone Receptor and Ki-67 levels in pre- and post-treatment tumor biopsies in patients with accessible tumor tissue

CBR, clinical benefit rate

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ARV-471 Phase 1 Dose Escalation— First Cohort Pharmacokinetics

Preclinical Efficacious Exposure Range

Dose (po, qd)	Mean AUC_{0-24} (ng*hr/ml)	Mean C_{max} (ng/ml)
3 mpk	658	84
10 mpk	2538	312
30 mpk	5717	962

Phase 1 Data

Dose po, qd	Day 1 AUC_{TAU} (ng*h/mL) Mean	Day 1 C_{max} (ng/ml) Mean	Day 15 AUC_{TAU} (ng*h/mL) Mean[a]	Day 15 C_{max} (ng/ml) Mean
30 mg	1690	109	**4100**	**224**

[a] Day 15 AUCs calculated using imputed 24 hour values

- Accumulation occurs between Day 1 and Day 15
- Exposure at 30 mg has entered the preclinical efficacious range associated with tumor growth inhibition

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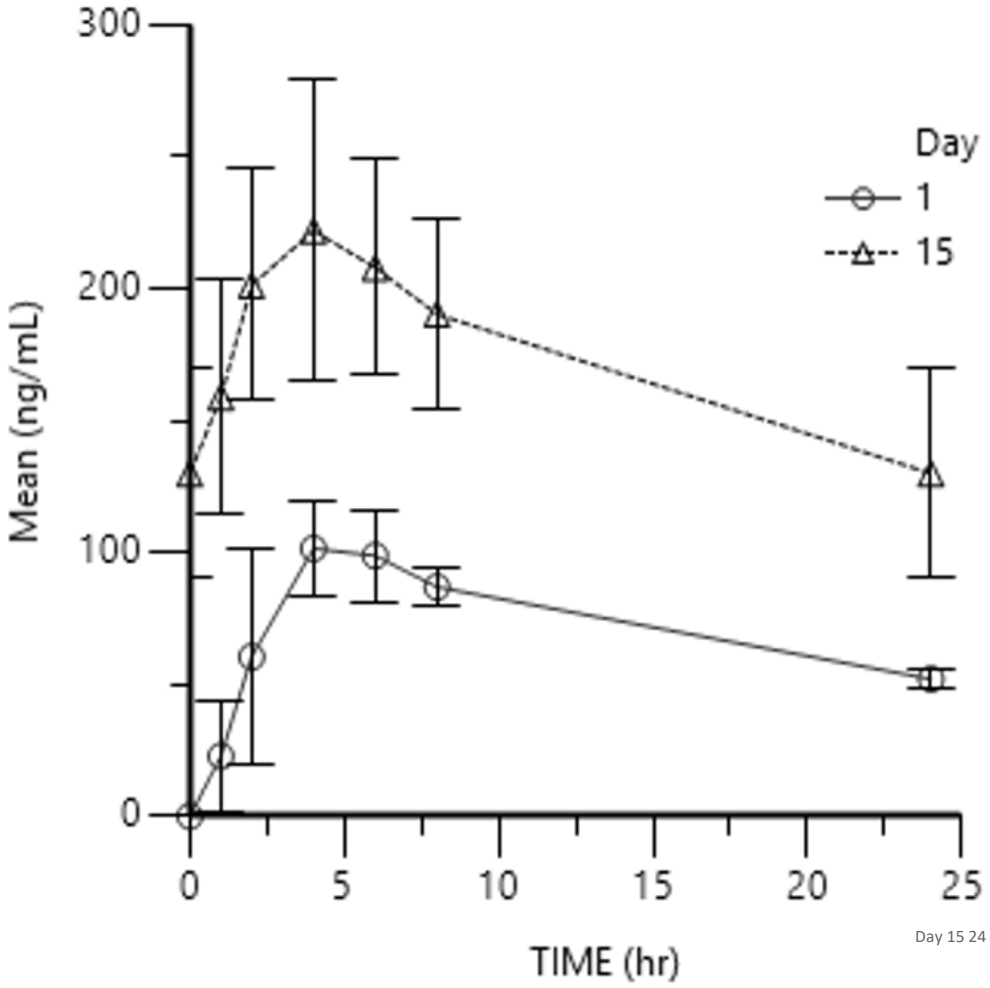
ARV-471 Phase 1 Dose Escalation—First Cohort Pharmacokinetics



Day 15 24 hour value is imputed from time zero

T_{max} = 4 hours

$t_{1/2}$ = estimated to be ~24 hours

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ARV-471 Phase 1 Dose Escalation—Safety/Tolerability

- First cohort through 28 day dose limiting toxicity evaluation period; second cohort enrolling

Dose Level[a]	N	Key Safety Findings
30 mg[b]	3	• No DLTs • No Treatment Related AEs
60 mg	3	• TBD

[a] Orally, once daily

[b] Data not yet 100% source verified

- Trial update planned in 2nd half 2020

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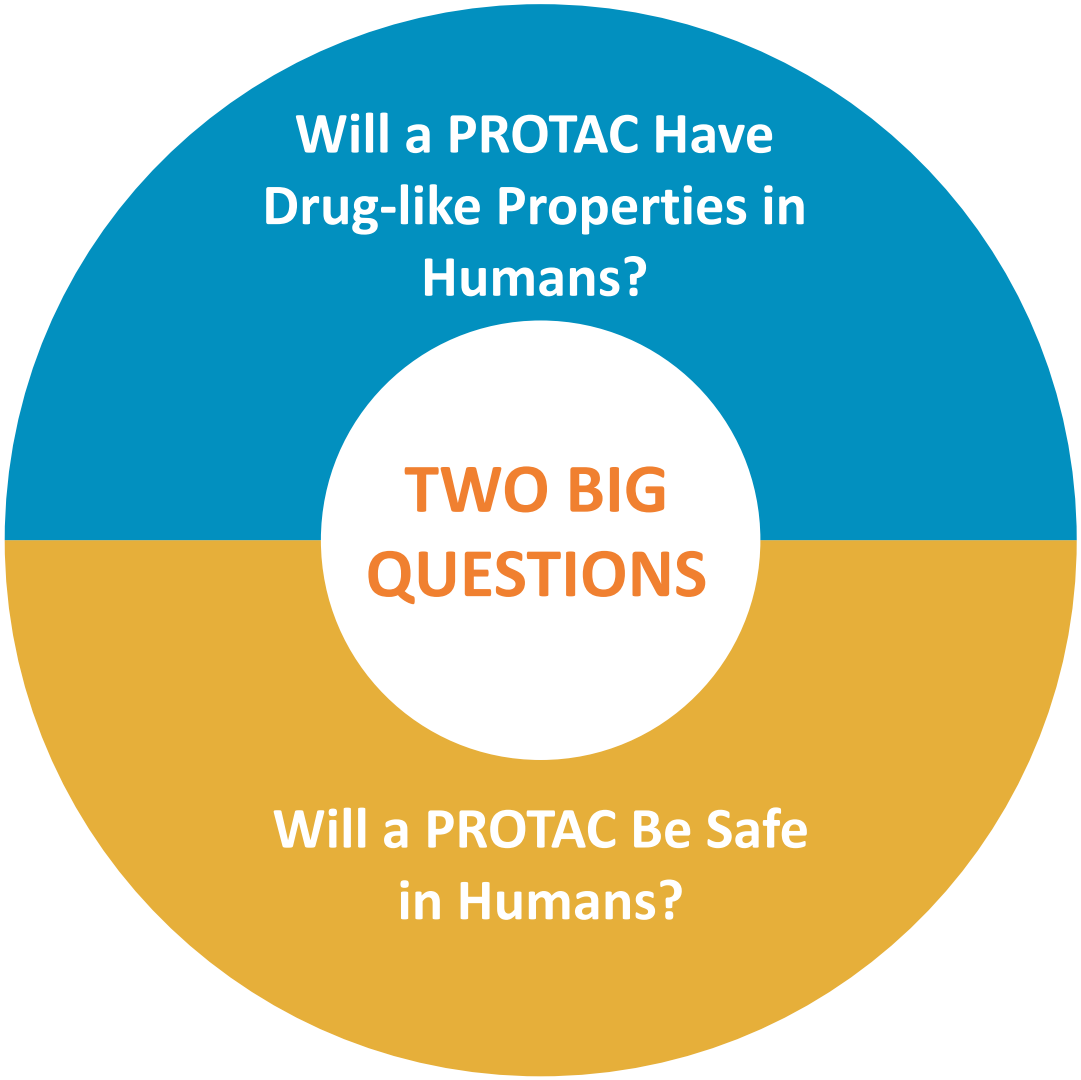
Two Big Questions of the PROTAC® Platform



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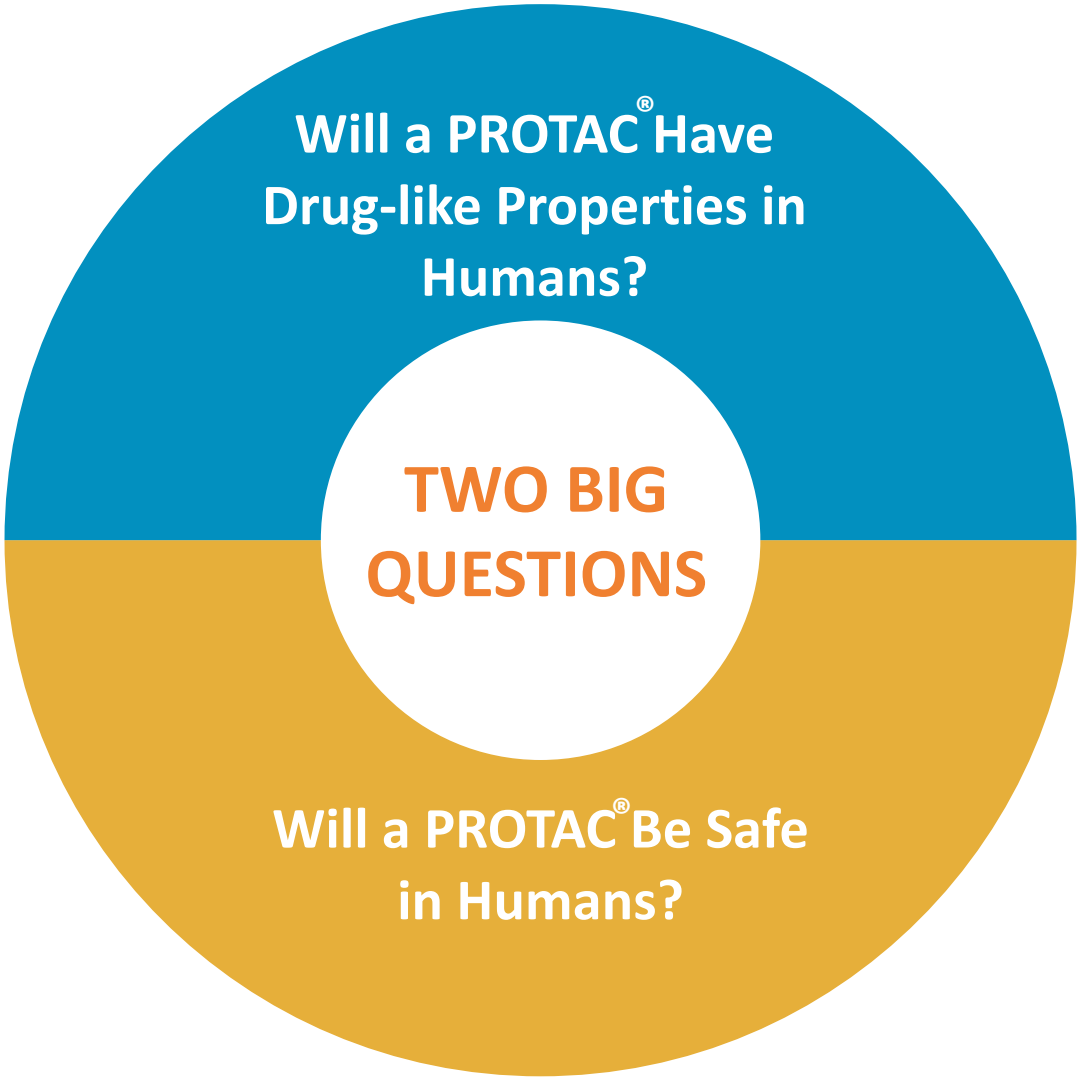
Two Big Questions of the PROTAC® Platform



Today:

Favorable Initial Clinical Data from PROTAC® Platform:

- Two Different PROTAC® Degraders
- Two Different Cancer Indications
- Two Different Patient Populations

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The Next Big Question:
Will a PROTAC® Demonstrate Efficacy in the Clinic?

Planned Milestone Updates

- 1H20: Topline Data on Completed ARV-110 Phase 1 Dose Escalation

- 2H20: ARV-471 Phase 1 Update

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The Patients, Their Families and Caregivers

Investigators and Clinical Trial Site Staff

Thank You

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And All Arvinas Colleagues!

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