AACR American Association for Cancer Research
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VIRTUAL #AACR21
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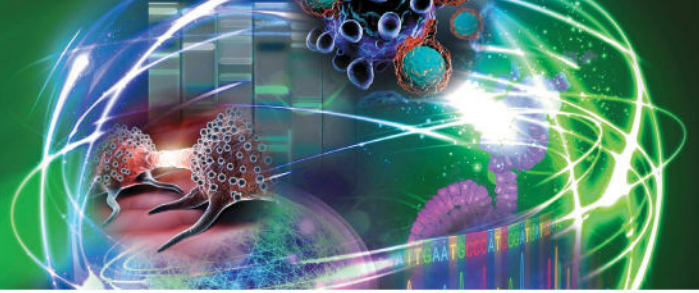

Discovery of ARV-110, a first in class androgen receptor degrading PROTAC® for the treatment of men with metastatic castration resistant prostate cancer

Lawrence B. Snyder, PhD
Executive Director Medicinal Chemistry
Arvinas Inc, New Haven, CT

Author Block: *Lawrence B. Snyder, Taavi K. Neklesa, Xin Chen, Hanqing Dong, Caterina Ferraro, Deborah A. Gordon, Jennifer Macaluso, Jennifer Pizzano, Jing Wang, Ryan R. Willard, Nicholas Vitale, Ron Peck, Marcia Dougan Moore, Craig M. Crews, John Houston, Andrew P. Crew, Ian Taylor.* Arvinas, New Haven, CT, Arvinas, New Haven, CT, Yale, New Haven, CT

Disclosure Information

Lawrence Snyder

I have the following financial relationships to disclose:

Stockholder in: Arvinas Inc

Employee of: Arvinas Inc

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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, 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, the potential benefits of our arrangements with Yale University, our collaborative partnerships, and the Bayer joint venture, 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 1/2 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, each party’s ability to perform its obligations under our collaborations and/or the Bayer joint venture, 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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PROTAC® protein degraders harness the UPS to induce the degradation of disease-causing proteins

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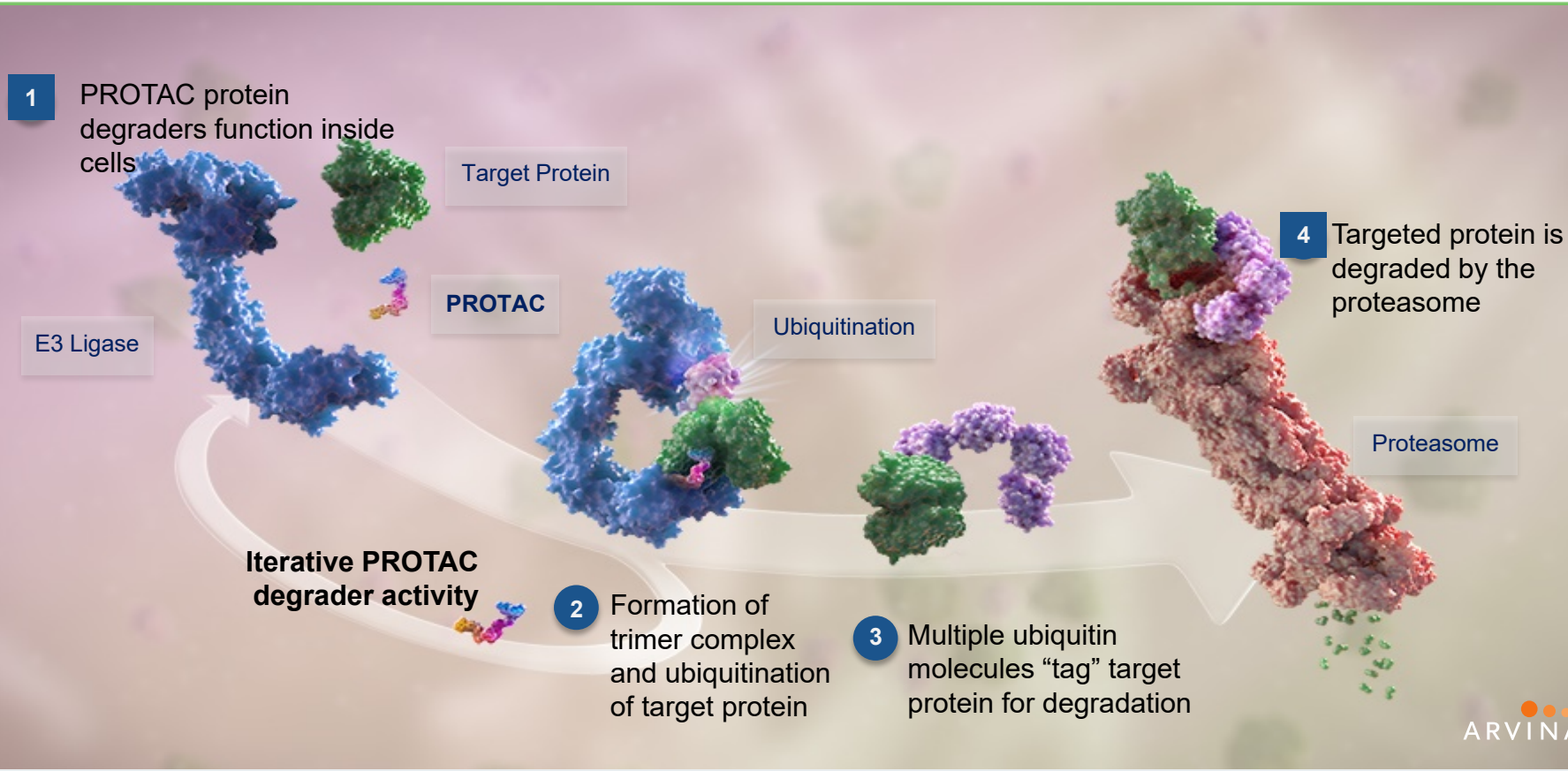

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PROTAC® protein degraders combine the advantages of gene-based medicines and small molecule inhibitors

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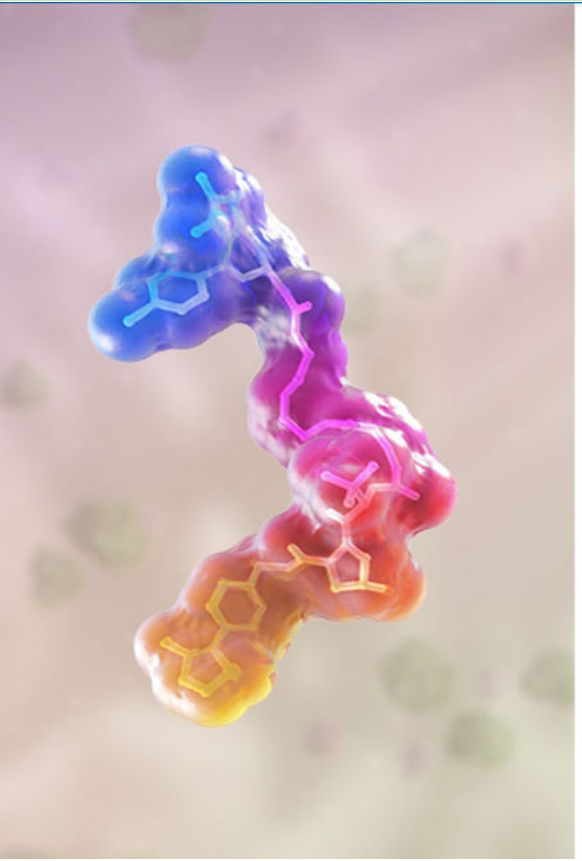
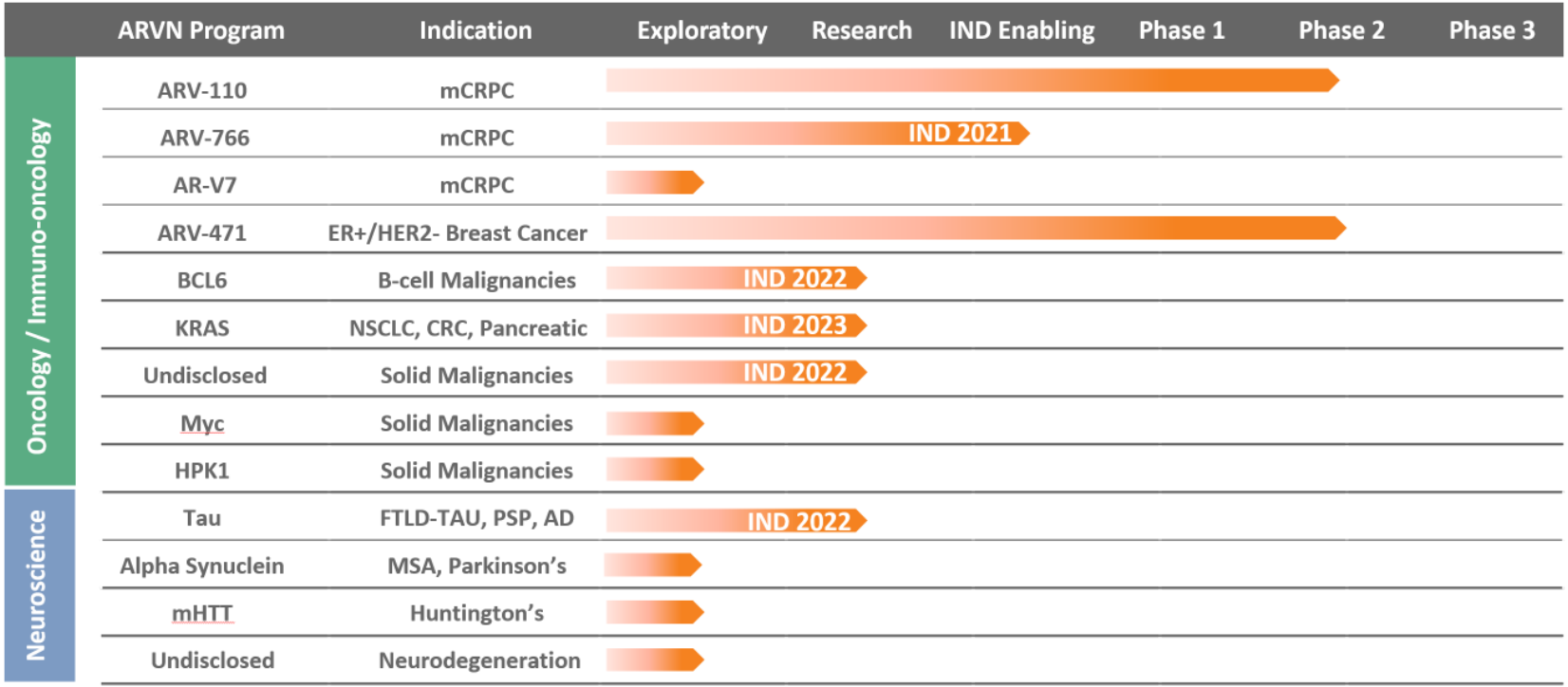


PROTAC protein degraders have distinct advantages over both small molecule inhibitors and gene-based medicines	PROTAC™ Protein Degraders	Small Molecule Inhibitors	Gene-Based Medicines
Eliminate pathogenic proteins	✓	✗	
Target scaffolding function	✓	✗	
Potential to treat "undruggable" proteins	✓	✗	
Iterative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

Arvinas' pipeline encompasses a range of validated and undruggable targets in oncology, I-O, and neuroscience



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

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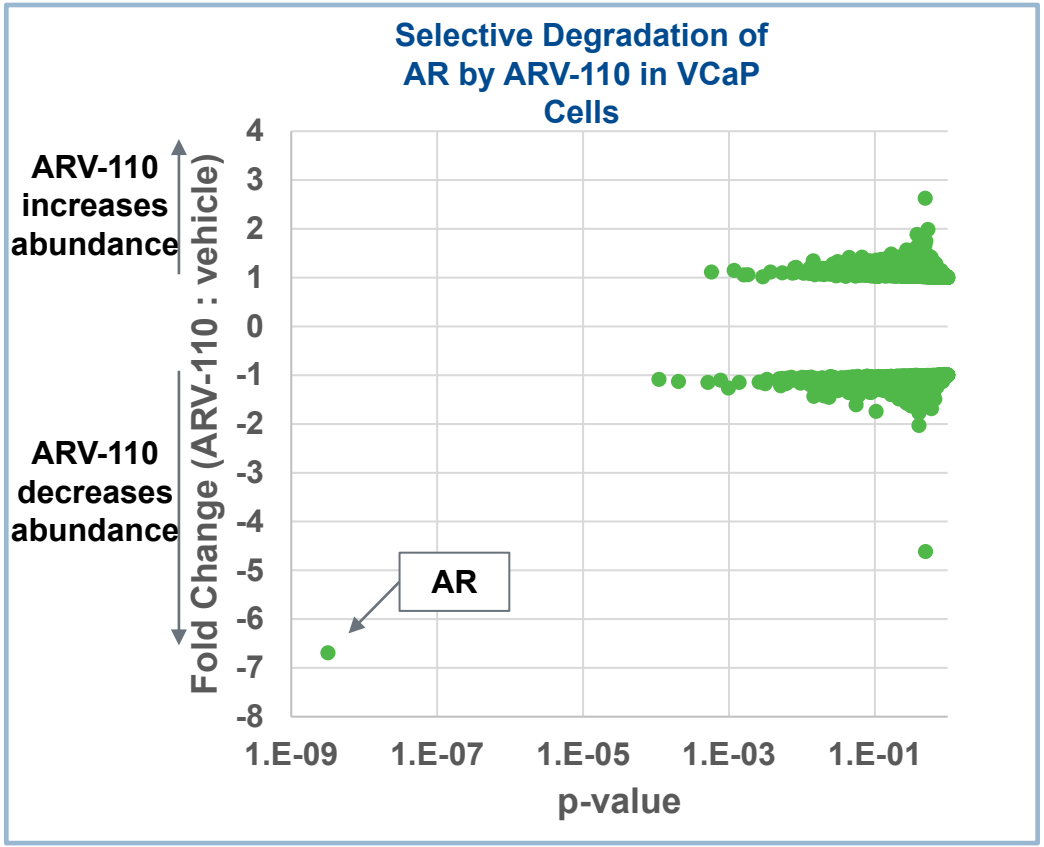
ARV-110 is a Potent and Selective Degrader of AR in Vcap Cells

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

ARV-110 Demonstrates Efficacy and Plasma PSA Reduction in an Enzalutamide-Insensitive PDX Model

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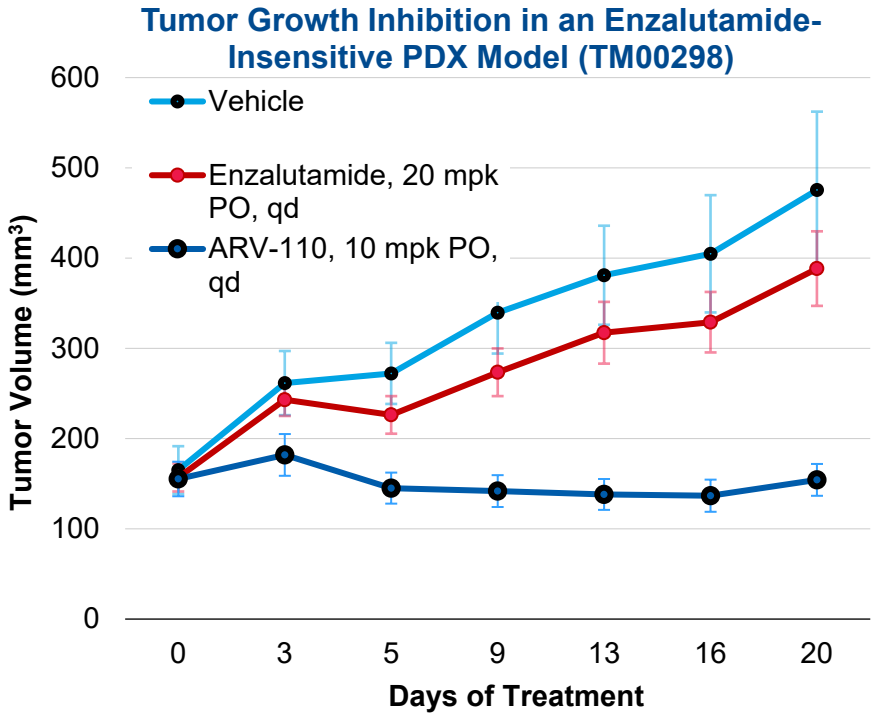
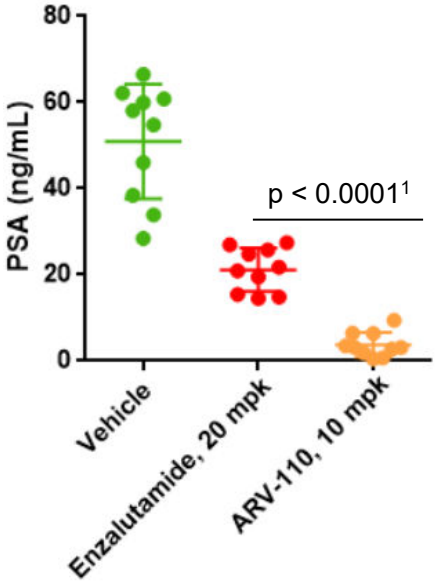
- Orally delivered ARV-110 significantly inhibited tumor growth in these enza-insensitive tumors (TGI: 100%)



- 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 is showing early clinical benefit in highly refractory patients

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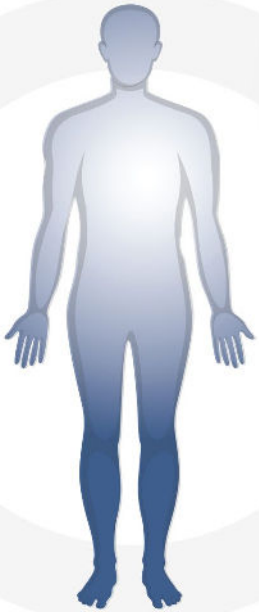
Data as presented 12/14/2020

Median prior therapies **5**

76% Patients treated with prior chemotherapy



Patients treated with both abiraterone and enzalutamide **82%**

84% Patients with non-AR mutations

Existing AR-directed therapies **expected to be ineffective**

High tumor heterogeneity suggests **low dependence on AR**

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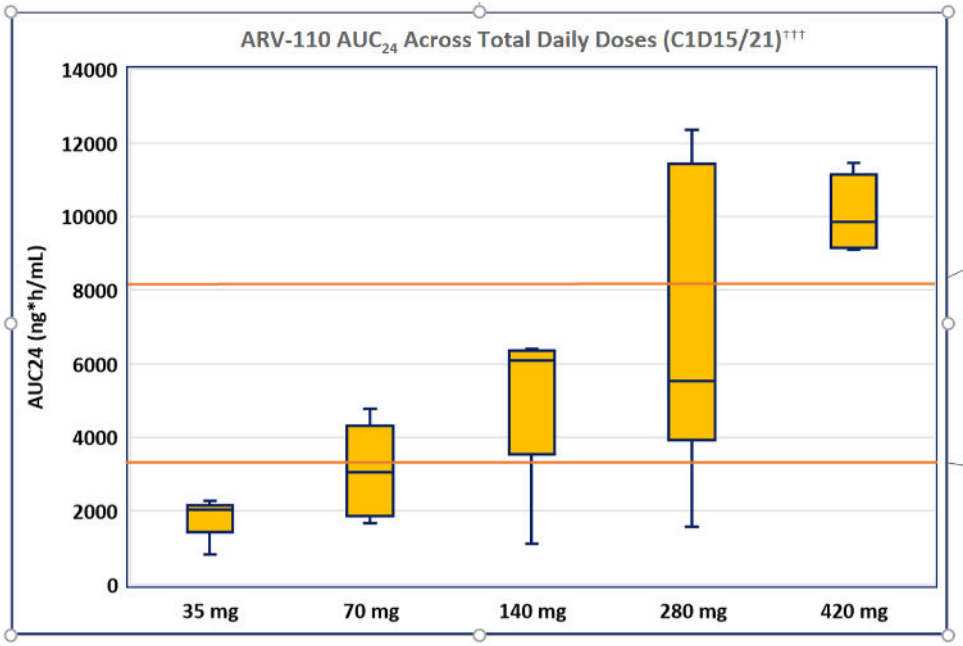
At 420 mg, exposures exceed the predicted efficacious threshold observed in a preclinical enzalutamide-resistant model



Data as presented 12/14/2020

Predicted efficacious threshold based on an **enzalutamide-resistant prostate cancer** model ††

Predicted **minimum** efficacious threshold based on a standard prostate cancer model†

† The minimum preclinical efficacious threshold represents the AUC associated with tumor growth inhibition in standard VCAP models, †† This efficacious threshold represents the AUC associated with tumor growth inhibition in a preclinical enzalutamide-resistant VCaP model, ††† Includes both qd and bid dosing for the 420 mg total daily dose

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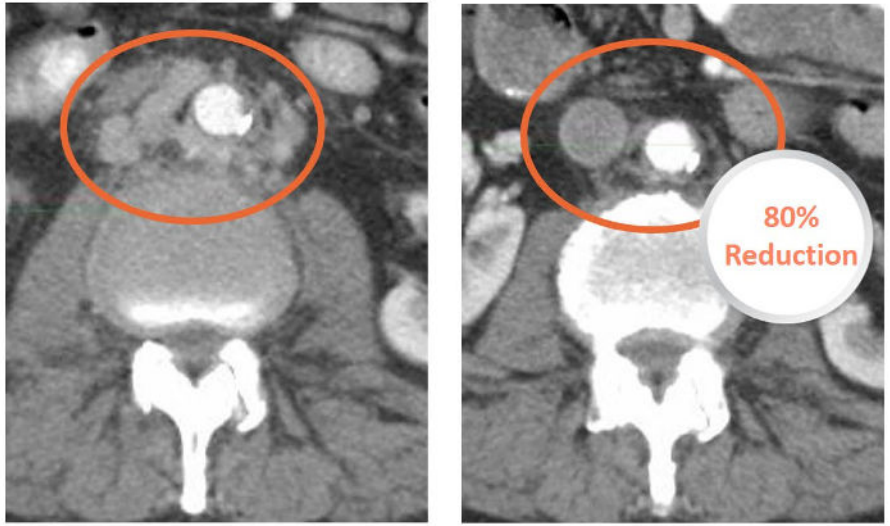
Results include one confirmed RECIST partial response

Patient Characteristics	
PSA response	**97%** decline
RECIST response	**80%** reduction
Duration of ARV-110	18+ weeks ongoing
Biomarker status	AR H875Y and T878A mutations (associated with resistance to abiraterone or enzalutamide)[1]
Common prior therapies	Enzalutamide, Abiraterone, Bicalutamide
Other prior therapies	Provenge Cabazitaxel
History	Extensive disease involving adrenal gland, aortocaval nodes, multiple cone metastases



BASELINE CT SCAN

Extensive retroperitoneal adenopathy compressing the inferior vena cava

AFTER 4 CYCLES

Near complete regression of adenopathy

RECIST: Response evaluation criteria in solid tumors
[1]Jernberg E, Endocrine Connections, 2017

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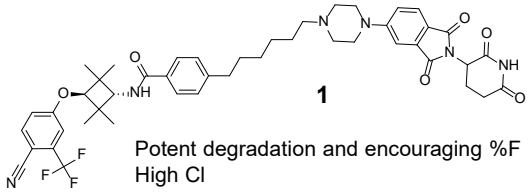
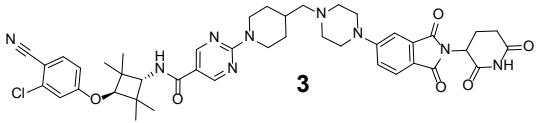
Evolution of AR Degrading PROTACs Leading to ARV-110

Early Discovery Efforts
Multiple E3 recruiting ligands
Multiple AR binders



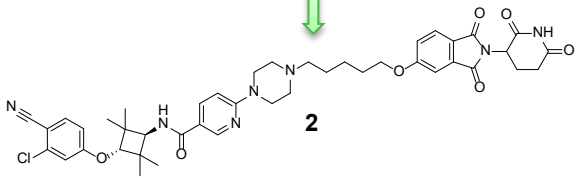
1

Potent degradation and encouraging %F
High Cl



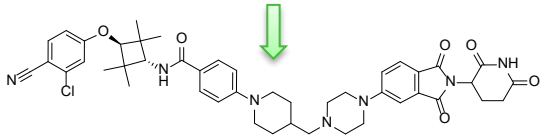
3

Good in vitro degradation potency
Possible autoinduction signal
AR ligand by itself agonist
In vivo potency superseded by **4**



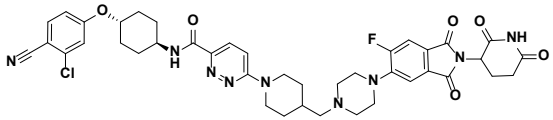
2

Possible candidate
In vivo potency suboptimal
Crystallized to high melting solid



4

Possible candidate
Dose escalation exposure suboptimal



ARV-110

Drug Discovery and Development is a Team Sport