

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

FORM 8-K

**CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): March 13, 2023

Acrivon Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

001-41551
(Commission
File Number)

82-5125532
(IRS Employer
Identification No.)

480 Arsenal Way, Suite 100
Watertown, Massachusetts
(Address of Principal Executive Offices)

02472
(Zip Code)

(617) 207-8979
(Registrant's Telephone Number, Including Area Code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.001 par value	ACRV	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 2.02 Results of Operations and Financial Condition

As discussed below, in connection with its participation in the Oppenheimer 33rd Annual Healthcare Conference taking place virtually, Acrivon Therapeutics, Inc. (the “Company”) updated its corporate presentation to include disclosure that the Company had \$169.6 million of cash and marketable securities as of December 31, 2022.

Because the Company’s consolidated financial statements for the year ended December 31, 2022 have not been finalized or audited, the preliminary statement of the Company’s cash and marketable securities as of December 31, 2022 in this Item 2.02 is subject to change, and the Company’s actual cash and marketable securities as of December 31, 2022 may differ materially from this preliminary estimate. Accordingly, you should not place undue reliance on this preliminary estimate.

Item 7.01 Regulation FD Disclosure

Beginning on March 13, 2023, the Company will participate in the Oppenheimer 33rd Annual Healthcare Conference taking place virtually. The Company has updated its corporate presentation that it intends to use in connection with its presentation on Monday, March 13, 2023 at 3:20 PM Eastern Time and in meetings with investors. The presentation includes, among other things, an update regarding the Company’s clinical progress, disclosure regarding the Company’s cash and marketable securities as of December 31, 2022 and confirmation of its projected cash runway into at least the fourth quarter of 2024.

A copy of the Company’s corporate presentation is attached hereto as Exhibit 99.1 and is hereby incorporated by reference herein.

The information furnished under Item 2.02 and Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1, is being furnished and shall not be deemed to be “filed” for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.**(d) Exhibits:**

Exhibit Number	Exhibit Description
99.1	Acrivon Therapeutics, Inc. Presentation
104	Cover Page Interactive Data File (formatted as Inline XBRL).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Acrivon Therapeutics, Inc.

Dated: March 13, 2023

By: /s/ Peter Blume-Jensen
Name: Peter Blume-Jensen, M.D., Ph.D.
Title: Chief Executive Officer and President

Acrivon
Therapeutics



ACRIVON PREDICTIVE PRECISION PROTEOMICS (AP3):
DRUG-TAILORED PATIENT SELECTION FOR CLINICAL SUCCESS

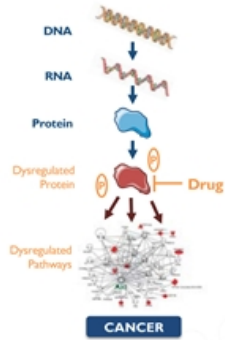
MARCH, 2023

ACRIVON THERAPEUTICS: DRUG-TAILORED PATIENT SELECTION

AIMING TO OVERCOME THE KEY ATTRITION FACTOR PREVENTING CLINICALLY ACTIVE DRUGS FROM REACHING MARKET

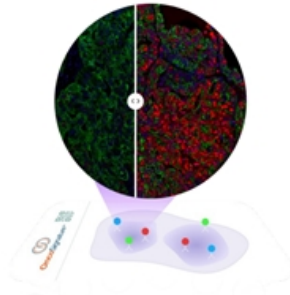
AP3 Platform

- Acrivon's proprietary proteomics-based predictive precision medicine platform
- Applied where NGS/genetics is insufficient and for our internal pipeline



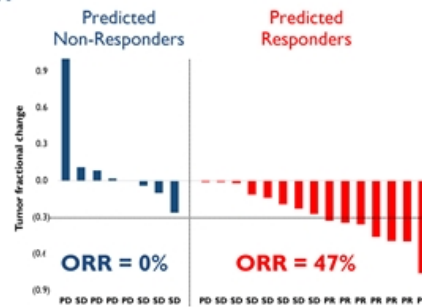
OncoSignature®

- Our proprietary predictive drug-tailored biopsy test
- Extensively evaluated in prospective preclinical studies, including prediction on blinded pretreatment tumor biopsies from past trials resulting in ORR 47% and 58%



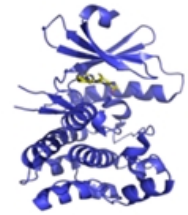
ACR-368 (Prexasertib)

- Clinically active (15-20% ORR) Phase 2 DNA Damage Response (DDR) inhibitor licensed from Eli Lilly & Co.
- Now being developed with OncoSignature patient selection for increased ORR with registrational intent



Pipeline

- Two co-crystallography- and AP3-driven preclinical programs targeting WEE1 and PKMYTI, proximal and redundant DDR nodes
- Single digit nM inhibitors, wholly-owned, opportunity for AP3 patient selection and pipeline combinations



ACCOMPLISHED LEADERSHIP TEAM



Peter Blume-Jensen, M.D., Ph.D.
CEO, Founder

- Executive Serono, Merck & Co., Daiichi Sankyo
- CSO Metamark - Marketed prostate proteomic test ProMark®
- Inventor AP3 pt. selection platform



Rasmus Holm-Jorgensen
Chief Financial Officer

- Novo Nordisk Finance and IR
- Synageva pipeline expansion and \$9bn sale to Alexion
- Kiniksa founding team, IPO and commercial launch



Erick Gamelin, M.D., Ph.D.
Chief Medical Officer

- Professor, CEO, large national cancer center and hospital
- Executive Amgen, Pfizer, Dynavax, MacroGenics; CMO STEP Pharma
- Led >100 ph I-3 oncology trials



Eric Devroe, Ph.D.
Chief Operating Officer

- Founder and CEO, Oponix
- Business executive MD Anderson Cancer Center and Metamark
- EIR Wyss Institute, Harvard
- Associate, Flagship Pioneering



Kristina Masson, Ph.D.
Co-Founder, CEO, Acrivon AB
EVP Business Operations

- Cross-functional Leadership Merrimack Pharmaceuticals, MIT/BROAD
- Founder and CEO, OncoSignature AB (acquired by Acrivon Therapeutics)



John van Duzer, Ph.D.
VP, CMC

- VP/SVP Acetylon, Collegium, Eloxx, Mersana, ActivBiotics
- Inventor of HDACi's Ricolinostat and Citarinostat and COX2i Lumiracoxib



Jeremy Barton, M.D., M.R.C.P.
Chief Medical Advisor

- CMO Mirati Therapeutics, Biogen-Idec, Effector
- Head Early Oncology Drug Development Pfizer



David Proia, Ph.D.
VP, Drug Discovery and Biology

- VP, Rome Therapeutics, C4 Therapeutics
- Previously Synta, Astra-Zeneca, Boston Biotech
- Multiple recognition awards



Joon Jung, Ph.D.
VP, Head, Data Science

- VP/Head, Theonys, Inc. Cyclieron/Ironwood
- Previously Merck & Co., J&J, Triad Therapeutics
- Multiple recognition awards



Katie Peterson, C.P.A.
VP, Finance and Accounting

- Head, Financial Planning and Analysis Wave Life Sciences, Spero Therapeutics, and Merrimack Pharmaceuticals
- Audit Manager, CPA Ernst & Young LLP



Michail (Misha) Shipitsin, Ph.D.
VP, Biomarker Development

- Head clin. biomarkers, Metamark
- Scientific lead on marketed, prostate test, ProMark®
- Expert digital imaging & clinical protein biomarker tests



ACRIVON THERAPEUTICS AT A GLANCE

Development Site (Boston)

- Drug and clinical biomarker assay development
- Clinical trials
- Market access pending approval

OUR HQ IS LOCATED IN BOSTON - ACCESS TO LEADING DRUG DISCOVERY, BIOTECH, AND PHARMA



Precision-Proteomics Site (Lund/Copenhagen)

- Early pipeline drug programs
- BM identification and drug profiling
- Mass spectrometry

OUR PROTEOMIC HUB IS LOCATED IN MEDICON VALLEY - NORTHERN EUROPE'S LEADING LIFE SCIENCE CLUSTER



Peter Blume-Jensen
CEO, President,
Co-Founder



Kristina Masson
EVP, Bus Ops,
Site Head and
Co-Founder

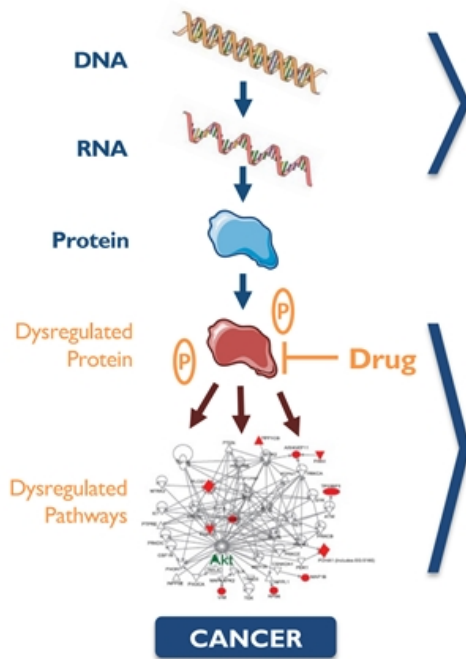


Jesper V. Olsen
Academic Co-Founder,
Novo-Nordisk Foundation
Protein Center, Cph.

Acrivon was founded in early 2018 and is backed by top-tier investors



ACRIVON PREDICTIVE PRECISION PROTEOMICS, AP3



Genomic Biomarkers are useful for patient selection in the smaller subset of cancers (<10%) with single gene driver mutations or known synthetic lethal context*

CANCER IS CAUSED BY DYSREGULATED PROTEIN ACTIVITY

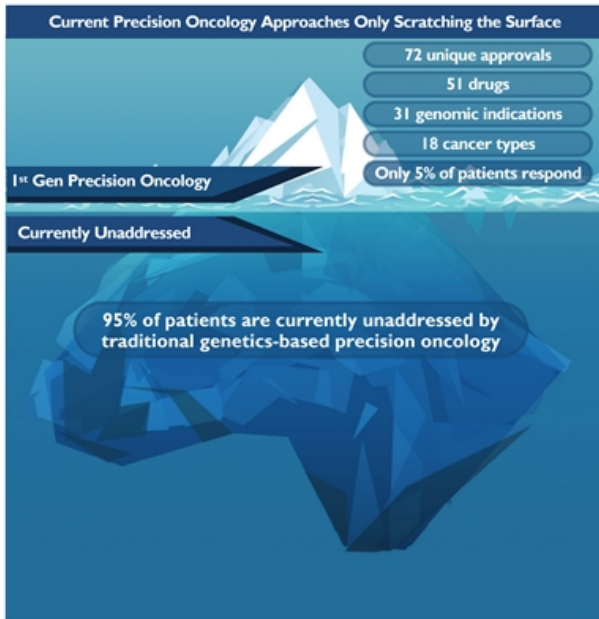
Proteomic Biomarkers directly measure the disease-driving, dysregulated proteins and enable an exact match with the drug mechanism-of-action independent of genetic alterations

(Acrivon meaning: "Exact, Accurate")

*Oncogenic Kinase Signaling: Blume-Jensen, P. and Hunter, T. Nature (2001)

Synthetic lethality as an engine for cancer drug target discovery: Huang, A. et al. NatRevDrugDisc (2020)

AP3 PLATFORM ADDRESSES HIGH UNMET NEED BEYOND NGS-BASED PRECISION MEDICINE



Sources: Company Filings, ACS, CDC, NCI, Wall Street Research

Acrivon Positioned to Increase Precision Oncology Market Size

Precision Oncology 1.0

Herceptin
trastuzumab

Approved indications:
HER2+ Breast Cancer
HER2+ Gastric Cancer

gleevec
imatinib mesylate

Approved indications:
CML (BCR-ABL)
Ph+ ALL

Precision Oncology 2.0

LOXO
Solid Tumors (NTRK)

agios
IDH mutation in AML

ignyta
NSCLC (NTRK) and
CRC (ROS1, ALK)

MIRATI
NSCLC (KRAS G12C)

TYRA
Bladder (FGFR3)

KINNATE
Class II and III BRAF
kinase alterations: N/A

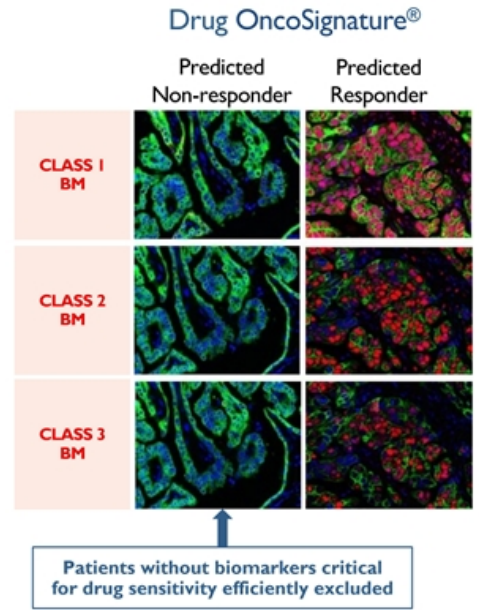
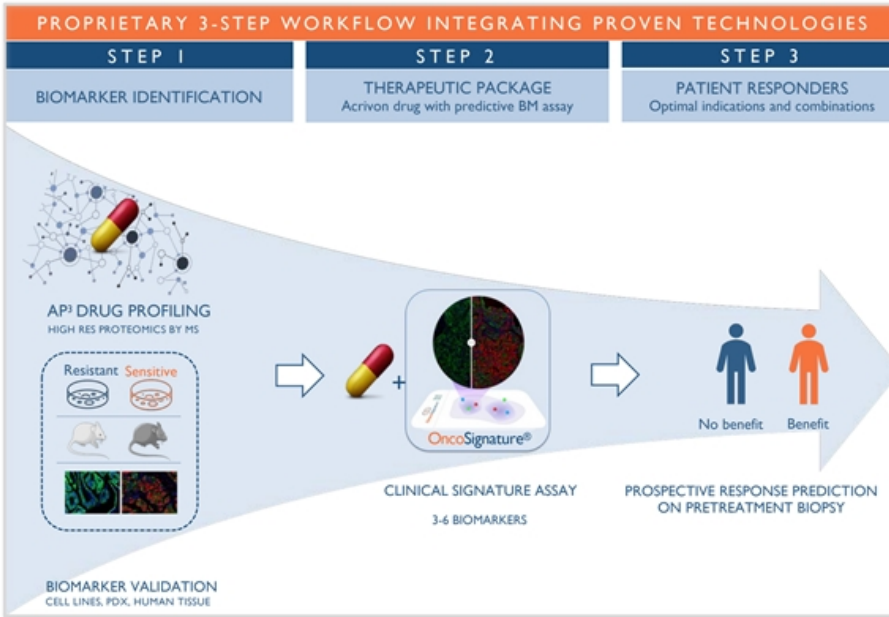
ELEVATION
Solid Tumors (NRG1)

Predictive Precision Proteomics

Acrivon
Therapeutics

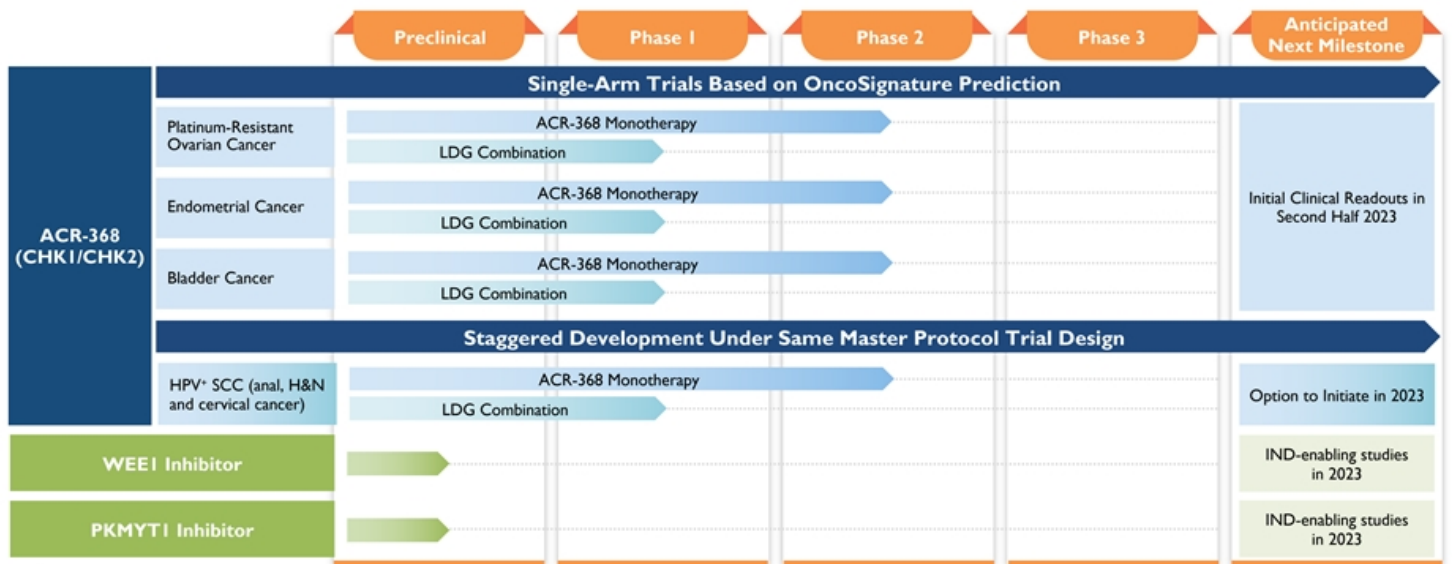
Aiming to make targeted therapeutic solutions available to broader group of cancer patients

AP3 PLATFORM: DRUG RESPONSE PREDICTION IN INDIVIDUAL PATIENTS



"Disease Pathway-Based Method to Generate Biomarker Panels Tailored to Specific Therapeutics for Individualized Treatments"; EP 2 229 589, issued June 10, 2015; US2017/0067877A9, pending. OncoSignature® is a Registered Trademark: US Reg. No. 5,718,472; Int. Cl. 5, 42. Int. Reg. 1382289

ACRIVON PIPELINE

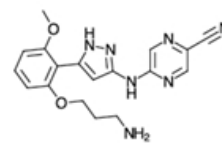


Notes

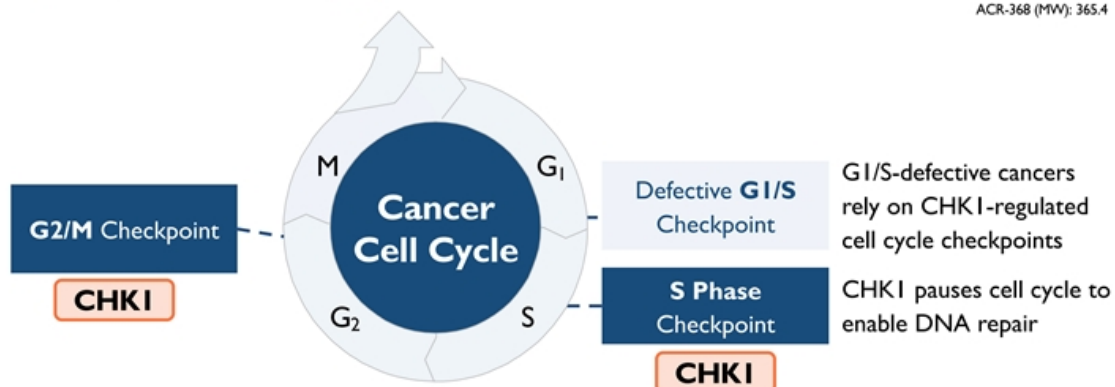
- ACR-368 Monotherapy → Registrational intent Phase 2 single arm trials based on predicted sensitivity to ACR-368 monotherapy in OncoSignature-positive patients
- LDG Combination → Exploratory Phase 1b/2 single arm trials of ACR-368 in combination with low dose gemcitabine, or LDG, in OncoSignature-negative patients

ACR-368: A CLINICALLY ACTIVE PHASE 2 CHK1/2 INHIBITOR

- ATP-competitive inhibitor of CHK1 (0.9 nM) and CHK2 (8 nM)
- Good ADME properties, minimal drug-drug interaction (DDI) potential
- Discovered by Array Biopharma, acquired by Eli Lilly & Company
- CoM patent exp. Oct., 2030; Salt-form exp. Apr., 2037



ACR-368 (MW): 365.4



- **Durable monotherapy activity:** Platinum-resistant ovarian and squamous cell cancers (Anal and H&N)
- **Large safety database, favorable safety profile:** >1,000 patients treated (~50% mono, ~50% in combination)
- **Ideal for AP3 method:** Proven clinical activity, but requires patient responder identification to achieve sufficient ORR

CLINICAL OVERVIEW OF ACR-368 MONOTHERAPY (PAST DATA)

Indication	Trial	ORR [#] (confirmed)	Median DoR ^o	Reference
HGSOC* (BRCA wild type, primarily platinum-resistant)	Phase 2 single center (NCI)	29%	>10 months [^]	Lee et al, Lancet Oncology, 2018
HGSOC (BRCA wild type and mutant; platinum-resistant and refractory)	Phase 2 multi-center (Lilly)	12.1% (platinum-resistant)	5.6 months	Konstantinopoulos et al; Gynec. Oncol.: 2022
Squamous cell cancer (anal cancer, head & neck cancer [H&N])	Phase 1b multi-center (Lilly)	19% HPV+ H&N 15% anal cancer	7 months (HPV+ H&N) 12 months anal cancer	Hong et al, CCR, 2018

Dosing and Administration

- IV q14d (RP2D = 105 mg/m²)

Safety summary

- Acceptable safety profile in >1,000 patients
 - No clinical or regulatory holds imposed across all clinical studies to date
- Primary adverse events ≥ grade 3 were hematological (manageable neutropenia and thrombocytopenia)
- Limited ≥ grade 3 non-hematological toxicities (≤7% for all AEs)
- Drug-related discontinuations <1-2%

*High grade serous ovarian cancer; [^]Updated post-publication; [#] Overall response rate; ^oDuration of Response

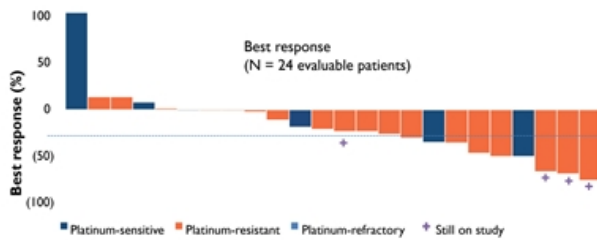
PAST PHASE 2 TRIALS IN HIGH GRADE SEROUS OVARIAN CANCER

NCI single-center Phase 2 study (N=28)

- Heavily pre-treated patients; median 5 prior lines
- Pretreatment tumor biopsies mandated

RESULTS

- ORR 29%; mDoR >10 months (post-publication)
- No genetic correlation with p53^{mut}, DDR^{mut}, or CCNE1



Lee et al; *Lancet Oncology*: 2018

Lilly-sponsored multi-center (46 center, 8 country) Phase 2 study (N=169)

- All lines of prior therapy, BRCA wt and mt, incl. prior PARPi
- Pretreatment tumor biopsies mandated

RESULTS

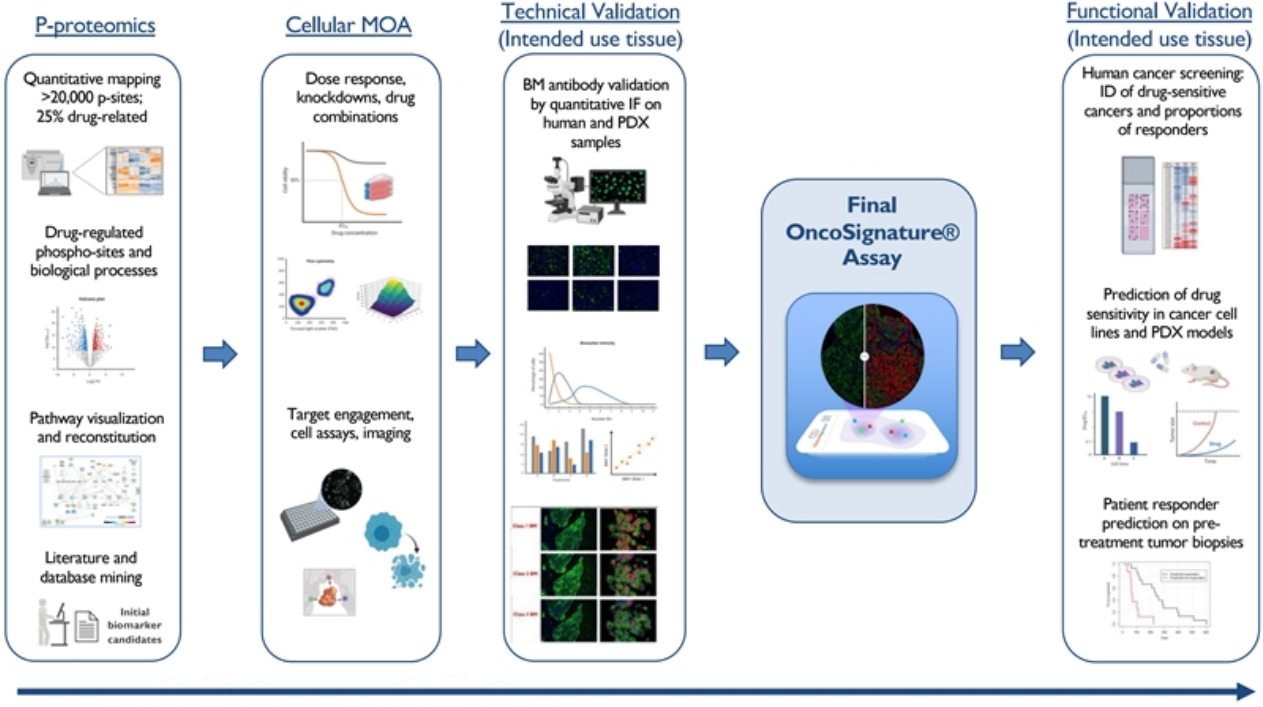
- ORR 12.1% (excl. unconfirmed); mDoR =5.6 months
- No correlation with genetic alterations

N = 169 PATIENTS	COHORT DESCRIPTION	PERCENT CONFIRMED ORR (95 % C.I.)
Cohort 1 (53)	Plat resistant BRCA wt; ≥3 lines of prior therapy	11.3 (4.3 to 23.0)
Cohort 2 (46)	Plat resistant BRCA wt; < 3 lines of prior therapy	13.0 (4.9 to 26.3)
Cohort 3 (41)	Plat resistant BRCA mt, any line of therapy (must include prior PARPi)	12.2 (4.1 to 26.2)
Cohort 4 (29)	Plat refractory, any BRCA, any line of therapy	6.9 (0.8 to 22.8)

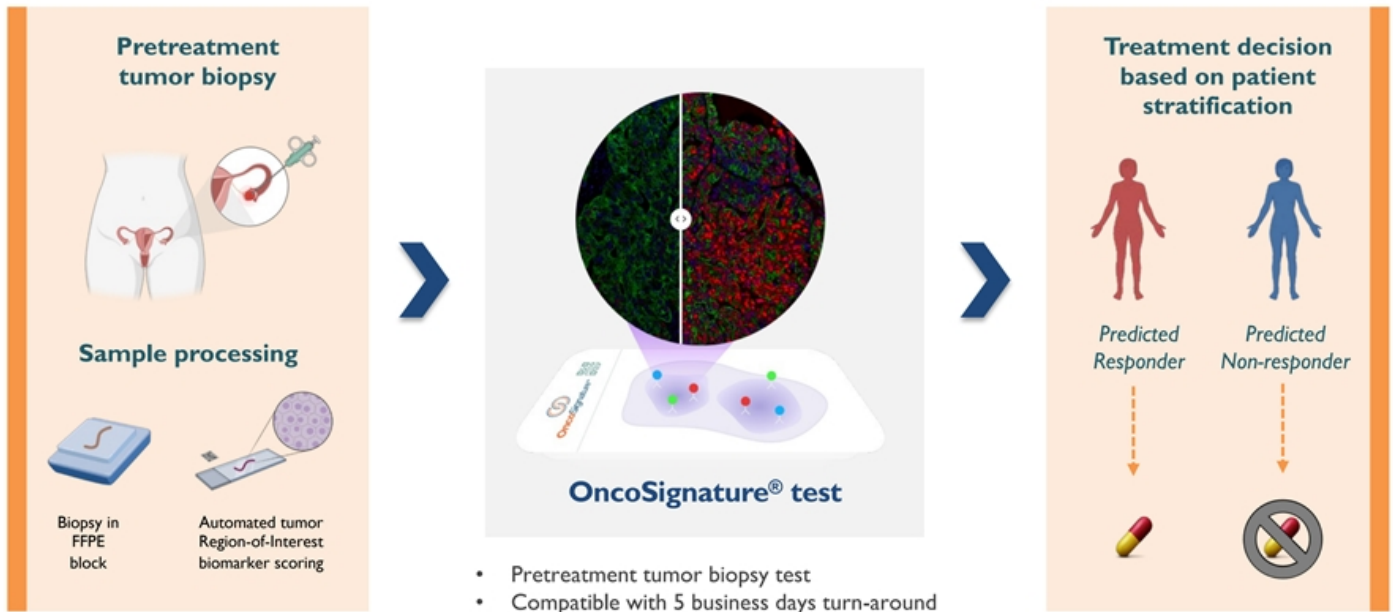
Konstantinopoulos et al; *Gynec. Oncol.*: 2022

- ✓ Past trials suggest unenriched all-comer ORR in HGS ovarian cancer is ~15-20%
- ✓ Durable clinical activity in most responders
- ✓ No predictive biomarkers identified, need for alternative biomarker approach (ideal for AP3)

DEVELOPMENT OF AP3-BASED PATIENT SELECTION ONCOSIGNATURE® TESTS

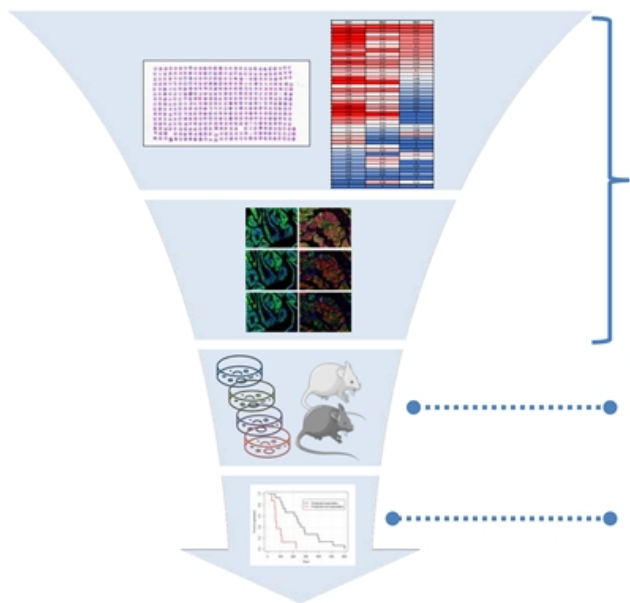


ONCOSIGNATURE® TESTS: USAGE IN THE CLINIC



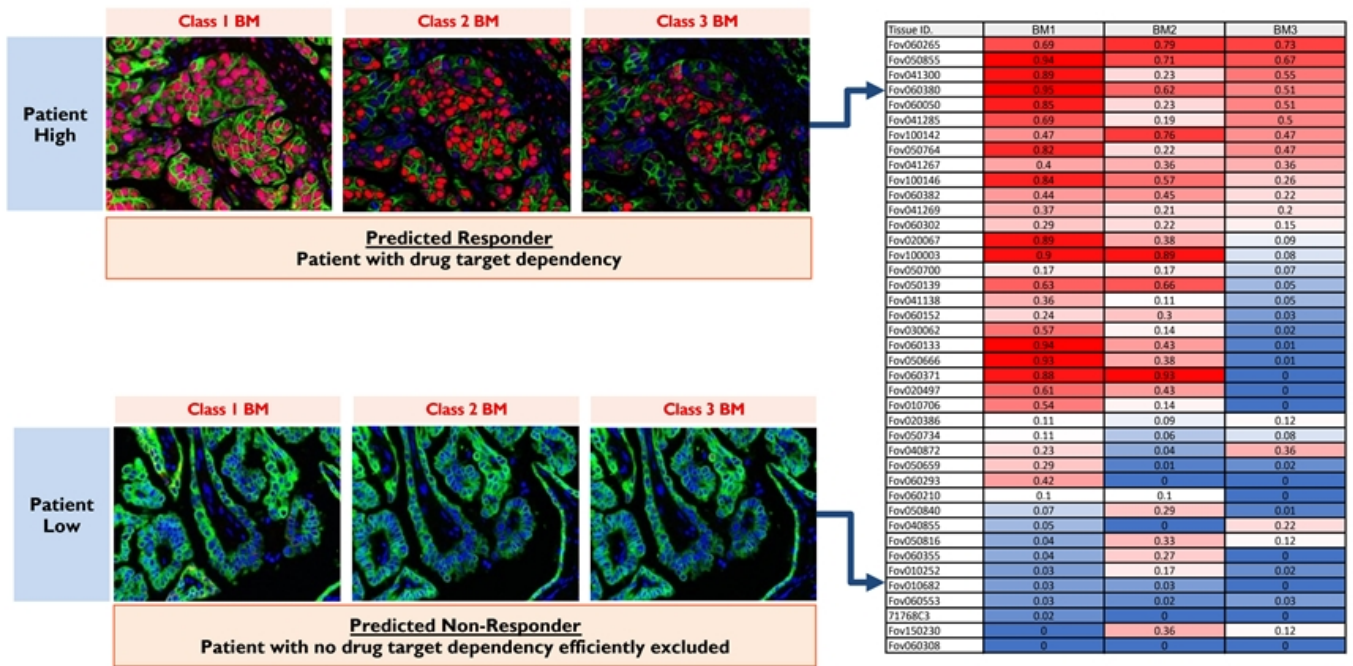
- Pretreatment tumor biopsy test
- Compatible with 5 business days turn-around
- Offered by CDx partner under exclusive license from Acrivon

CONSISTENT ACR-368 ONCOSIGNATURE® PERFORMANCE ACROSS PRECLINICAL STUDIES



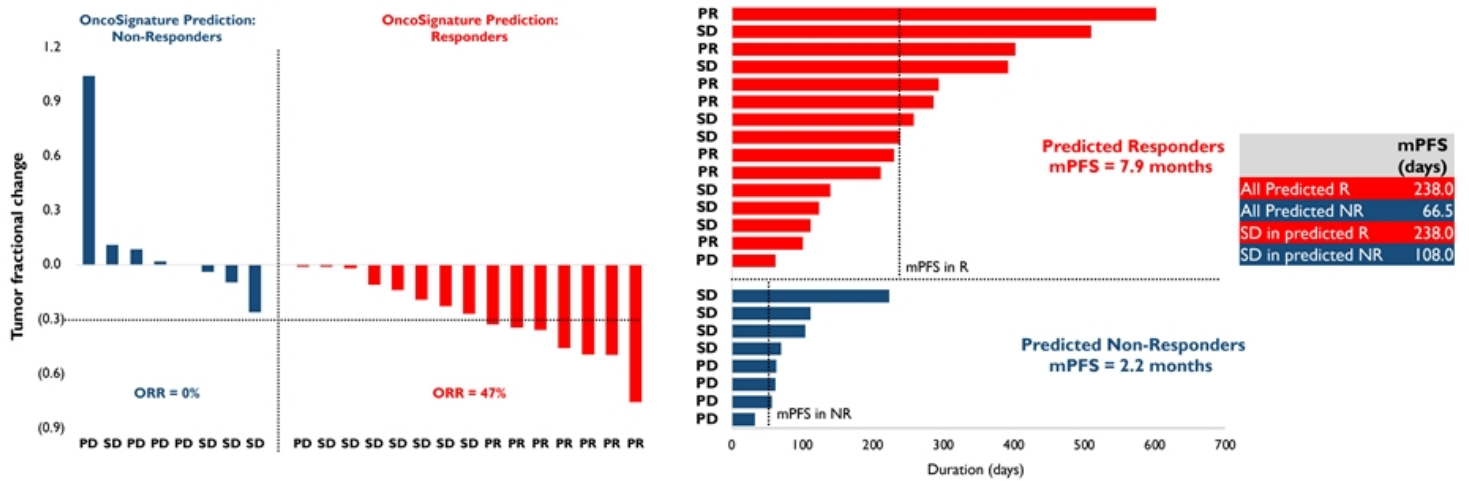
- Prediction of the fraction of human tumors sensitive to single agent ACR-368
 - Selection rate 30-40% across lead indications
- Identification of additional human tumor types predicted sensitive to single agent ACR-368
 - Endometrial and bladder cancer
- Prediction of treatment outcome in human PDX models
 - ORR enrichment to $\geq 55\%$; AUC of 0.88 and 0.9
- Two separate, prospectively designed, blinded studies of biopsies from past Phase 2 trials with ACR-368 in patients with platinum-resistant ovarian cancer
 - ORR enrichment to 47% (NCI) and 58% (Lilly multi-center)

ACR-368 ONCOSIGNATURE® PREDICTION OF DRUG SENSITIVITY: BIOMARKER QUANTITATION ACROSS HUMAN CANCER PATIENT SAMPLES



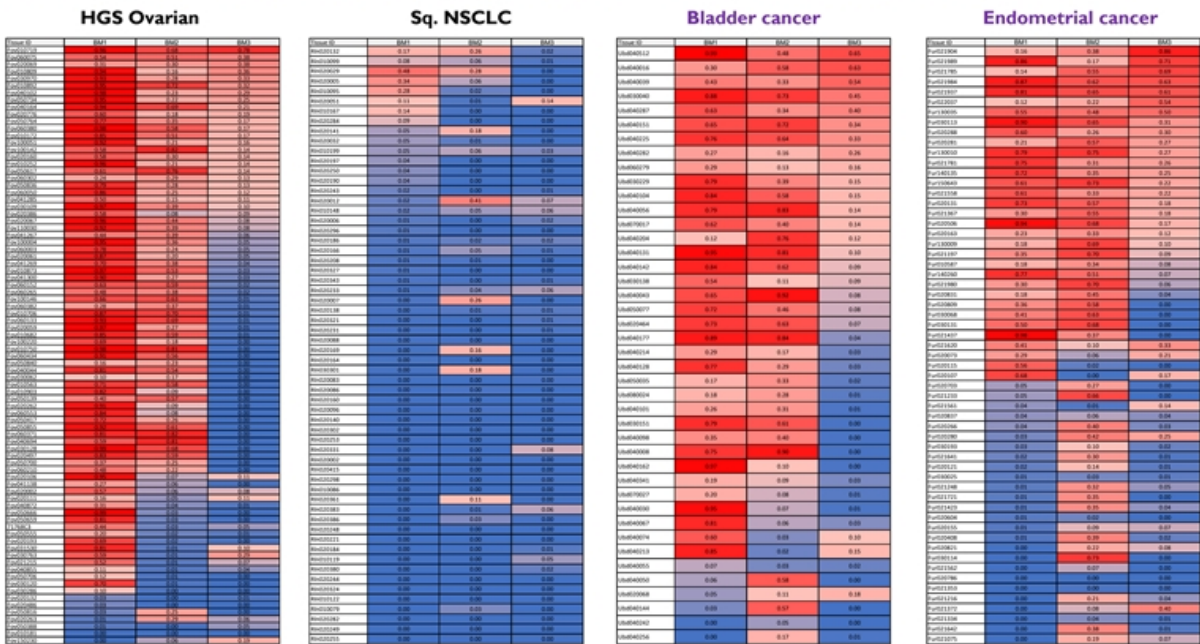
BIOPSY STUDY 1: SUBSTANTIAL RESPONSE AND PFS BENEFIT IN PREDICTED RESPONDERS (BLINDED, PROSPECTIVELY DESIGNED STUDY)

- Available pretreatment tumor biopsies from past phase 2 trials at NCI with ACR-368 in platinum-resistant ovarian cancer were obtained
- OncoSignature® scores were generated **blinded to treatment outcome** at Acvion and analyzed by **3rd party biostatistician** in **prospectively designed study**



Result: ORR ~47%; mPFS = 7.9 months

TWO ADDITIONAL HIGH UNMET NEED SOLID CANCERS PREDICTED ACR-368-SENSITIVE THROUGH HUMAN TUMOR SAMPLE SCREENING



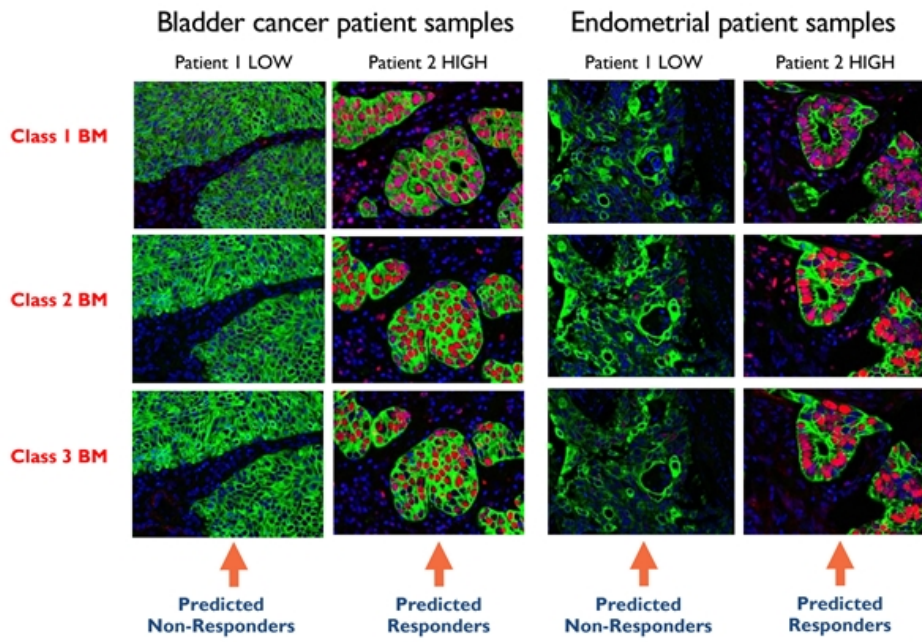
OncoSignature-positive = 30%
(ORR in past trials: 12+% and 29%)

OncoSignature-positive = 0%
(ORR in past trial: 0%)

OncoSignature-positive = 30-50%

OncoSignature-positive = 30-40%

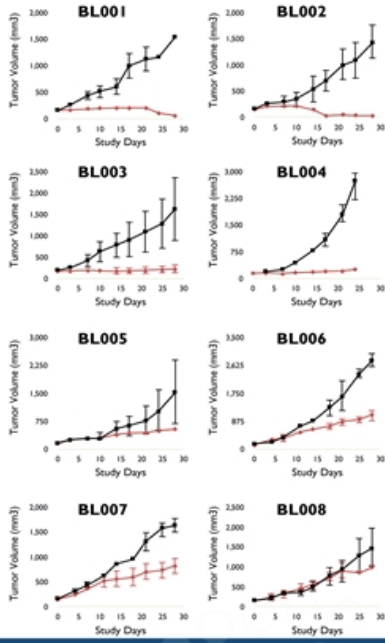
TWO ATTRACTIVE ACR-368-SENSITIVE CANCER TYPES IDENTIFIED



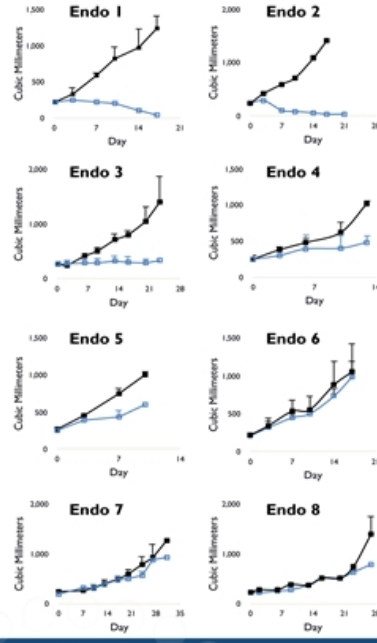
ACR-368 OncoSignature screening of human cancer samples

A SUBSET OF ENDOMETRIAL AND BLADDER PDX MODELS ARE HIGHLY SENSITIVE TO ACR-368

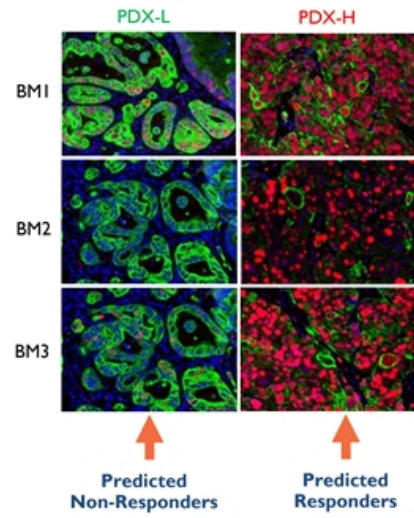
Bladder PDX



Endometrial PDX



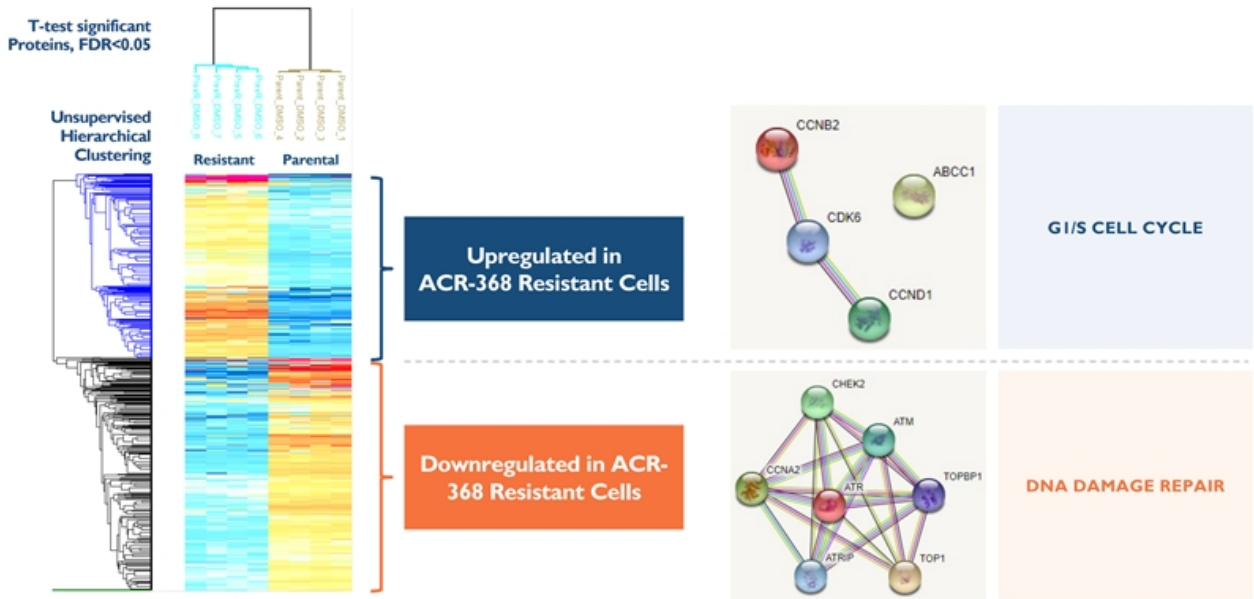
ACR-368-sensitive responders



Predicted Non-Responders

Predicted Responders

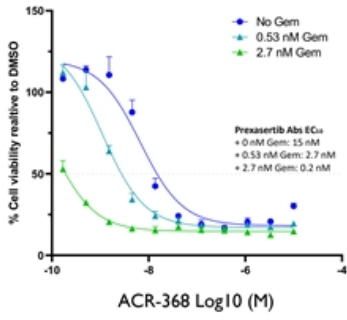
AP3 UNCOVERS ACTIONABLE ACR-368 RESISTANCE MECHANISMS UNBIASED AND INDEPENDENT OF GENETIC INFORMATION



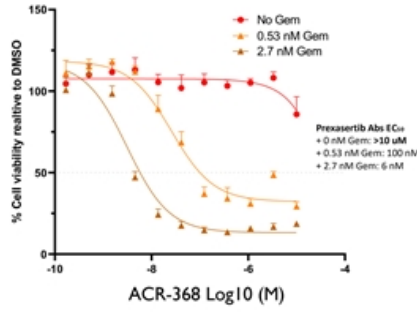
Data suggest that gemcitabine might be a rational combination to overcome DDR suppression

LDG SENSITIZES OVARIAN CANCER CELL LINES TO ACR-368

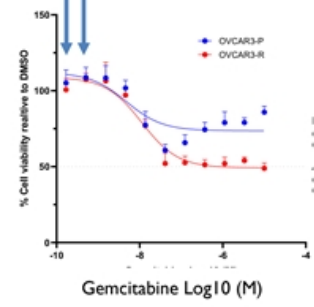
Ovarian-Parental



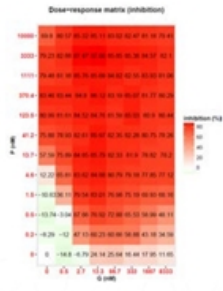
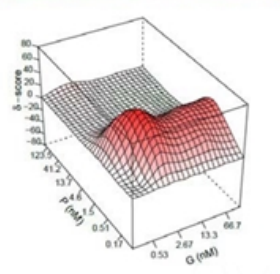
Ovarian-Resistant



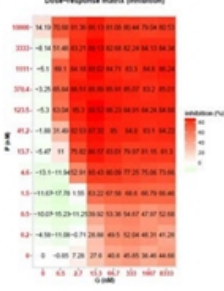
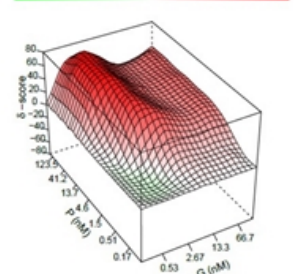
Gemcitabine alone



Bliss synergy score: 14.82



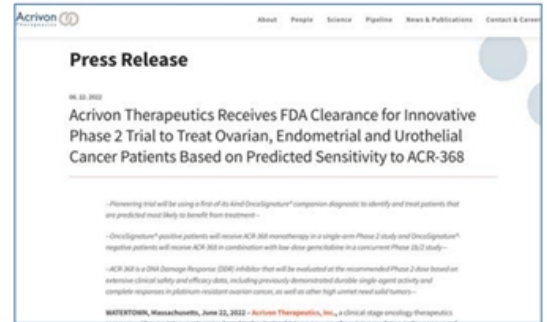
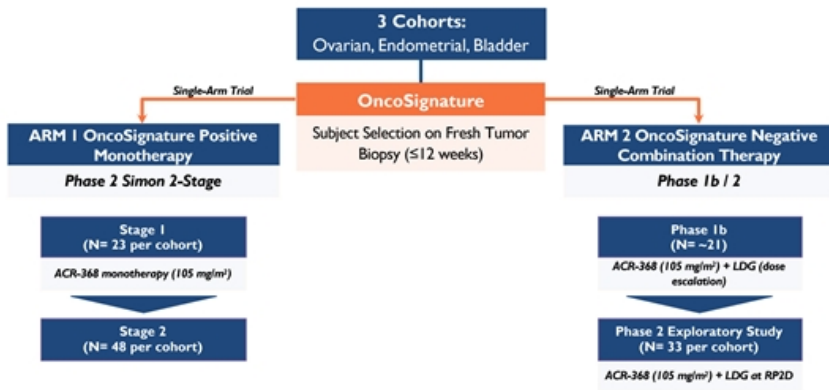
Bliss synergy score: 36.125



Bliss Synergy score:

- <-10: Drug interaction is likely antagonistic
- 10 to 10: Drug interaction is likely additive
- >10: Drug interaction is likely synergistic

ACR-368 PHASE 2 CLINICAL TRIAL HAS BEEN INITIATED



INTERNAL PIPELINE: WEE1 AND PKMYT1 - LEVERAGING AP3

Rationale

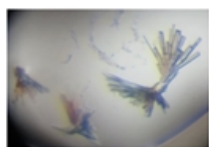
- Complement to in-licensing, leveraging our AP3 patient selection platform for high clinical POS
- Potential within DDR drug target class to pursue combinations (ACR-368, WEE1i, and PKMYT1i)

Approach:

- Targets with promising clinical activity or strong rationale and no obvious patient selection path (DDR)
- Expert crystallography/Med Chem CRO; privileged access to world's brightest synchrotron MAX IV in Lund
- Structure-based drug design and SAR guided by Target Product Profile, AP3 profiling, and parallel FTO analysis

Progress:

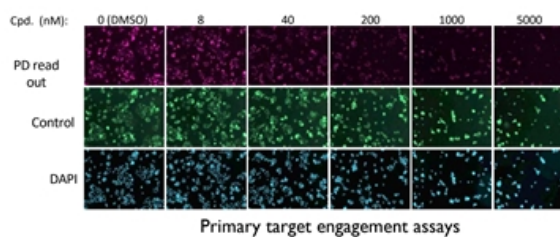
- High resolution co-crystals generated, drug target engagement imaging assays established, single digit nM candidate lead series identified and profiled by our AP3 approach



PKMYT1 co-crystals

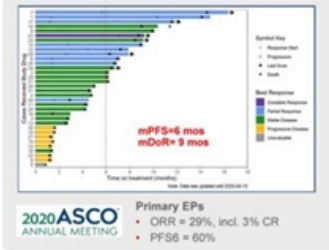
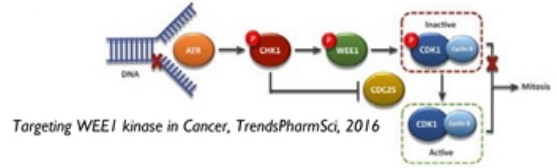


WEE1 co-crystallized with Ref. Cpd



WEE1 PROGRAM: IDEAL FOR THE AP3 PLATFORM

- WEE1 is a mitotic cell cycle regulatory kinase; inhibition propagates genomic instability by premature DNA replication and cell cycle progression, resulting in mitotic catastrophe.
- Strong preclinical data and emerging clinical data:
 - AZD1775/MKI775/adavosertib (AstraZeneca)
 - Debio0123 (Debiopharm)
 - ZN-c3 (Zentalis Pharmaceuticals)



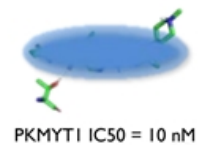
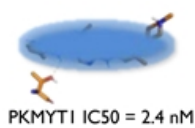
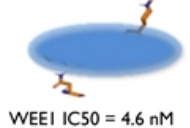
✓ Clinical activity
 ✓ Correlation with genetic alterations insufficient for responder identification
 ✓ Competitors have no obvious patient selection path

STRUCTURE- AND AP3-GUIDED DRUG DESIGN

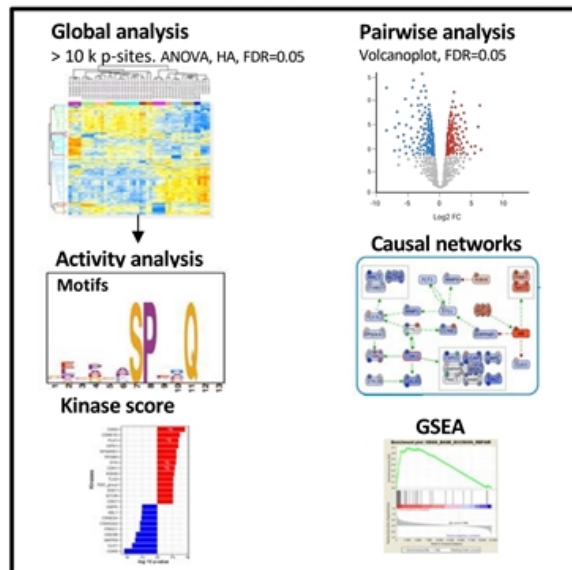
WEE1 and PKMYT1 programs

Lead optimization ongoing in several prioritized series based on high resolution co-crystals (WEE1: 2.1-2.6 Å; PKMYT1: 1.65-2.1 Å)

- Potent target inhibition ($IC_{50} < 10$ nM)
- Confirmed target engagement in cells
- Novel structural series (FTO analyses)
- Kinase selectivity (IVKA and AP3 profiling)
- PK studies ongoing



High throughput AP3 profiling



Leveraging AP3 for biologically relevant selectivity profiling

ACRIVON CORPORATE PRIORITIES

IP

- MoU for ACR-368 OncoSignature® (filed)
- CoM & MoU on all programs

Team-building

- Key positions to support growth

Optionality and value

- NDAs and Commercial Launch pending results
- Pipeline expansion
- Co-development deals/in-licensing



Clinical

- Advance phase 2 trials in multiple solid tumor indications with OncoSignature® patient selection

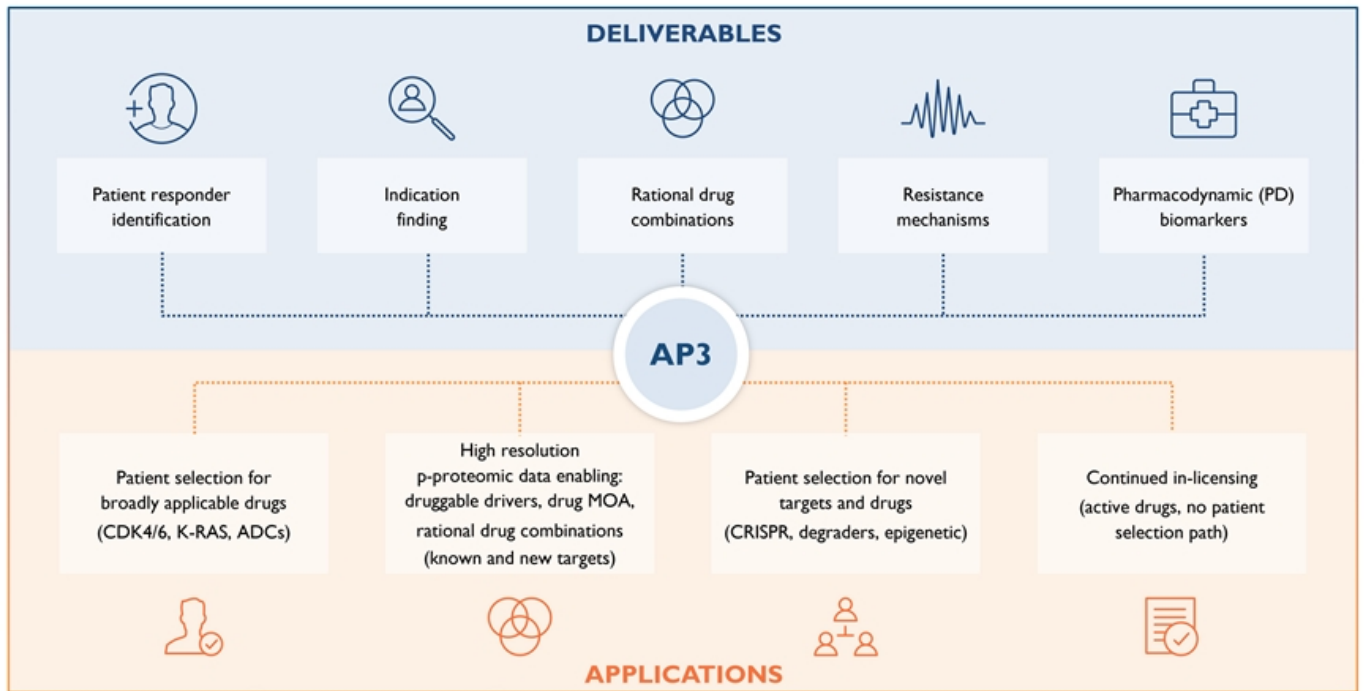
CMC

- DS and DP CMC for confirmatory trials

AP3 platform and pipeline

- Preclinical programs into IND-enabling phase
- OncoSignature® tests for Acrivon programs and potential co-development partnerships

AP3: BROAD APPLICABILITY AND UNTAPPED POTENTIAL



FINANCIAL HIGHLIGHTS

Cash and marketable securities

\$169.6M

Balance sheet
31-December-2022

Projected runway at least into

Q4'24

Current operating plan with no
additional financing

Fully Diluted Shares Outstanding

27.0M

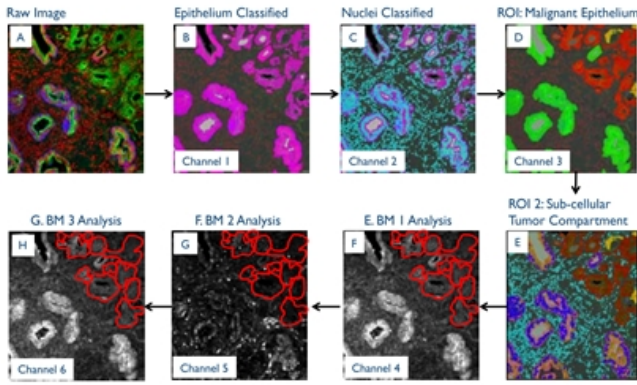
Shares and equity grants
outstanding 31-December-2022

Unaudited.



TEAM HAS PIONEERED OUTCOME-PREDICTIVE QUANTITATIVE PROTEOMIC MULTIPLEX IN SITU TEST

Prostate cancer 8-marker biopsy test developed and launched by Founding team



- **ProMark®:** Marketed, automated *in situ* proteomic test for human outcome prediction included under NCCN guidelines
- **Founding team:** Has pioneered p-proteomics and quantitative multiplex imaging including double-blinded clinical validation*

Ideal test	Protein multiplex <i>in situ</i> test	Current CDx tests
Quantitative and automated	✓	(✓)
Validated Abs and reagents	✓	(✓)
Drug target and pathway activation context	✓	
Biomarkers measured in relevant region on tumor biopsy	✓	
Imaging algorithm (tissue pattern)	✓	
Addresses tumor heterogeneity	✓	
Double-blinded, prospective validation	✓	(✓)

*Blume-Jensen et al: Development and clinical validation of an *in situ* biopsy-based multimarker assay for risk stratification in prostate cancer. *Clinical Cancer Research* (2015)

SIGNATURE :
MARKETED, OUTCOME-PREDICTIVE MULTIPLEX CANCER
TEST

Biology of Human Tumors

Clinical
Cancer
Research

**Development and Clinical Validation of an *In Situ*
Biopsy-Based Multimarker Assay for Risk
Stratification in Prostate Cancer** 

(2015)

Peter Blume-Jensen¹, David M. Berman², David L. Rimm³, Michail Shipitsin¹, Mathew Putzi⁴, Thomas P. Nifong¹, Clayton Small¹, Sibgat Choudhury¹, Teresa Capela¹, Louis Coupal⁵, Christina Ernst¹, Aeron Hurley¹, Alex Kaprelyants¹, Hua Chang¹, Eldar Giladi¹, Julie Nardone¹, James Duniak¹, Massimo Loda⁶, Eric A. Klein⁷, Cristina Magi-Galluzzi⁸, Mathieu Latour⁹, Jonathan I. Epstein¹⁰, Philip Kantoff⁶, and Fred Saad⁹

- Third-party blinded clinical validation, bioinformatic analysis (U. Montreal)
- Validation of locked ProMark™ test on single institution biopsy cases (N=274)
- Secondary validation on multi-center biopsy cohort (N=359) for clinical use indication
- Marketed test included under NCCN Guidelines and Medicare coverage

PIONEERING PHOSPHO-PROTEOMICS STUDY IDENTIFIES NOVEL PI3K PATHWAY INHIBITOR BIOMARKERS

Science Translational Medicine AAAS	RESEARCH ARTICLE
Sci Transl Med 2: 1-14 (2010)	CANCER DRUG DEVELOPMENT
Pathway-Based Identification of Biomarkers for Targeted Therapeutics: Personalized Oncology with PI3K Pathway Inhibitors	
Jannik N. Andersen, ^{1*} Sriram Sathyanarayanan, ^{1*} Alessandra Di Bacco, ¹ An Chi, ¹ Theresa Zhang, ¹ Albert H. Chen, ¹ Brian Dolinski, ¹ Manfred Kraus, ¹ Brian Roberts, ¹ William Arthur, ² Rich A. Klinghoffer, ^{1†} Diana Gargano, ^{1‡} Lixia Li, ¹ Igor Feldman, ¹ Bethany Lynch, ¹ John Rush, ³ Ronald C. Hendrickson, ^{4§} Peter Blume-Jensen, ^{1§} Cloud P. Paweletz ¹	

Editorial Highlights:

VOLUME 28 NUMBER 10 OCTOBER 2010 NATURE BIOTECHNOLOGY	Science Translational Medicine AAAS	TOWARD CUSTOMIZING TUMOR TREATMENT
Tracing cancer networks with phosphoproteomics		Just as our view of Earth has become increasingly global, cells are now seen as complex networks of interacting and intersecting signaling pathways rather than a collection of regulated genes.
David B Solit & Ingo K Mellinghoff		
A mass-spectrometry approach for identifying downstream events in cancer signaling pathways may help to tailor therapies to individual patients.		

Nature Reviews Cancer | AOP, published online 19 August 2010; doi:10.1038/nrc2922



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A discovery strategy for novel cancer biomarkers

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Adj. Prof. UCSD

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- Previously SVP and WW Head, Oncology R&D, Pfizer
- VP, Oncology Res., Wyeth
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Queen's Cancer Res. Inst.,
Ontario Canada

- GU Pathologist; bladder cancer expert
- Expert on protein biomarkers and quantitative tissue imaging
- Academic lead on ProMark®



Jesper V. Olsen, Ph.D.
Academic Co-Founder
Professor, Novo-Nordisk
Foundation Protein
Center, Cph. University

- Recognized pioneer and leading authority in phosphoproteomics and proteomic systems analyses
- Top 0.1% most cited scientist in protein sciences



Jung-Min Lee, M.D.
NCI Collaborator
Investigator, Lasker
Clinical Research
Scholar, NCI

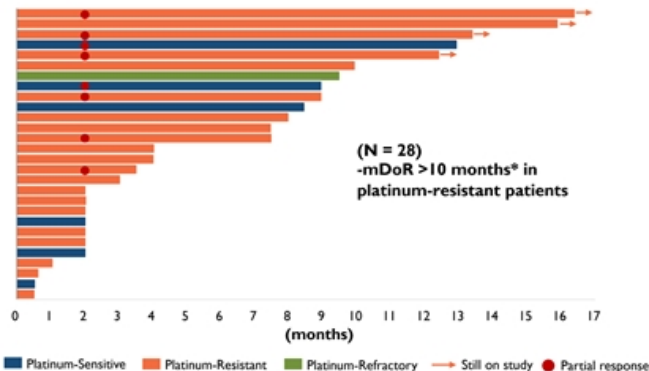
- Expert on women's cancers and DNA damage response (DDR)
- Lead and co-PI on numerous HGSOC & TNBC trials
- Lead PI on ACR-368 platinum-resistant ovarian trials

NATIONAL CANCER INSTITUTE (NCI) TRIAL IN HIGH GRADE SEROUS OVARIAN CANCER

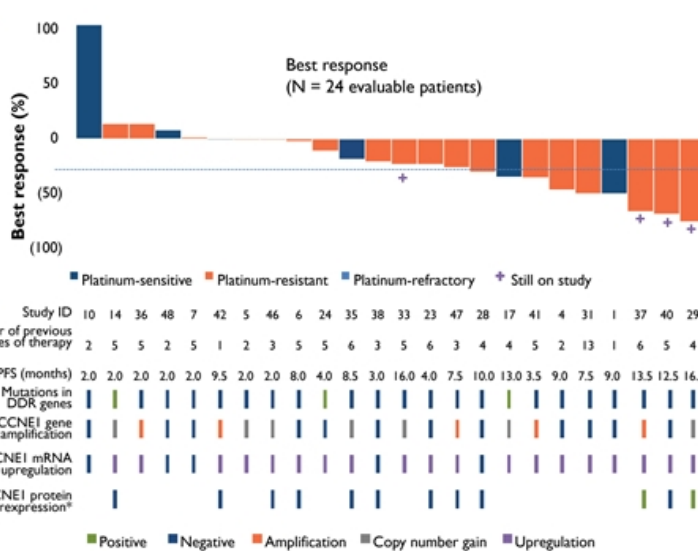
- Single-arm, Phase 2 POC study (Dr. Jung-Min Lee)
- N=28 (21 platinum resistant, 6 sensitive, 1 refractory)
- Heavily pre-treated; median of 5 prior systemic therapies
- Pretreatment biopsies mandated

Results:

- 8 PR in 28 intent to treat (ITT) patients (ORR 29%)
- 6 PR in 21 platinum-resistant patients (ORR 29%)
- No correlation with p53*, DDR*, or CCNE1 gene expression



*Updated post-publication



Lee et al; Lancet Oncology: 2018

Durable clinical activity in most responders (ideal for AP3)

MULTICENTER CLINICAL TRIAL IN ADVANCED HIGH GRADE SEROUS OVARIAN CANCER

Study design (Lilly-sponsored)

- Multi-center (46 centers, 8 countries), Ph. 2 (N =169)
- Pretreatment biopsies mandated

N = 169 PATIENTS	COHORT DESCRIPTION	PERCENT CONFIRMED ORR (95 % C.I.)	DURATION OF RESPONSE (DOR) IN MONTHS (95 % C.I.)	OVERALL SURVIVAL (OS) IN MONTHS (95 % C.I.)
Cohort 1 (53)	Plat resistant BRCA wt ≥3 lines of prior therapy	11.3 (4.3 to 23.0)	8.57 (5.55 to NA)	13.04 (7.46 to 19.25)
Cohort 2 (46)	Plat resistant BRCA wt < 3 lines of prior therapy	13.0 (4.9 to 26.3)	3.84 (2.79 to NA)	14.32 (11.76 to 16.46)
Cohort 3 (41)	Plat resistant BRCA mt , any line of therapy (must include prior PARPi)	12.2 (4.1 to 26.2)	5.55 (3.65 to 9.36)	11.14 (7.23 to 16.43)
Cohort 4 (29)	Plat refractory, any BRCA , any line of therapy	6.9 (0.8 to 22.8)	5.31 (5.06 to NA)	8.18 (6.18 to 11.93)

Konstantinopoulos et al; Gynec. Oncol.: 2022

Target indication: platinum resistant ovarian cancer (cohorts 1-3, N = 140)

Observed clinical activity in cohorts 1-3:

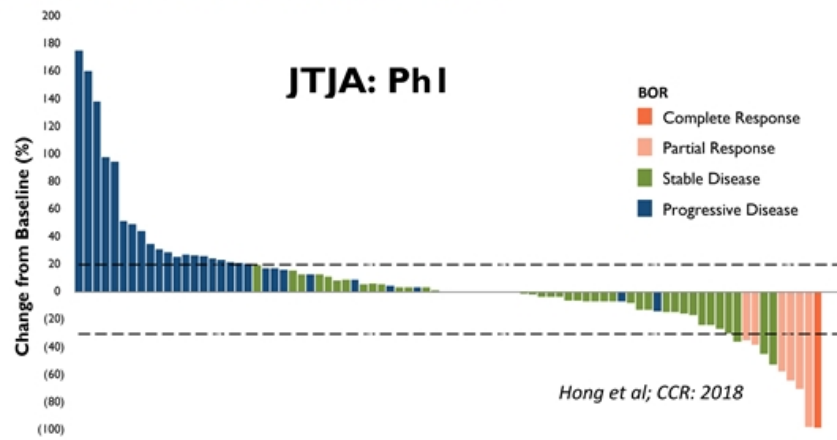
- ORR = 12.1%; DoR = 5.6 months; OS = 11.9 months

Past trials suggest unenriched all-comer ORR in HGS ovarian cancer is ~15-20%

SINGLE AGENT CLINICAL ACTIVITY IN OTHER TUMOR TYPES

ACR-368 activity in other heavily pretreated tumor types (primarily squamous cell cancer SCC):

- 15% ORR in **Anal** (N = 26), incl. 1 CR; mDoR = 12 mths*
- 19% ORR in **HPV+ H&N** (N=16); 5% ORR in all-comer **H&N** (N = 57); mDoR = 7 mths
- (5% ORR plat-sensitive SCLC (N =58); mDoR = 5 mths)

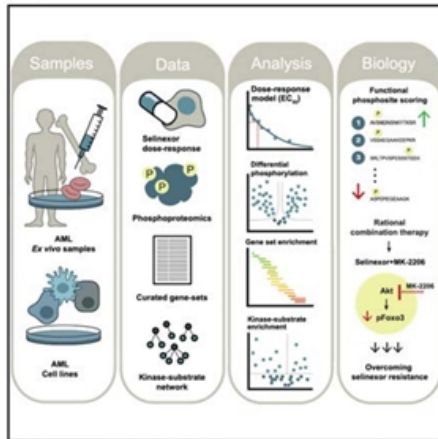


*ACR-368 Orphan Drug Designation for Anal Cancer transferred to Acrivon

Cell Reports

Phosphoproteomics of primary AML patient samples reveals rationale for AKT combination therapy and p53 context to overcome selinexor resistance

Graphical abstract



Authors

Kristina B. Emdal, Nicolás Palacio-Escat, Caroline Wigerup, ..., Kristina Masson, Peter Blume-Jensen, Jesper V. Olsen

Correspondence

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In brief

Emdal et al. combine phosphoproteomics of samples from patients with AML and functional phosphosite scoring to uncover clinically actionable molecular context for selinexor efficacy. Sensitivity to selinexor correlates with functional p53 and is enhanced with nutlin-3a, while resistance is associated with dysregulated AKT-FOXO3 signaling and overcome by combining with MK-2206.

Using spatial phosphoproteomics developed in co-founder Jesper Olsen's lab (*Nat. Commun.*, 2021) Acrivon's AP3 platform uncovers single agent sensitivity and rational drug combination for treatment with Selinexor, a selective inhibitor of nuclear export, in patients with AML

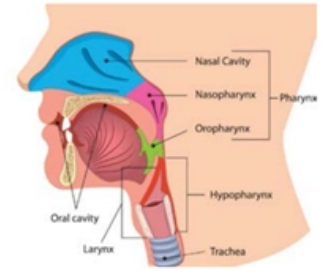
Cell Reports, August 9, 2022

ELI LILLY ACR-368 HIGH LEVEL LICENSE TERMS

- In-licensing completed 27 January 2021
 - WW exclusive rights with rights to sub-license
 - \$5M up front and low single digit percentage equity subject to ordinary dilution going forward
 - Aggregate development and commercial milestone payments of up to \$168M, of which \$5M is due prior to NDA
 - Tiered percentage royalty on annual net sales ranging from low single-digit up to a maximum of 10% subject to certain specified reductions
 - Drug product as well as drug substance sufficient to treat several hundred patients
 - Limited right of first negotiation expiring 45 days upon completion of certain clinical milestones

HPV-POSITIVE CANCERS: STRONG RATIONALE AND INCREASING POTENTIAL MARKET OPPORTUNITY

- Significant upregulation and tumor dependency on DDR in HPV+ cancers
 - Strong preclinical evidence demonstrating activation of Chk1 and Chk2
 - Durable activity of ACR-368 in HPV-positive SCCHN and anal cancer
- **Oral and Oropharyngeal cancer:** 54,000 new cases/year: 50 to 70% HPV+ (SEER 2022)
 - 7,500 new cases of HPV-associated diagnosed in women and about 19,200 diagnosed in men each year
 - 2.7% annual increase in oropharyngeal cancer incidence among men
- **Cervico-vaginal cancers: 90% HPV-related** (CDC 2022)
 - Cervical cancer: 14,100 new cases per year
 - Vulvar cancer: 5,580 new cases
 - Vaginal cancer: 1,370 new cases
- **Anal cancer** 9,090 new cases (6,070 in women and 3,020 in men): 95% HPV-related (SEER 2022)
 - 3% annual increase



Total: 39,000 HPV-associated oropharyngeal, cervical, and anal cancers diagnosed annually, including 23,000 (59%) among females and 15,793 (41%) among males (CDC 2022)