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): April 25, 2023

Acrivon Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-41551**	**82-5125532**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(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 7.01 Regulation FD Disclosure

Beginning on April 25, 2023, Acrivon Therapeutics, Inc. (the "Company") will participate in the Stifel 2023 Targeted Oncology Days Conference taking place virtually. The Company has updated its corporate presentation that it intends to discuss in connection with its fireside chat on Tuesday, April 25, 2023 at 3:00 PM Eastern Time and in meetings with investors during the day. The presentation includes, among other things, an update regarding the Company's pipeline and AP3 platform, 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 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: April 25, 2023

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

Exhibit 99.1

Acrivon Therapeutics

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

CORPORATE PRESENTATION

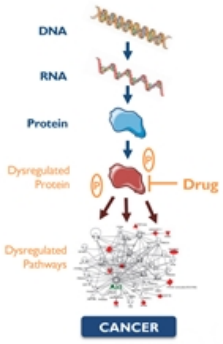
APRIL 2023

ACRIVON THERAPEUTICS: DRUG-TAILORED PATIENT SELECTION

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

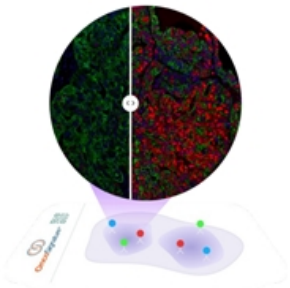
AP3 Platform

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



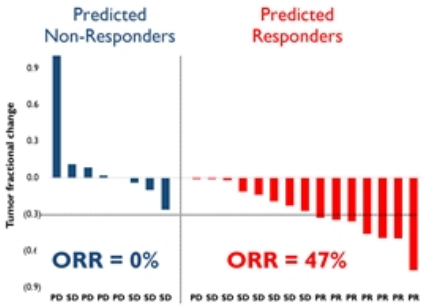
OncoSignature®

- 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%



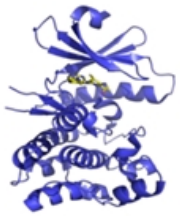
ACR-368 (Prexasertib)

- 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 PKMYT1, 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 1-3 oncology trials

Eric Devroe, Ph.D.
Chief Operating Officer

- Founder and CEO, Opsonix
- 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.
SVP, 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. Cyclerion/Ironwood
- Previously Merck & Co., J&J, Triad Therapeutics
- Multiple recognection 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

MERCK · MERCK SERONO · Daiichi-Sankyo · AMGEN · MIRATI THERAPEUTICS · Pfizer · Biogen · Roche · Shire · Metamark · MD Anderson Cancer Center · SALK INSTITUTE Where cures begin. · BROAD INSTITUTE · The Novo Nordisk Foundation Center for Protein Research

ACRIVON THERAPEUTICS AT A GLANCE

Development Site (Boston)

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

Precision-Proteomics Site (Lund/Copenhagen)

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

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

Peter Blume-Jensen
CEO, President,
Co-Founder

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

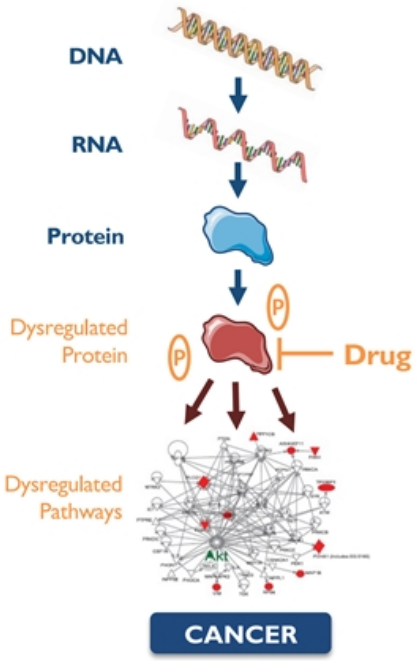
Jesper V. Olsen
Academic Co-Founder.
Novo-Nordisk Foundation
Protein Center, Cph.

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

WELLINGTON MANAGEMENT · SURVEYOR · RACAPITAL · PERCEPTIVE ADVISORS
SANDS CAPITAL · HBM Partners · MARSHALL WACE · PUREOS BIOVENTURES
HealthCor. · acorn BIOVENTURES · ALEXANDRIA Venture Investments · Chione Ltd

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

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*

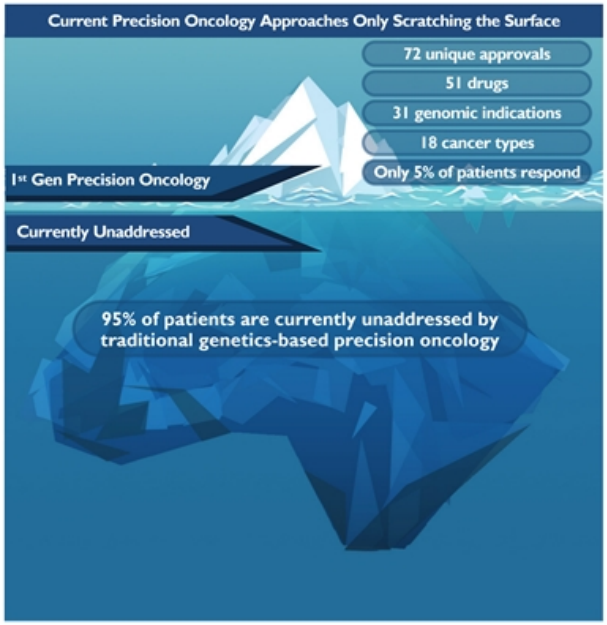
CANCER IS CAUSED BY DYSREGULATED PROTEIN ACTIVITY

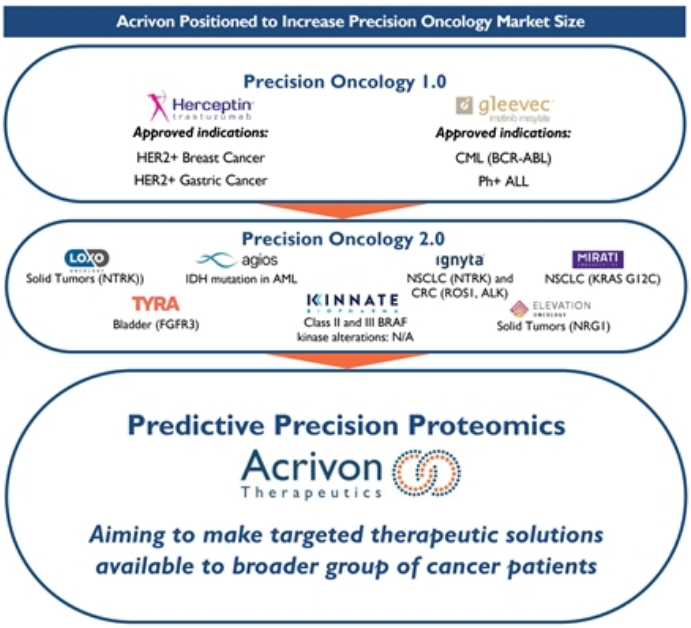
Acrivon's AP3 platform directly measure the disease-driving, dysregulated proteins and is designed to enable an exact match with the drug mechanism-of-action independent of genetic alterations

(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)

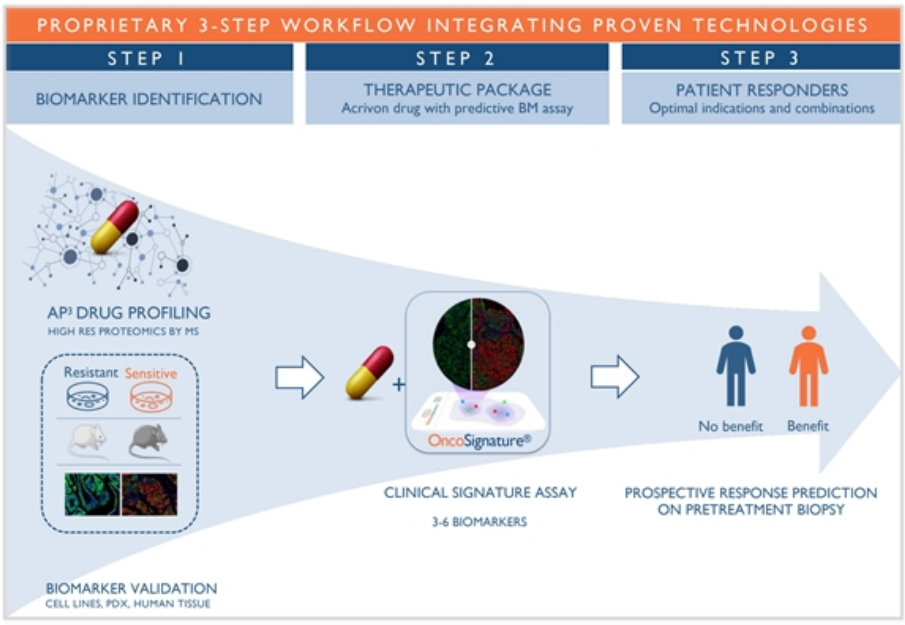
AP3 PLATFORM ADDRESSES HIGH UNMET NEED BEYOND NGS-BASED PRECISION MEDICINE

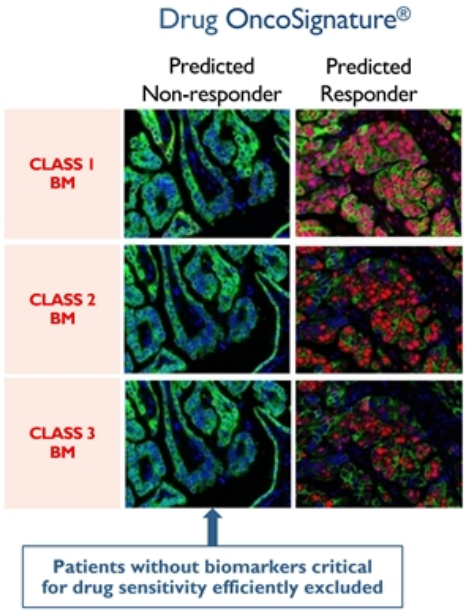




Sources: Company Filings, ACS, CDC, NCI, Wall Street Research

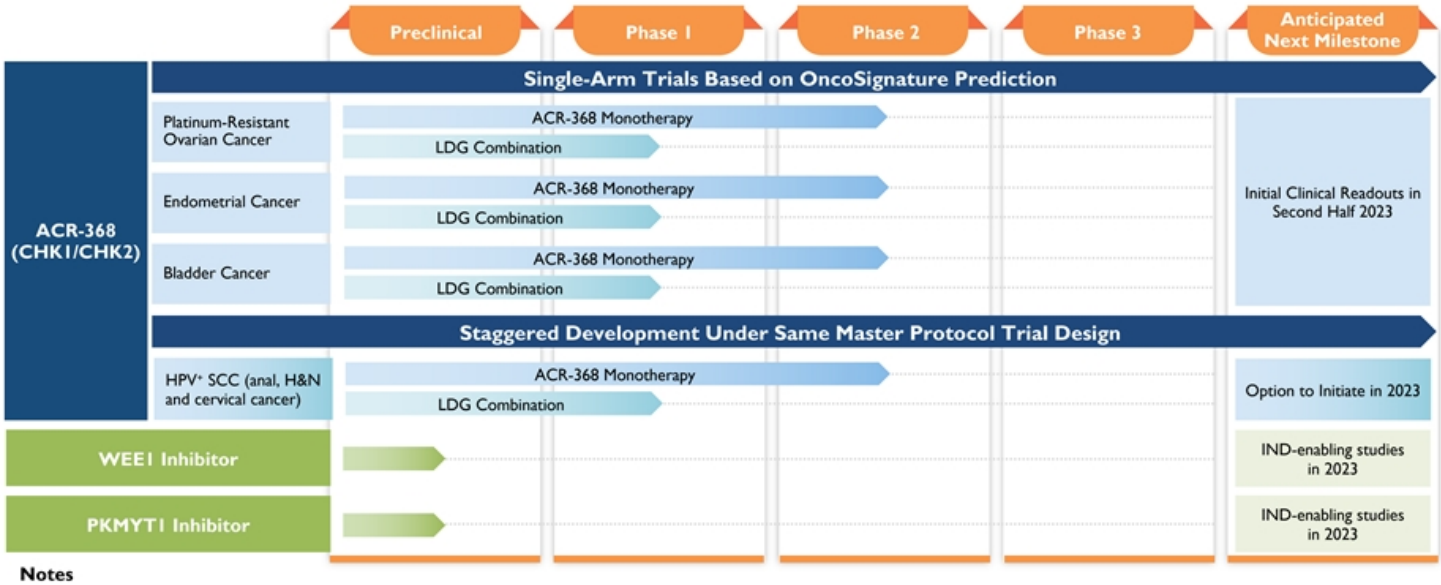
AP3 PLATFORM: DRUG RESPONSE PREDICTION IN INDIVIDUAL PATIENTS





"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. Intl. Reg. 1382289*

ACRIVON PIPELINE

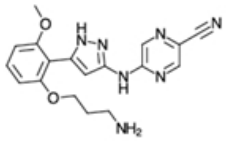


Notes

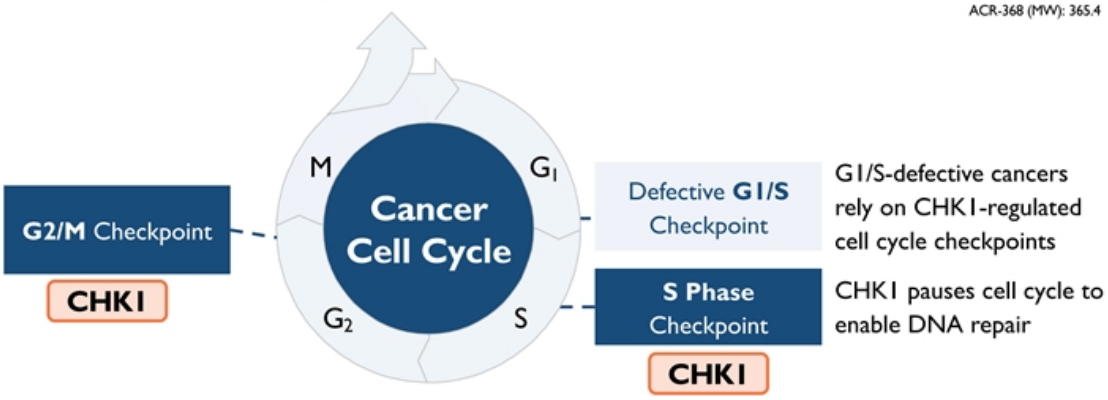
ACR-368 Monotherapy	Registrational intent Phase 2 single arm trials based on predicted sensitivity to ACR-368 monotherapy in OncoSignature-positive patients
LDG Combination	Exploratory Phase 1b/2 single arm trials of ACR-368 in combination with low dose gemcitabine, or LDG, in OncoSignature-negative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

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; °Duration of Response

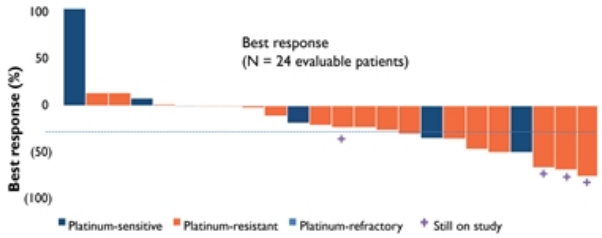
PAST PHASE 2 TRIALS IN HIGH GRADE SEROUS OVARIAN CANCER

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

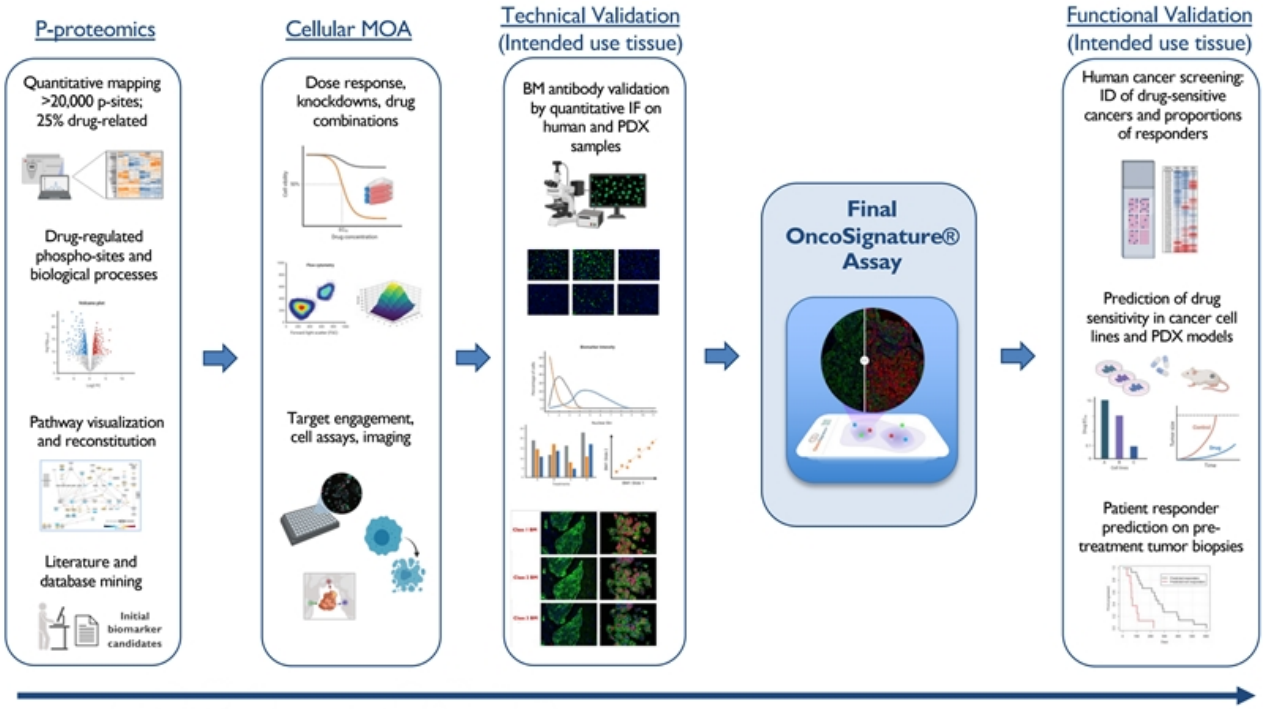
- ORR 12.1% (excl. unconfirmed); mDoR =5.6 months
- No correlation with genetic alterations

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

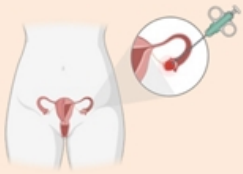
- ✓ Past trials suggest unenriched all-comer ORR in HGS ovarian cancer is ~15-20%
- ✓ Durable clinical activity in most responders
- ✓ No predictive biomarkers identified, need for alternative biomarker approach (ideal for AP3)

DEVELOPMENT OF AP3-BASED PATIENT SELECTION ONCOSIGNATURE® TESTS

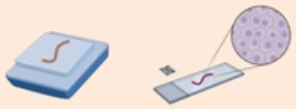


ONCOSIGNATURE® TESTS: USAGE IN THE CLINIC

Pretreatment tumor biopsy

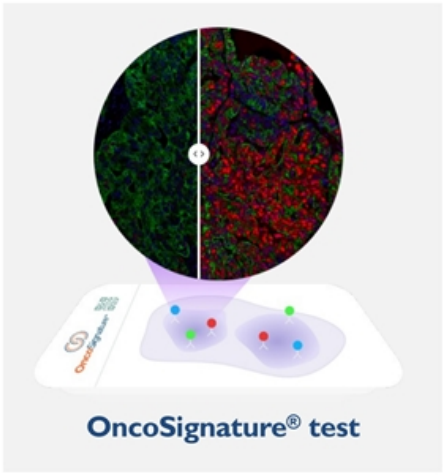


Sample processing



Biopsy in FFPE block

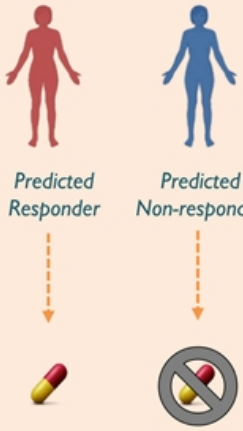
Automated tumor Region-of-Interest biomarker scoring



OncoSignature® test

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

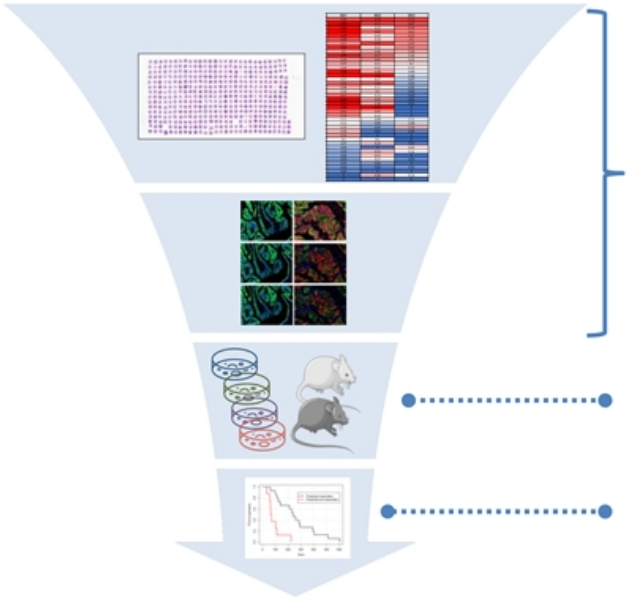
Treatment decision based on patient stratification



Predicted Responder

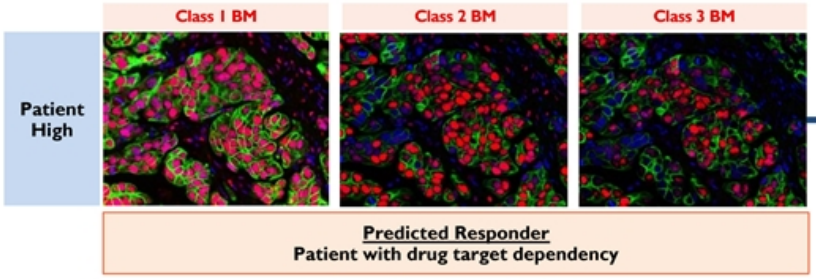
Predicted Non-responder

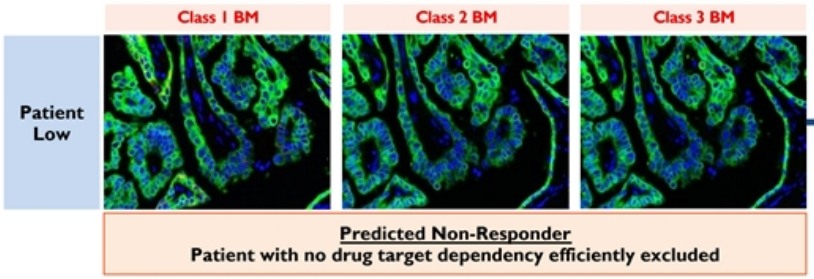
CONSISTENT ACR-368 ONCOSIGNATURE® PERFORMANCE ACROSS PRECLINICAL STUDIES



- 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 ≥ 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

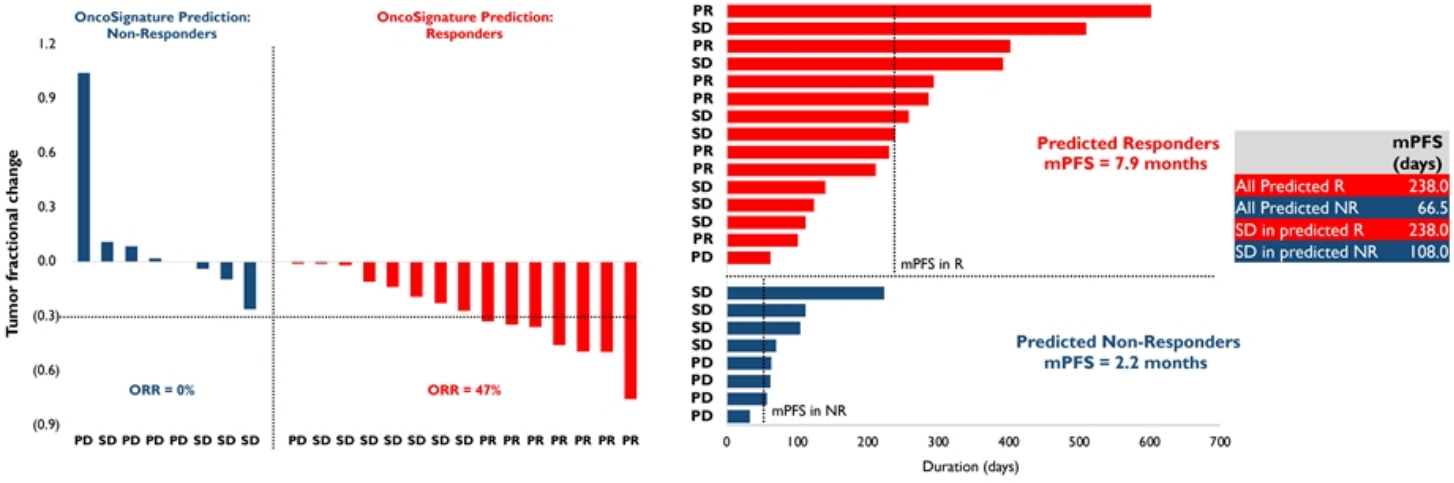




Tissue ID.	BM1	BM2	BM3
Fov060265	0.69	0.79	0.73
Fov050855	0.94	0.71	0.67
Fov041300	0.89	0.23	0.55
Fov060380	0.95	0.62	0.51
Fov060050	0.85	0.23	0.51
Fov041285	0.69	0.19	0.5
Fov100142	0.47	0.76	0.47
Fov050764	0.82	0.22	0.47
Fov041267	0.4	0.36	0.36
Fov100146	0.84	0.57	0.26
Fov060382	0.44	0.45	0.22
Fov041269	0.37	0.21	0.2
Fov060302	0.29	0.22	0.15
Fov020067	0.89	0.38	0.09
Fov100003	0.9	0.89	0.08
Fov050700	0.17	0.17	0.07
Fov050139	0.63	0.66	0.05
Fov041138	0.36	0.11	0.05
Fov060152	0.24	0.3	0.03
Fov030062	0.57	0.14	0.02
Fov060133	0.94	0.43	0.01
Fov050666	0.93	0.38	0.01
Fov060371	0.88	0.93	0
Fov020497	0.61	0.43	0
Fov010706	0.54	0.14	0
Fov020386	0.11	0.09	0.12
Fov050734	0.11	0.06	0.08
Fov040872	0.23	0.04	0.36
Fov050659	0.29	0.01	0.02
Fov060293	0.42	0	0
Fov060210	0.1	0.1	0
Fov050840	0.07	0.29	0.01
Fov040855	0.05	0	0.22
Fov050816	0.04	0.33	0.12
Fov060355	0.04	0.27	0
Fov010252	0.03	0.17	0.02
Fov010682	0.03	0.03	0
Fov060553	0.03	0.02	0.03
71768C3	0.02	0	0
Fov150230	0	0.36	0.12
Fov060308	0	0	0

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 Acrivon and analyzed by **3rd party biostatistician** in **prospectively designed** study

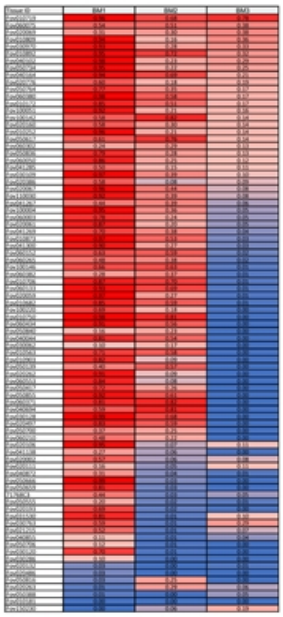


	mPFS (days)
All Predicted R	238.0
All Predicted NR	66.5
SD in predicted R	238.0
SD in predicted NR	108.0

Result: ORR ~47%; mPFS = 7.9 months

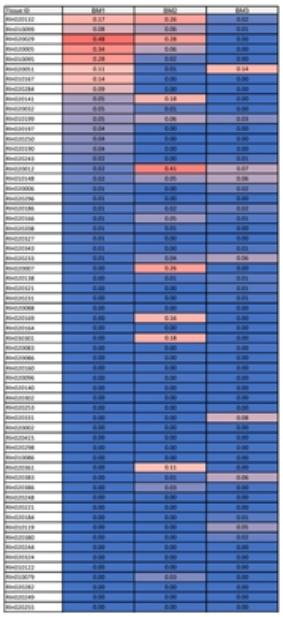
TWO ADDITIONAL HIGH UNMET NEED SOLID CANCERS PREDICTED ACR-368-SENSITIVE THROUGH HUMAN TUMOR SAMPLE SCREENING

HGS Ovarian



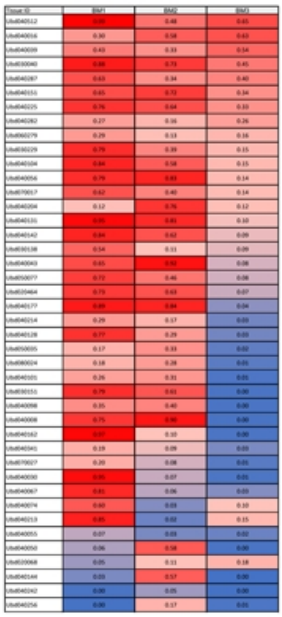
OncoSignature-positive = 30%
(ORR in past trials: 12+% and 29%)

Sq. NSCLC



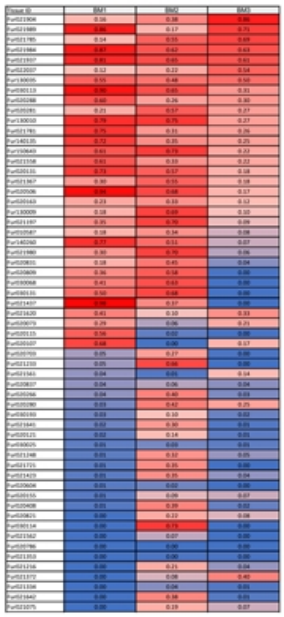
OncoSignature-positive = 0%
(ORR in past trial: 0%)

Bladder cancer



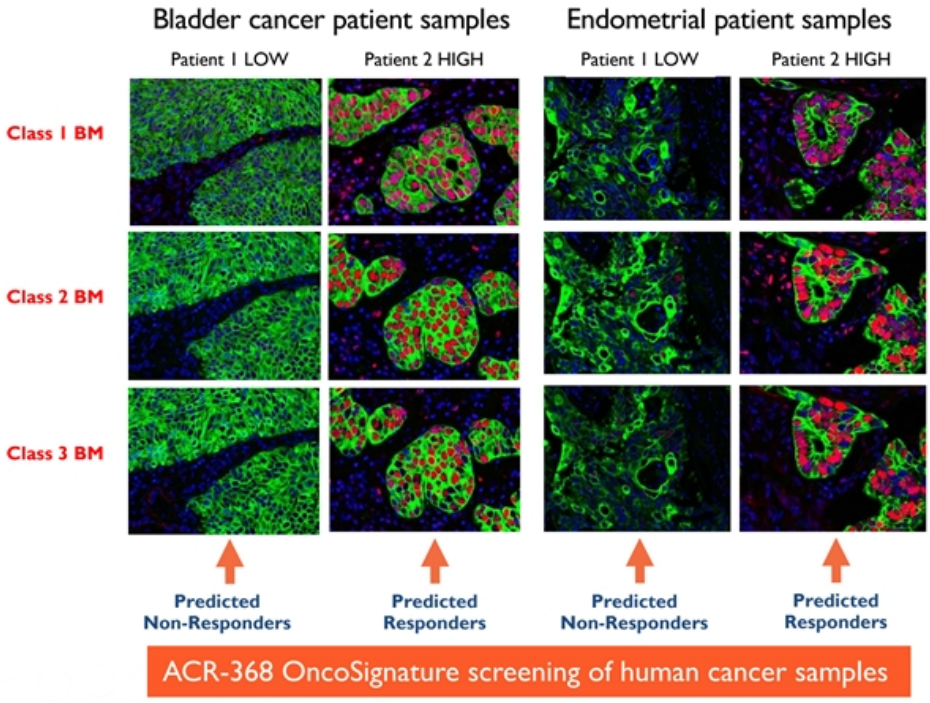
OncoSignature-positive = 30-50%

Endometrial cancer



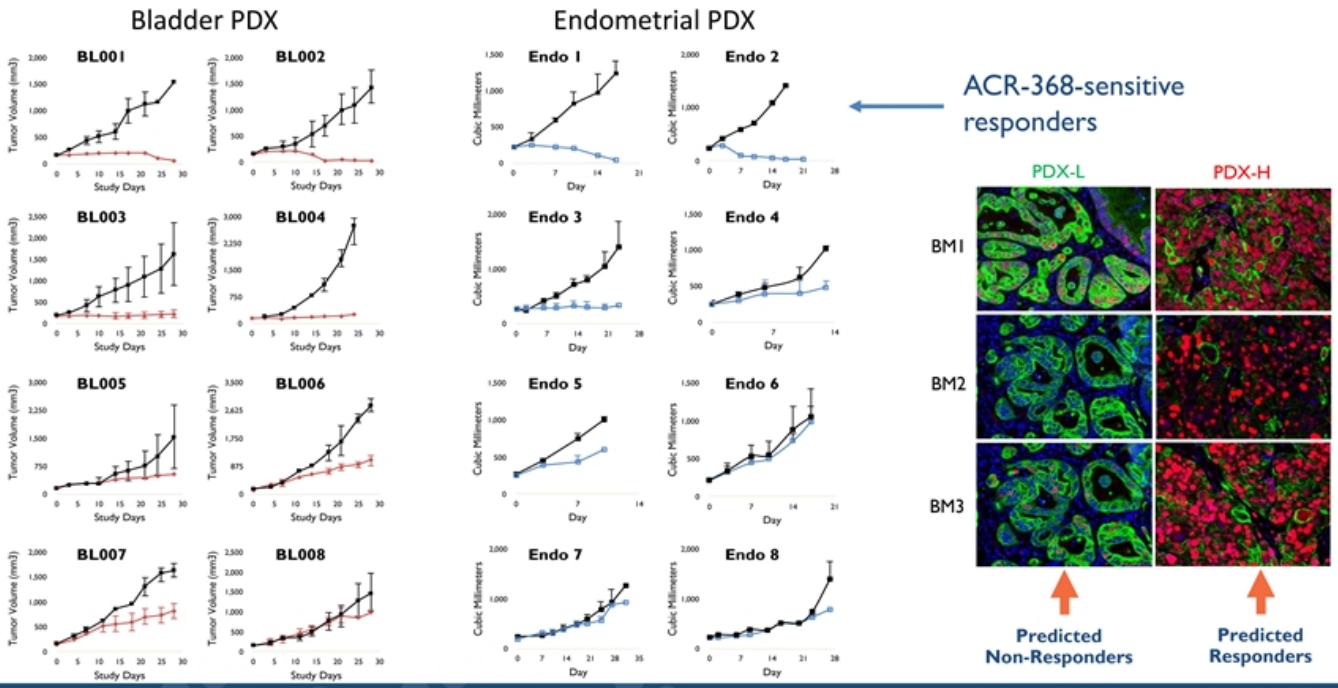
OncoSignature-positive = 30-40%

TWO ATTRACTIVE ACR-368-SENSITIVE CANCER TYPES IDENTIFIED

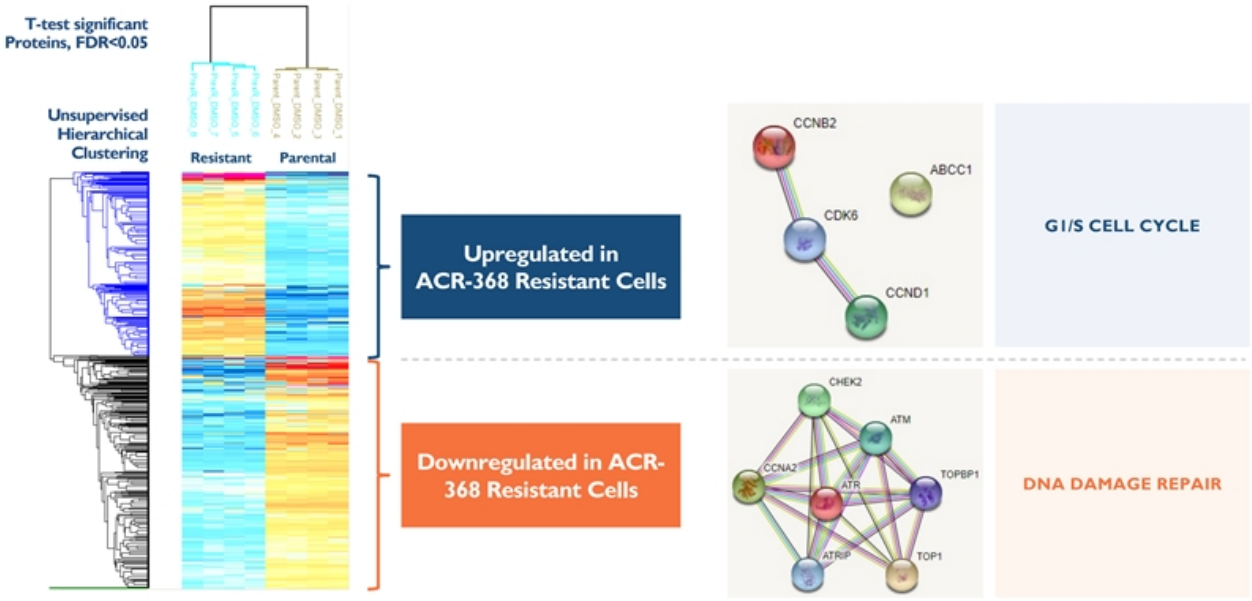


ACR-368 OncoSignature screening of human cancer samples

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

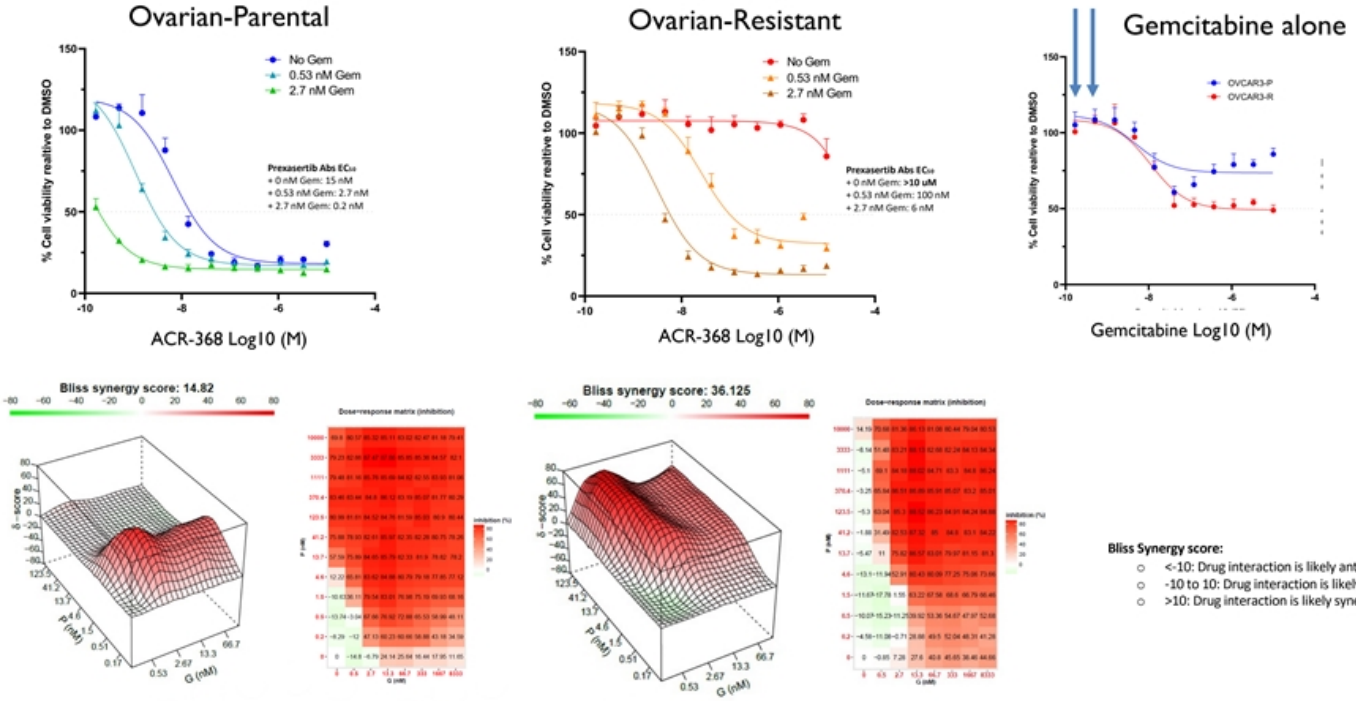


AP3 UNCOVERS ACTIONABLE ACR-368 RESISTANCE MECHANISMS UNBIASED AND INDEPENDENT OF GENETIC INFORMATION



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

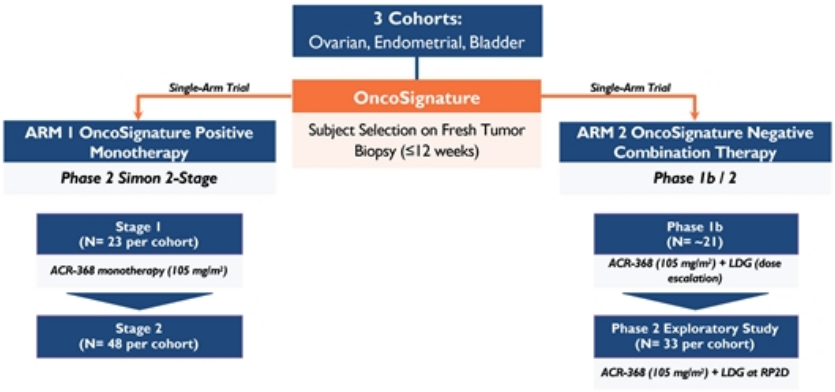
LDG SENSITIZES OVARIAN CANCER CELL LINES TO ACR-368



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




Acrivon

About People Science Pipeline News & Publications Contact & Career

Press Release

Acrivon Therapeutics Receives FDA Clearance for Innovative Phase 2 Trial to Treat Ovarian, Endometrial and Urothelial Cancer Patients Based on Predicted Sensitivity to ACR-368

INTERNAL PIPELINE: WEE1 AND PKMYT1 - LEVERAGING AP3

Rationale

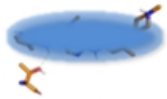
- *Complement to in-licensing, leveraging our AP3 patient selection platform for high clinical POS*
- *Potential within DDR drug target class to pursue combinations (ACR-368, WEE1i, and PKMYT1i)*

WEE1 and PKMYT1 programs

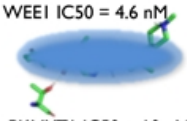
Lead optimization ongoing in several prioritized series based on high resolution co-crystals (WEE1: 2.1-2.6 Å; PKMYT1: 1.65-2.1 Å)

- 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

WEE1 IC50 = 4.6 nM



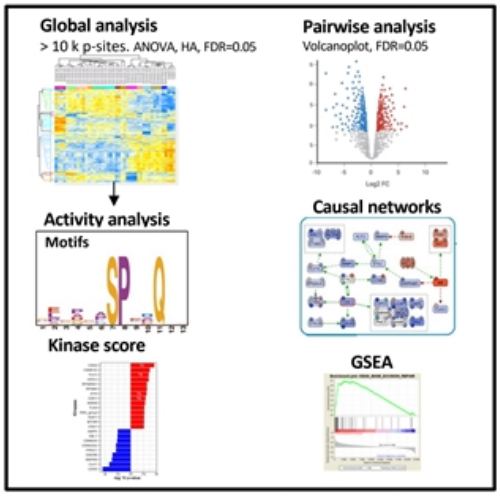
PKMYT1 IC50 = 2.4 nM



PKMYT1 IC50 = 10 nM

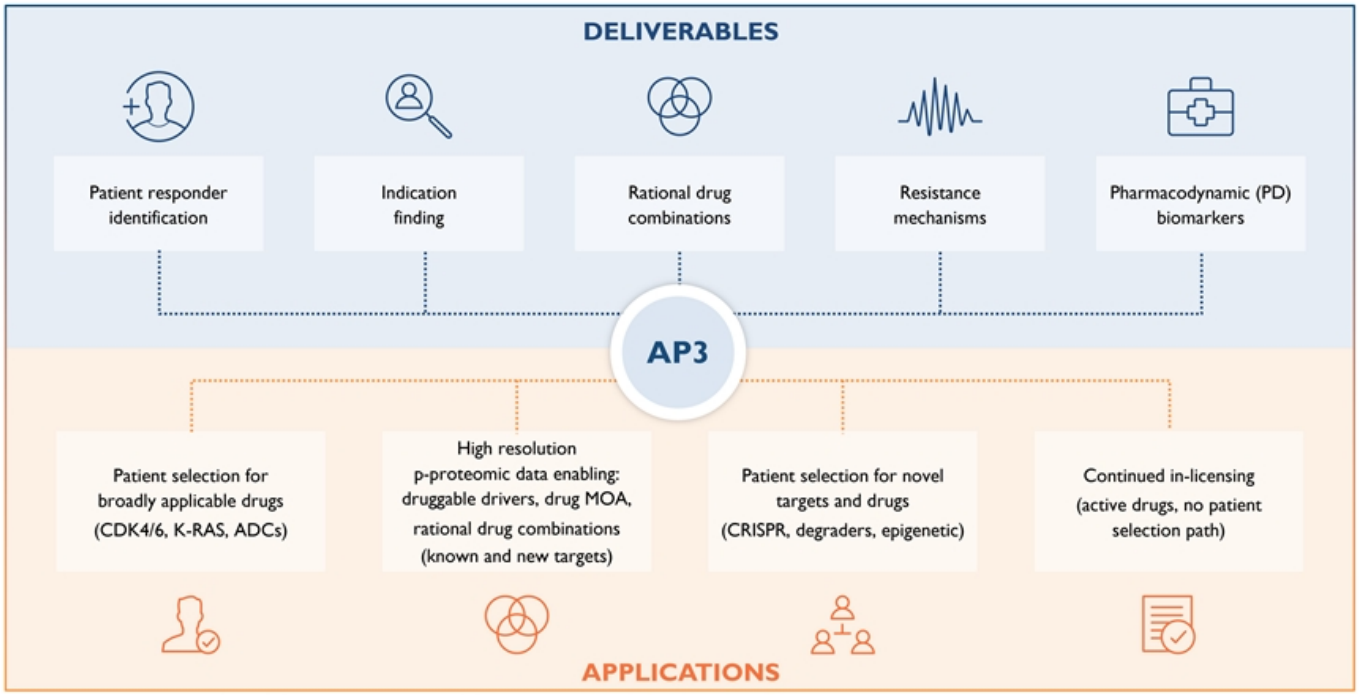
PKMYT1 co-crystallized with a candidate compound

High throughput AP3 profiling

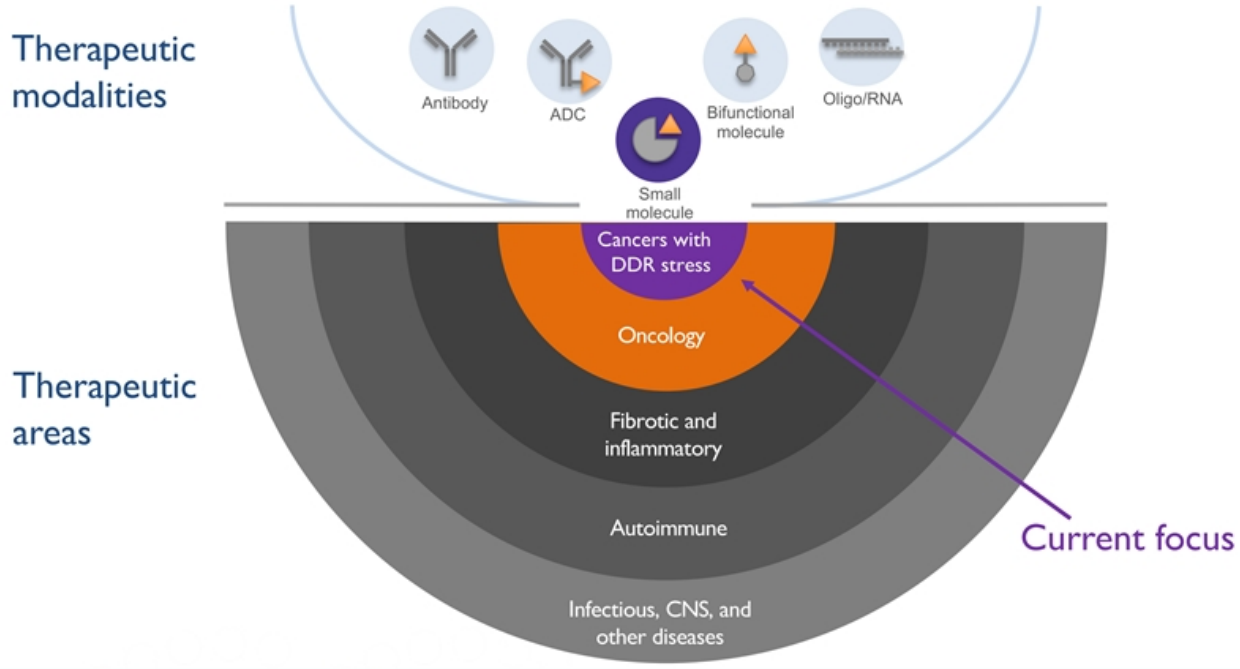


Leveraging AP3 for biologically relevant selectivity profiling

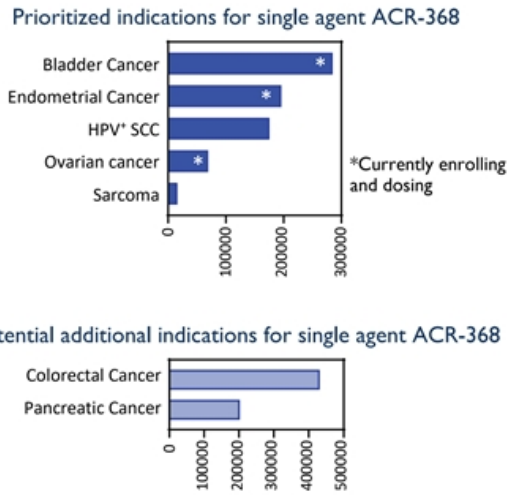
AP3: BROAD APPLICABILITY AND UNTAPPED POTENTIAL

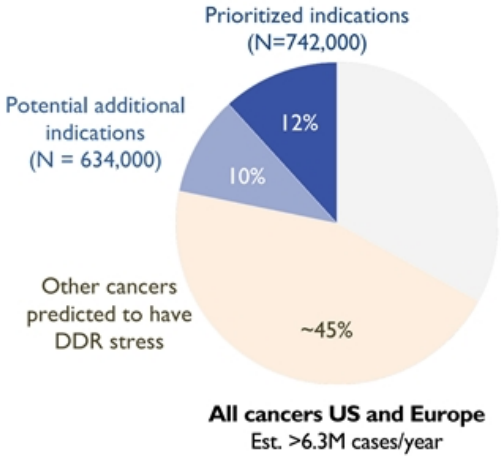


THE AP3 APPROACH IS MODALITY AND DISEASE AGNOSTIC



ACRIVON ADDRESSABLE MARKETS (US & EU INCIDENCE)





All cancers US and Europe
Est. >6.3M cases/year

- ~30% (N = 223,000) of prioritized indications predicted sensitive to single agent ACR-368
- WEE1 and/or PKMYT1 inhibitor combinations with ACR-368 might further expand addressable fraction within sensitive tumor types

US cancer stats are based on ACS 2022 publication and subtype estimation from literature; EU cancer stats are based on IARC 2020 publication and subtype estimation from literature.
Cancers with DDR stress are estimated to be 67% which is calculated from MSK-IMPACT patient samples with DDR relevant mutations and CNVs, such as TP53, KRAS, CCNE1, etc.

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

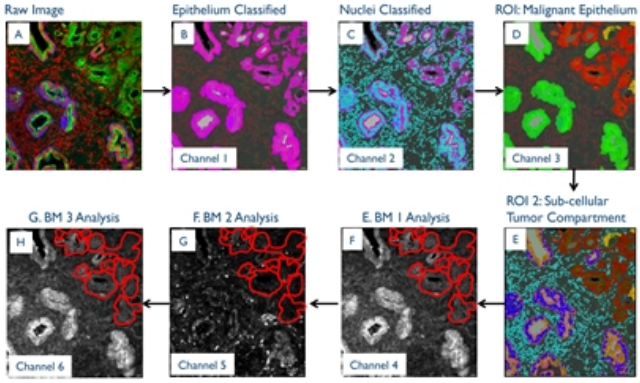
27.0M

Shares and equity grants outstanding 31-December-2022

APPENDIX

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 *in situ* 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

(2015)

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

Peter Blume-Jensen[1], David M. Berman[2], David L. Rimm[3], Michail Shipitsin[1], Mathew Putzi[4], Thomas P. Nifong[1], Clayton Small[1], Sibgat Choudhury[1], Teresa Capela[1], Louis Coupal[5], Christina Ernst[1], Aeron Hurley[1], Alex Kaprelyants[1], Hua Chang[1], Eldar Giladi[1], Julie Nardone[1], James Dunyak[1], Massimo Loda[6], Eric A. Klein[7], Cristina Magi-Galluzzi[8], Mathieu Latour[9], Jonathan I. Epstein[10], Philip Kantoff[6], and Fred Saad[9]

- 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 PI3'K PATHWAY INHIBITOR BIOMARKERS

Science Translational Medicine
AAAS

Sci Transl Med
2: 1-14 (2010)

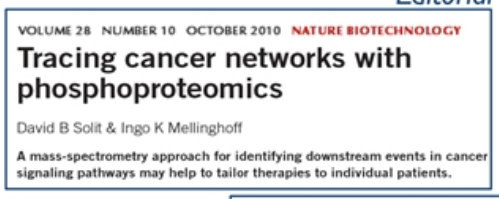
RESEARCH ARTICLE

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,[4,5] Peter Blume-Jensen,[1]§ Cloud P. Paweletz[1]

Editorial Highlights:

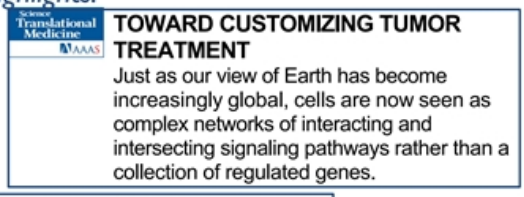


VOLUME 28 NUMBER 10 OCTOBER 2010 NATURE BIOTECHNOLOGY

Tracing cancer networks with phosphoproteomics

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.



Science Translational Medicine
AAAS

TOWARD CUSTOMIZING TUMOR TREATMENT

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.

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

A discovery strategy for novel cancer biomarkers

OLSEN LAB-EXAMPLES OF DEEP PROTEOMICS DRUG PROFILING

Science Signaling (2018)
ALK-i : LDK378, TAE684, crizotinib, lorlatinib.

SCIENCE SIGNALING | RESEARCH RESOURCE

CANCER

Integrated proximal proteomics reveals IRS2 as a determinant of cell survival in ALK-driven neuroblastoma

Cell Reports (2018)
SHP2-i: SHP099 -allosteric inhibitor.

Large-Scale Phosphoproteomics Reveals Shp-2 Phosphatase-Dependent Regulators of Pdgf Receptor Signaling

Cell Reports (2017)
CHK1-i: SCH900776, **ATM-i:** KU55933

Proteomics Reveals Global Regulation of Protein SUMOylation by ATM and ATR Kinases during Replication Stress

Cell Reports (2017)
CDK7-i: THZ-1

Phosphoproteomics of Primary Cells Reveals Druggable Kinase Signatures in Ovarian Cancer

Cell Systems (2017)
Deepest proteome resolution of a human cell to date

An Optimized Shotgun Strategy for the Rapid Generation of Comprehensive Human Proteomes

Cell (2019)
Functional mapping of differential signaling by RPTK mutants

Oncogenic Mutations Rewire Signaling Pathways by Switching Protein Recruitment to Phosphotyrosine Sites

Nature Communications (2020)
Highest throughput, sensitivity, and scalability to date

ARTICLE OPEN

Rapid and site-specific deep phosphoproteome profiling by data-independent acquisition without the need for spectral libraries

Nature Communications (2021)
Subcellular compartmental proteomics

ARTICLE OPEN

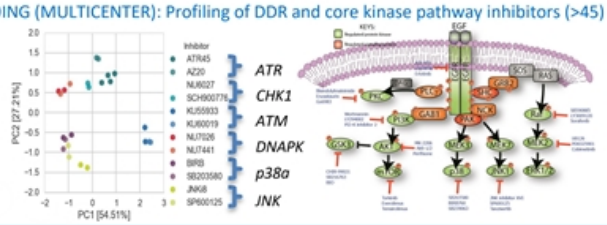
Spatial-proteomics reveals phospho-signaling dynamics at subcellular resolution

Nature Communications (2021)
Clinically actionable resistance mechanisms

ARTICLE OPEN

Proteomics of resistance to Notch1 inhibition in acute lymphoblastic leukemia reveals targetable kinase signatures

ONGOING (MULTICENTER): Profiling of DDR and core kinase pathway inhibitors (>45)



ADVISORS AND COLLABORATORS

SAB

George Demetri, M.D., FACP, FASCO, FAACR

Professor, Harvard Med. School, Dir. Dana-Farber Cancer Institute & Ludwig Center, Boston

- Leader in Precision Oncology
- Key contributor to development and rapid approvals of Gleevec, Sutent, Stivarga, Zelboraf, Votrient, and Yondelis

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EVP, Head Cancer Biology, Odyssey Therapeutics

Adj. Prof. , Burnham Inst. Adj. Prof. UCSD

- Expert in signal transduction-based R&D
- Previously SVP and WW Head, Oncology R&D, Pfizer
- VP, Oncology Res., Wyeth
- Professor, Burnham Institute
- Professor, Duke University

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Associate Prof., MD Anderson Cancer Center, Medical Director, Inst. for Applied Cancer Science

- Expert on DDR accelerated clinical development and predictive biomarkers
- Previously oncologist Royal Marsden, London and Inst. Cancer Res, London
- Lead/P.I. on numerous DDR trials

David Berman, M.D., Ph.D.

Professor, Director, 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

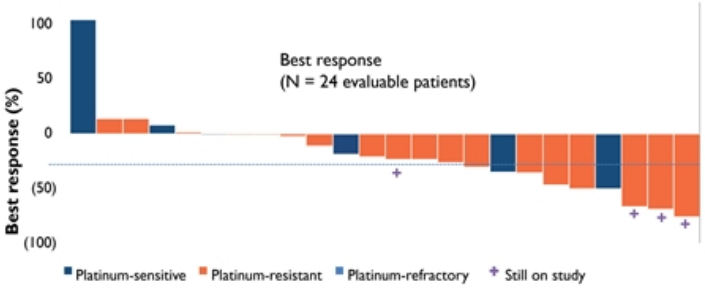
- Expert on women's cancers and DNA damage response (DDR)
- Lead and co-PI on numerous HGSOC &TNBC trials
- Lead PI on ACR-368 platinum-resistant ovarian trials

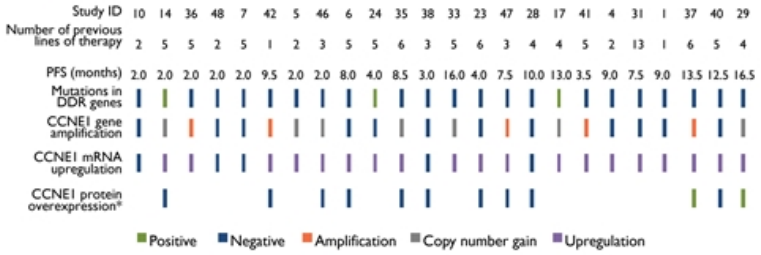
NATIONAL CANCER INSTITUTE (NCI) TRIAL IN HIGH GRADE SEROUS OVARIAN CANCER

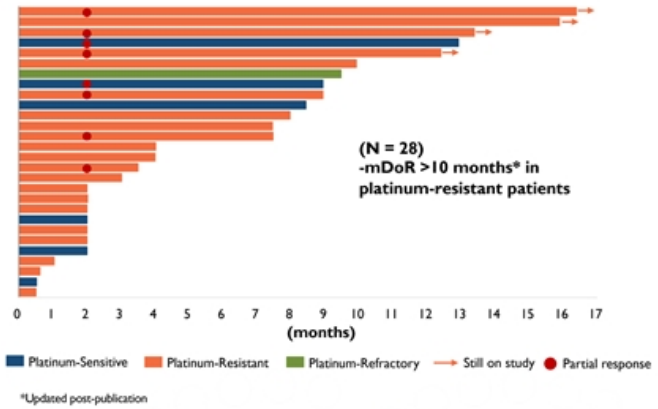
- Single-arm, Phase 2 POC study (Dr. Jung-Min Lee)
- N=28 (21 platinum resistant, 6 sensitive, 1 refractory)
- Heavily pre-treated; median of 5 prior systemic therapies
- Pretreatment biopsies mandated

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:

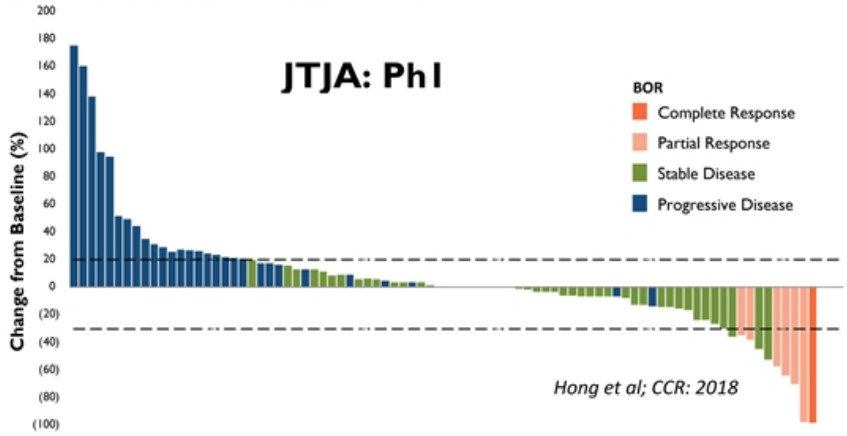
- ORR = 12.1%; DoR = 5.6 months; OS = 11.9 months

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)



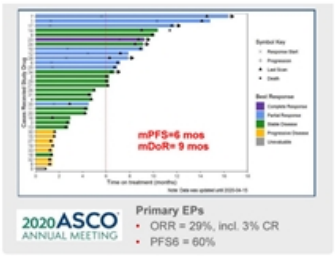
**ACR-368 Orphan Drug Designation for Anal Cancer transferred to Acrivon*

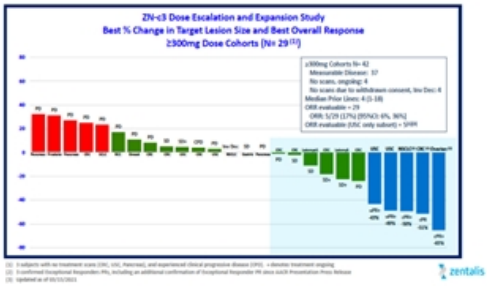
WEE1 PROGRAM: IDEAL FOR THE AP3 PLATFORM

- 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/MK1775/adavosertib (AstraZeneca)
  - Debio0123 (Debiopharm)
  - ZN-c3 (Zentalis Pharmaceuticals)

Targeting WEE1 kinase in Cancer, TrendsPharmSci, 2016





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

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

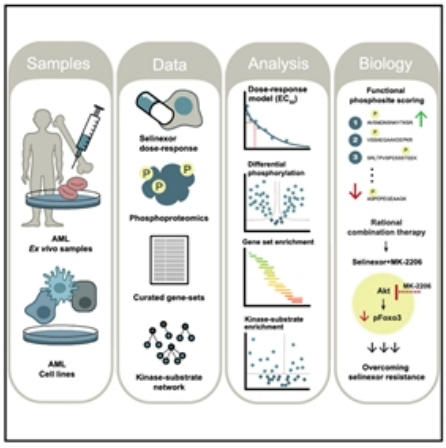
AP3 PHOSPHOPROTEOMICS PROOF-OF-CONCEPT STUDY

Article

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, Nicolàs Palacio-Escat, Caroline Wigerup, ..., Kristina Masson, Peter Blume-Jensen, Jesper V. Olsen

Correspondence

pub.saez@uni-heidelberg.de (J.S.-R.), kmasson@acrivon.com (K.M.), pblumejensen@acrivon.com (P.B.-J.), jesper.olsen@cpr.ku.dk (J.V.O.)

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

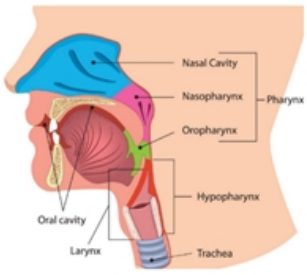
ELI LILLY ACR-368 HIGH LEVEL LICENSE TERMS

- 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 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)