



**Innovative Precision Medicine
for Serious Conditions Of
Unmet Medical Need in
Oncology**

FEBRUARY 2022

Forward-Looking Statements

Nuvectis Pharma, Inc.

Certain statements in this presentation constitute “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. Statements other than those of historical fact, as well as those statements identified by words such as “anticipate,” “estimate,” “intend,” “plan,” “expect,” “project,” “believe,” “may,” “will,” and “should,” “would,” “could,” and “probable,” or any variation of the foregoing and similar expressions, are forward-looking statements. Such statements also include, but are not limited to, any statements relating to our plans to submit one or more Clinical Trial Authorization and Investigational New Drug Application for NXP800, the potential timing and advancement of our clinical trial and preclinical studies for NXP800 and NXP900, and statements regarding the potential differentiation of NXP900, including a potentially favorable profile as compared to the currently available or in development SRC kinase inhibitors, statements relating to the unique mechanism of action of NXP800 and NXP900 translating into potential enhanced efficacy, any statements relating to our growth strategy, product development programs and commercial prospects. Forward-looking statements are based on management’s current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: the ongoing impact of the COVID-19 pandemic and mitigation efforts by governments and regulatory authorities; the risk that regulatory authorities will not accept an application to start clinical trials of NXP800 and NXP900 based on preclinical data; risks relating to our growth strategy and commercial prospects; our ability to obtain, perform under and maintain financing and strategic agreements and relationships; risks relating to the results of research and development activities; risks relating to the timing of starting and completing clinical trials, including the recently initiated Phase 1 clinical trial of NXP800; uncertainties and risks relating to preclinical and clinical testing including safety findings; our dependence on third-party suppliers; our ability to attract, integrate and retain key personnel; the early stage of products under development; our need for substantial additional funds; government regulation; patent and intellectual property matters; competition; as well as other risks described in our Securities and Exchange Commission filings. Therefore, you should not rely on these forward-looking statements. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law, and we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.



**Innovative Precision Medicine
for Serious Conditions of
Unmet Medical Needs in
Oncology**



Key Highlights

Management team with proven track record of clinical and regulatory success and significant shareholder value creation

Novel pipeline of precision targeted therapy drug candidates

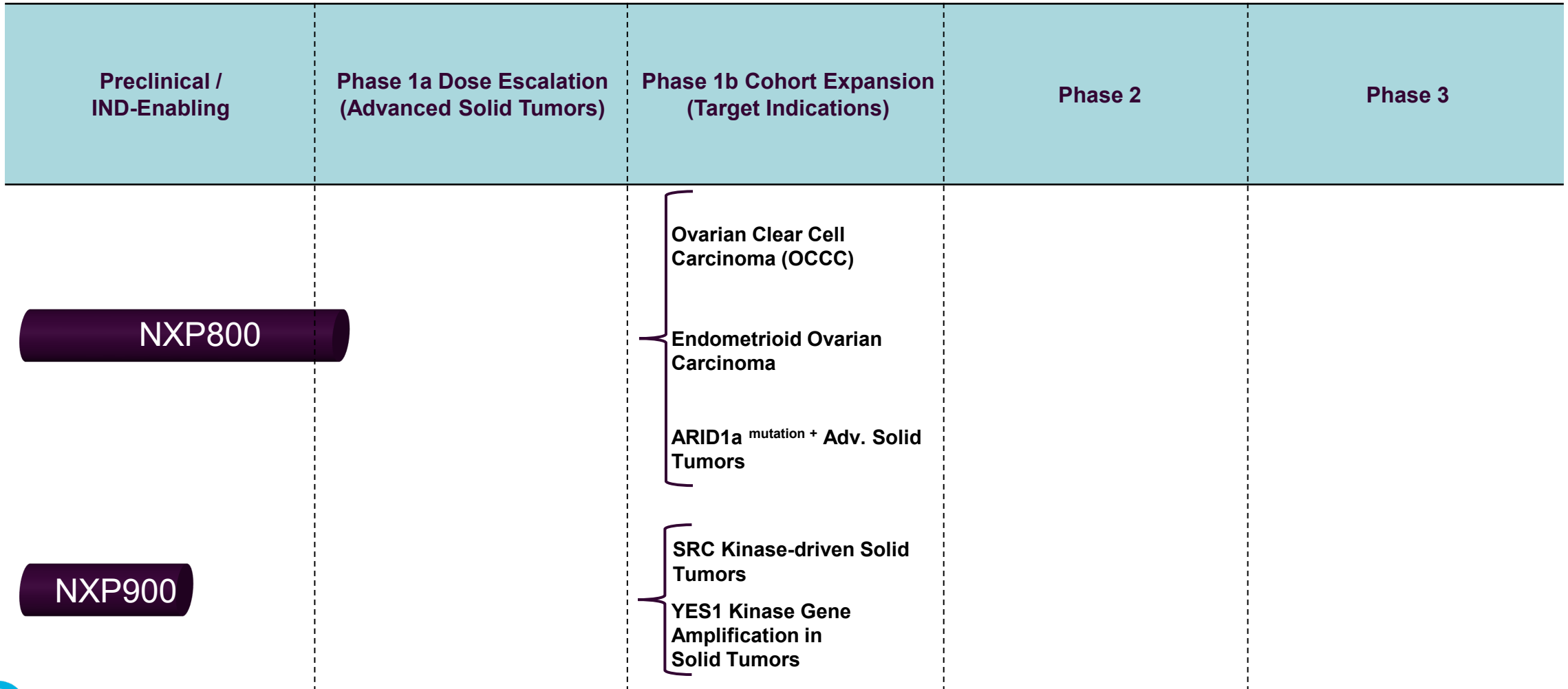
- NXP800: A potent clinical-stage HSF1-pathway inhibitor; development opportunities in several ARID1a-mutated solid tumors
 - NXP900: A novel SRC/YES1 kinase inhibitor
-

Strong **IP position**

Composition of matter and use patents issued in all key jurisdictions for both drug candidates

Nuvectis Pipeline

Unique precision-medicine drug candidates



Leadership Team

Track Record of Success

Leadership Team Achievements (Last 10 Years)

4 FDA approvals
2 EU approvals
1 approval in
Japan (via partner)

2 Breakthrough Therapy
Designations in oncology.
Multiple Orphan Drug
Designations (US/EU) and
Fast Track Designations (US)

Significant
shareholder value
creation

Successful Ex-US
partnerships and US
commercial infrastructure
buildouts and drug
launches

The team led the approvals of the following drugs:

Auryxia[®]
(ferric citrate) tablets

 **ELZONRIS**[®]
(tagraxofusp-erzs) Injection

Jelmyto[®]
(mitomycin)

NXP800

**A Novel HSF1-Pathway
Inhibitor**

About NXP800

NXP800

Key Highlights

Discovered and optimized at the Institute of Cancer Research (ICR) in the UK.

The ICR discovered Zytiga, a leading drug for metastatic prostate cancer.

Unique, novel molecule targeting a well-characterized biologic pathway with established relevance in oncology: Heat Shock Factor 1 (HSF1).

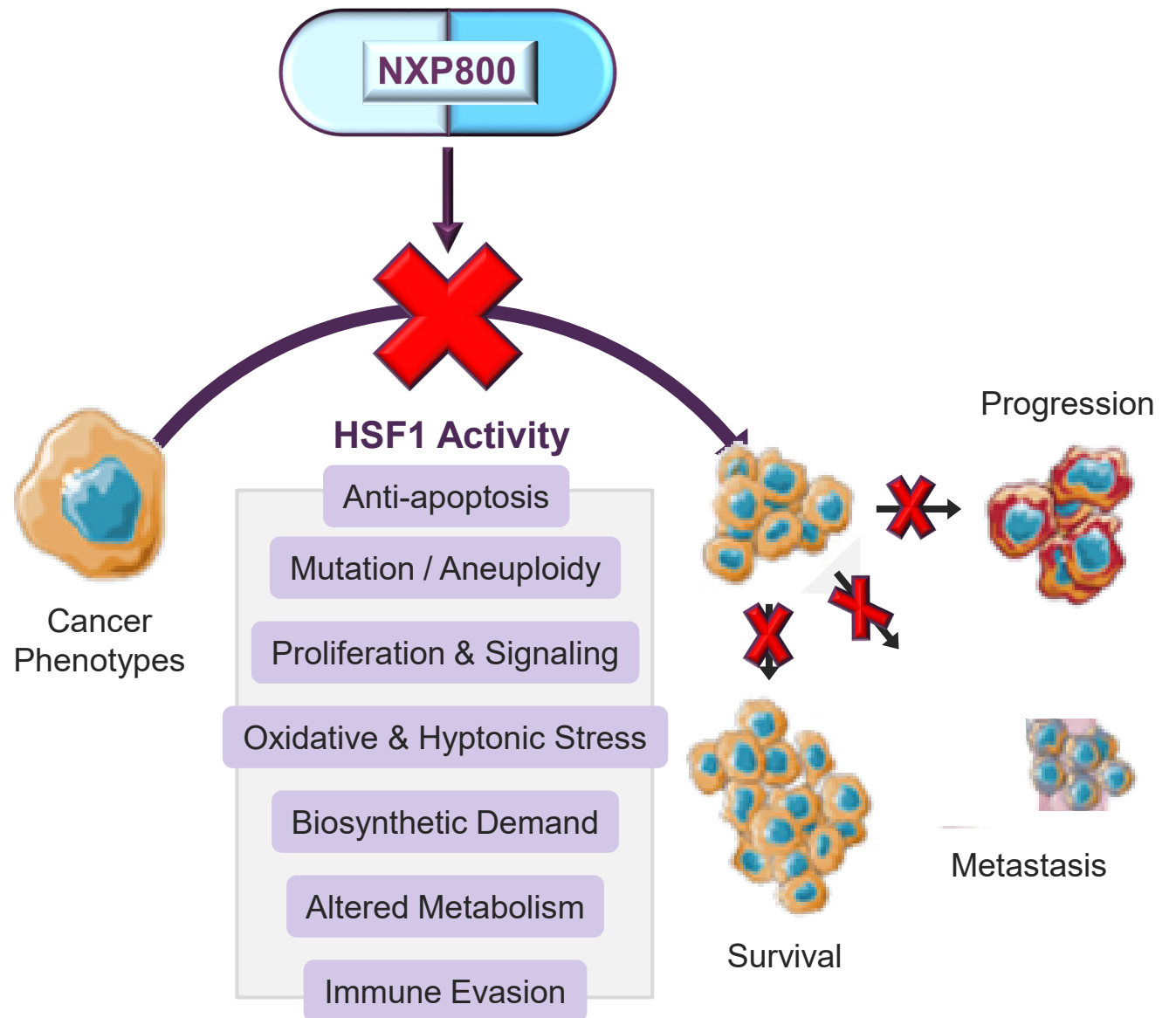
Substantial tumor growth inhibition demonstrated in ovarian clear cell carcinoma (OCCC) and endometrioid cancer xenograft models.

- ARID1a was mutated in these models, providing a marker for patient selection in clinical trials; HSF1-ARID1a synthetic lethality effect observed.
- ARID1a is mutated in multiple solid tumor types, potentially enabling a genetic mutation-based/tumor agnostic development opportunity.

Targeting the HSF1 Pathway in Oncology

HSF1 pathway addiction – enables cancer cells to overcome diverse stresses and promote biological activities crucial for cancer survival, progression, immune evasion and metastasis.

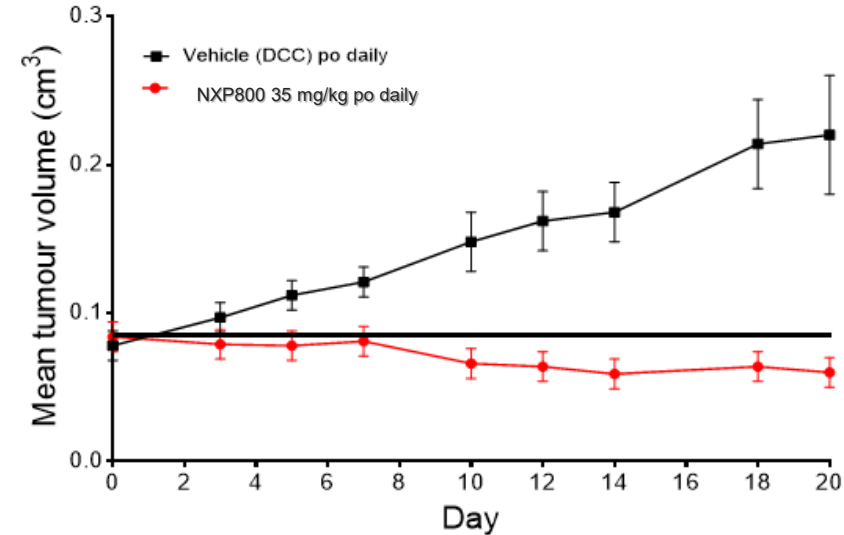
- Master transcription factor regulating protein homeostasis and survival in response to proteotoxic stresses.
- HSF1 also regulates a distinct gene expression pattern in response to “**oncogenic stress**”.



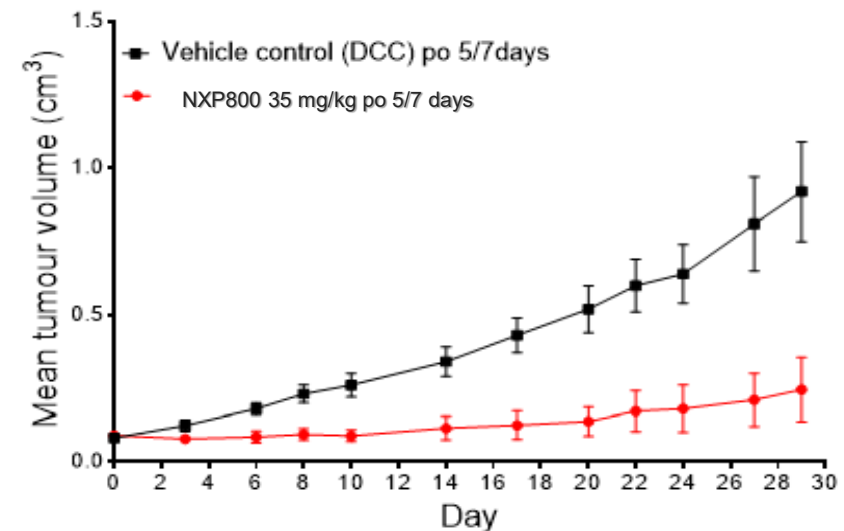
Adapted from Dong 2019. *Inhibiting Heat Shock Factor 1 in Cancer: A Unique Therapeutic Opportunity*. Trends in Pharmacological Sciences.

NXP800 Demonstrated Substantial Antitumor Activity in OCCC Xenografts with the ARID1a Mutation

Model 1: SKOV-3



Model 2: TOV-21G



NXP800 Clinical Development Plan

Phase 1a (Commenced in December 2021)

- Accelerated dose escalation (i.e., begin with single-patient cohorts)
- Objectives: Evaluation of safety and tolerability, and recommendation of dose and dosing schedule for Phase 1b

Phase 1b

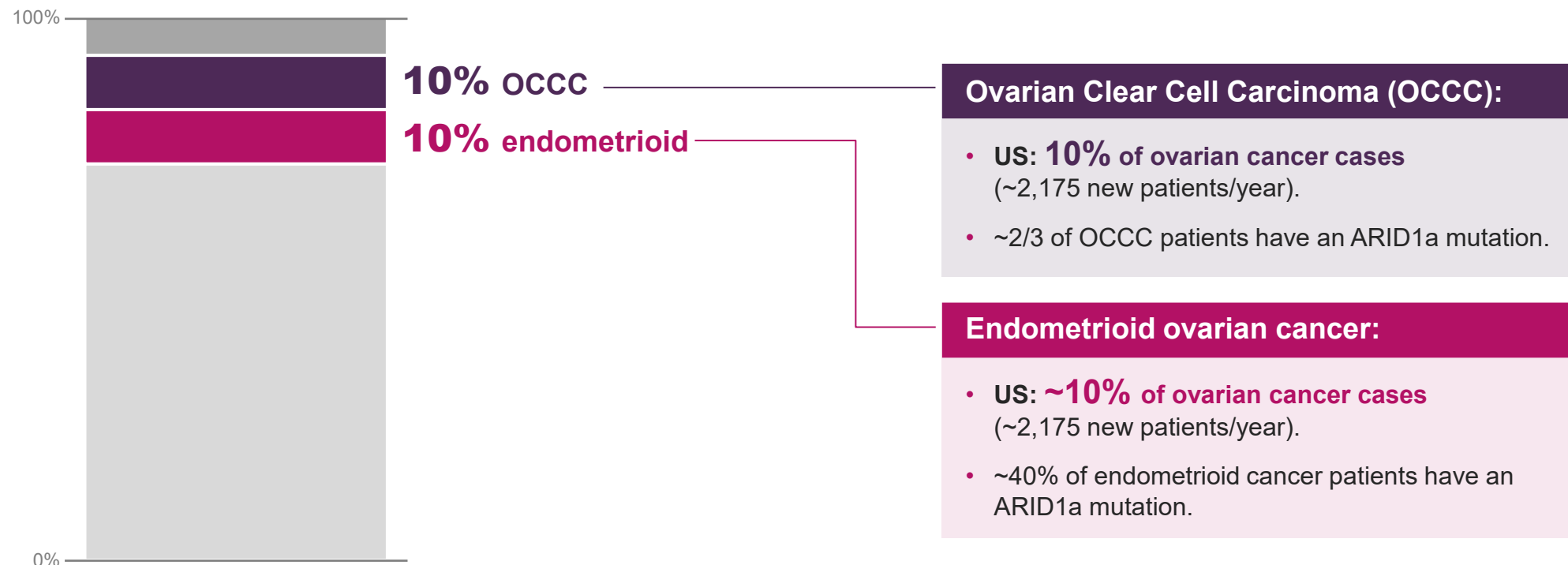
- OCCC and endometrioid ovarian cancer cohorts
- Objectives: preliminary efficacy, confirmation of dose and dosing schedule
- Potential for additional patient cohorts with the ARID1a mutation

OCCC and endometrioid Ovarian Cancer

Serious Conditions of Unmet Medical Needs

- Limited treatment options, low response rate to chemotherapy treatment poor prognosis.
- The American Cancer Society estimates that approximately 21,410 women will receive a new diagnosis of ovarian cancer in the United States in 2021 (<https://cancerstatisticscenter.cancer.org/#!/cancer-site/Ovary>).

Ovarian Cancer Net Incidence by Type



Significant Potential in Additional Tumor Types

Patient-selection strategy

ARID1a is a common genetic mutation that can potentially be used as a patient selection strategy in a variety of solid tumor types.

- The ARID1a mutation detection assay is a standard part of the commercially available screening panels.
- Broad in-vivo testing program ongoing to identify additional tumor types for clinical testing

Indication	Estimated Incidence (US)	Estimated Number of Patients with ARID1a protein loss (US)
Ovarian Clear Cell Carcinoma	2,175	1,410
Endometrioid Carcinoma	2,175	909
Uterine endometrioid	66,570	26,628
Urothelial	75,357	25,621
Hepatocellular	34,000	9,070
Gastric	26,550	6,615
Pancreatic	60,430	4,230
Esophageal	19,260	2,120

NXP800

A Novel HSF1-Pathway Inhibitor

First in class HSF1-pathway inhibitor

HSF1 activation implicated in several solid tumors.

Focused clinical/regulatory strategy

Phase 1 initiated, accelerated dose escalation

Broad Potential in ARID1a mutated patients in OCCC,

Endometrioid Ovarian, uterine endometroid, urothelial, hepatocellular, gastric, pancreatic and esophageal

NXP900

A Novel SRC / YES1 inhibitor

About NXP900

NXP900

Key Highlights

Novel, Selective and highly potent SRC/YES1 kinase inhibitor discovered at the University of Edinburgh, Scotland.

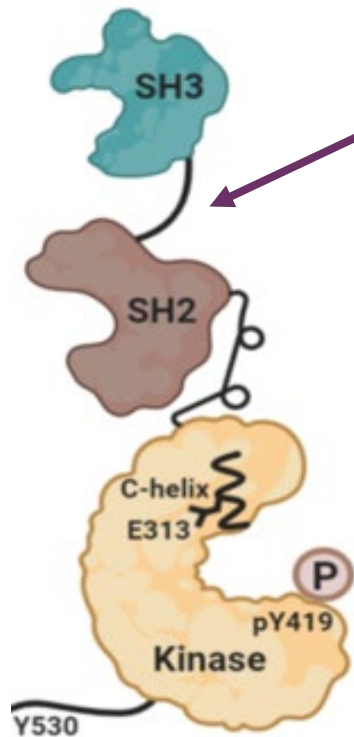
NXP900 is clearly differentiated from other SRC/YES1 inhibitors, due to:

- Unique MoA providing for the complete shutdown of the SRC signaling pathway
 - High selectivity without immune suppression effect
-

IND-enabling studies ongoing

SRC / YES1 Kinase Signaling

SRC-mediated signal transduction involves catalytic and scaffolding activities



Scaffold Domain

SH2 and SH3 domains of SRC kinase family members constitute a scaffold to which other pro-oncogenic signaling molecules are recruited inducing pro-oncogenic signals

Catalytic Domain

SRC kinase family members (such as Src and Yes1) transmit pro-oncogenic signals via phosphorylation of downstream targets

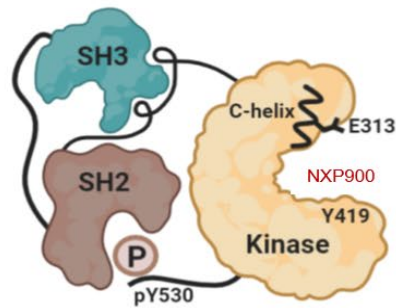
Complete shutdown of SRC signaling requires inhibition of both the catalytic and scaffold activities

NXP900

Novel and Differentiated Mechanism of Action

NXP900

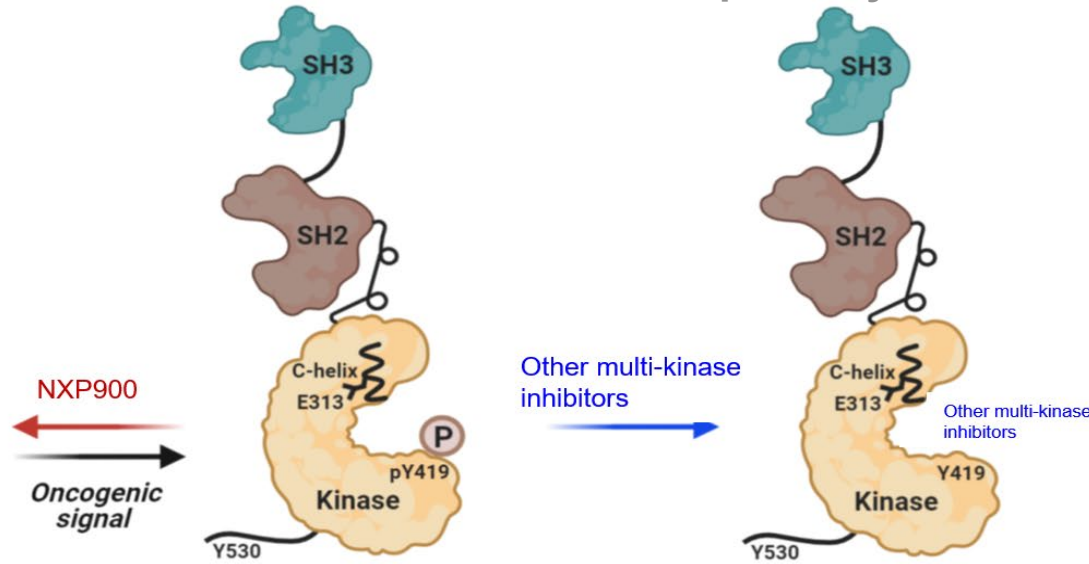
Complete shutdown of the SRC pathway



Closed conformation locked by
NXP900

No inhibitor

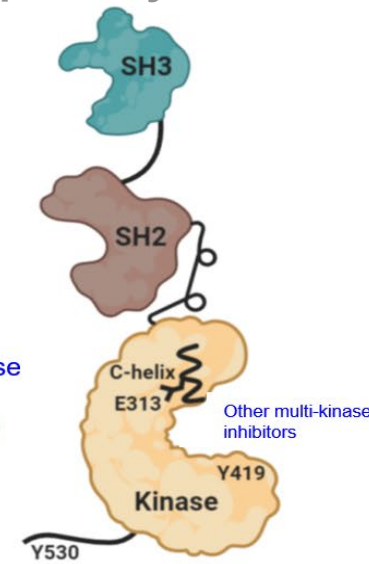
Fully active SRC



Open conformation
no inhibitor

Other multi-kinase inhibitors

Partial shutdown of the SRC pathway



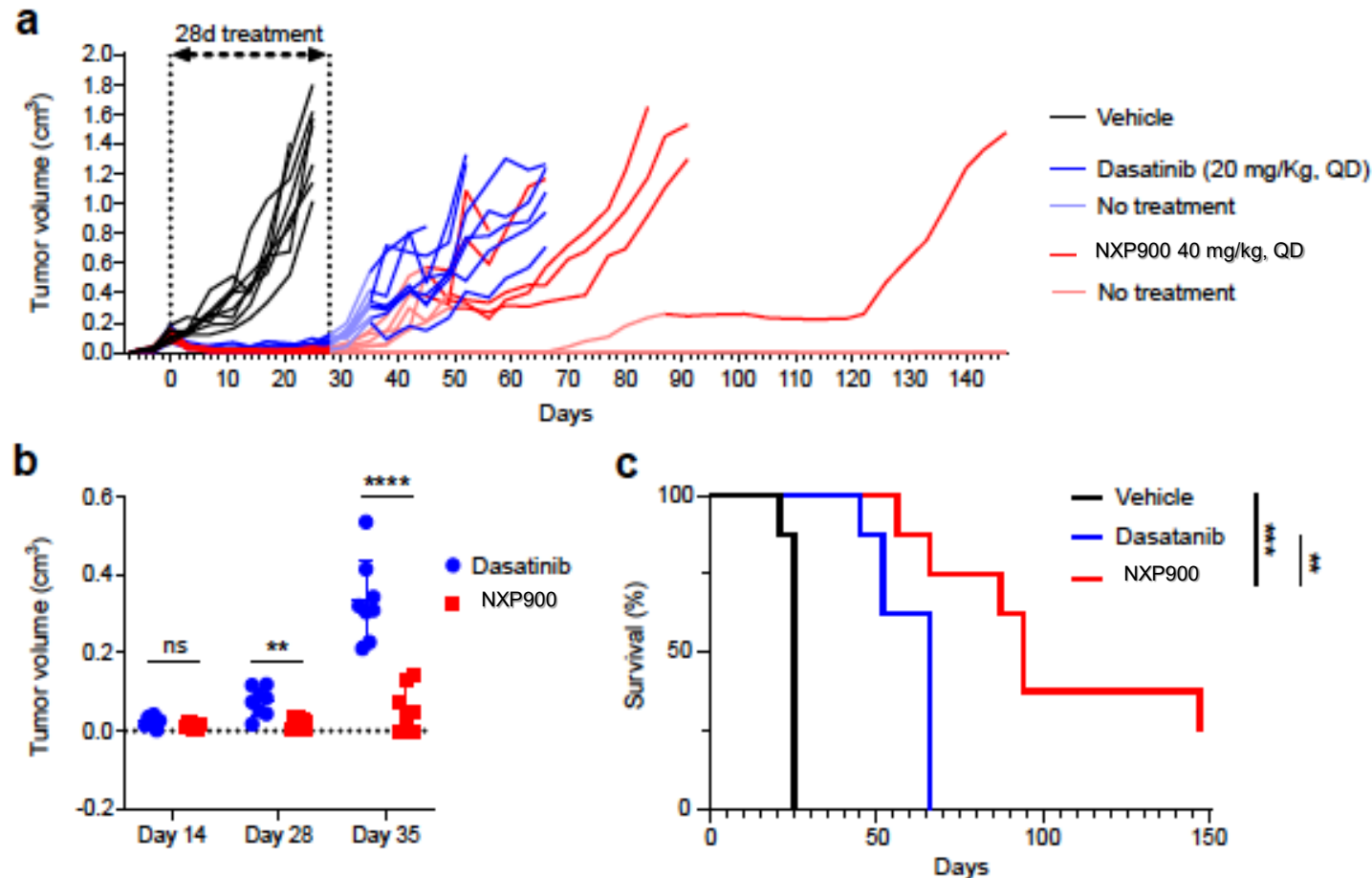
Open conformation stabilized by
other multi-kinase inhibitors

NXP900 in TNBC

Superior Preclinical Activity vs. Approved Compound

A Conformation Selective Mode of Inhibiting SRC Improves Drug Efficacy and Tolerability

Carolin Temps¹, Daniel Lietha², Emily R. Webb¹, Xue-Feng Li³, John C. Dawson¹, Morwenna Muir¹, Kenneth G. Macleod¹, Teresa Valero¹, Alison F. Munro¹, Rafael Contreras-Montoya¹, Juan R. Luque-Ortega², Craig Fraser¹, Henry Beetham¹, Christina Schoenherr¹, Maria Lopalco⁴, Mark J. Arends¹, Margaret C. Frame¹, Bin-Zhi Qian⁵, Valerie G. Brunton¹, Neil O. Carragher¹, and Asier Unciti-Broceta¹



NXP900 inhibited tumor growth in an orthotopic model of triple negative breast cancer (TNBC) in immunocompetent animals, showing superiority vs dasatinib, and substantial long-term effect after treatment completion.

A,B) Comparative analysis of tumor volumes vs dasatinib

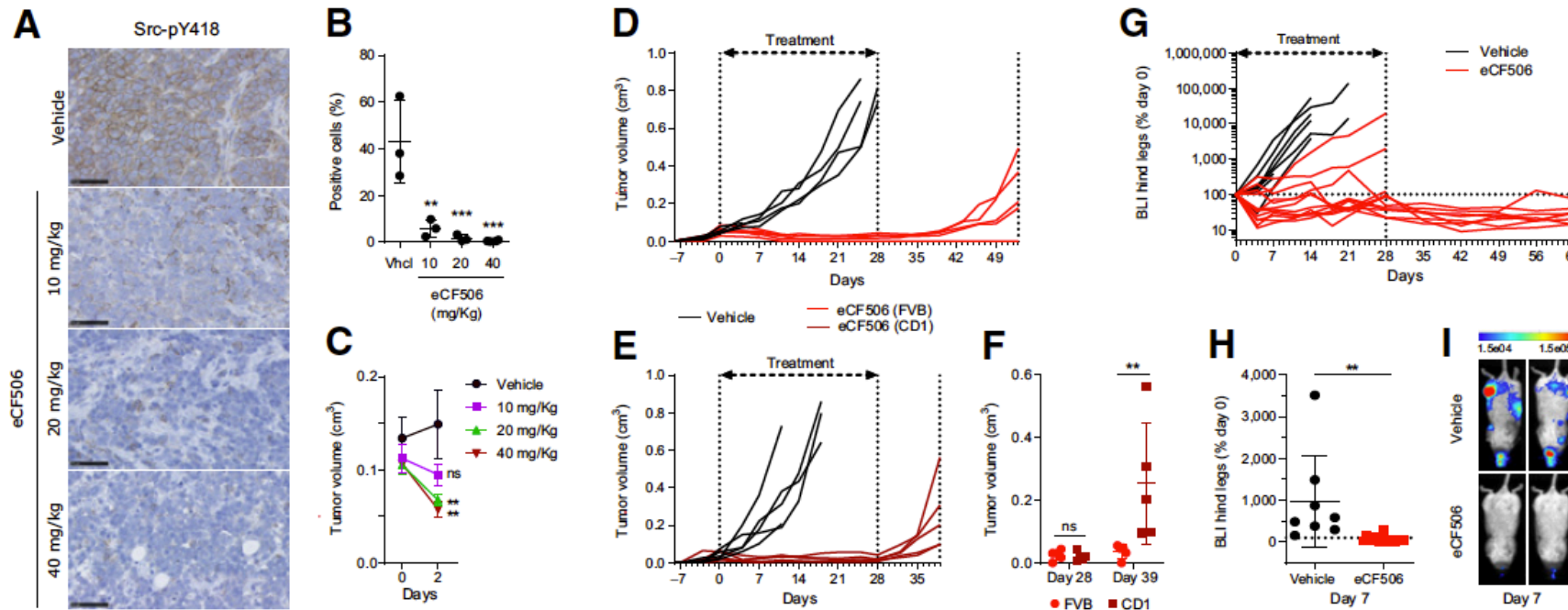
C) Kaplan-Meier Survival analysis.

NXP900 in TNBC (Con't)

Eradication of TNBC-induced bone metastatic lesions

A Conformation Selective Mode of Inhibiting SRC Improves Drug Efficacy and Tolerability

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- A) IHC - pY418 inhibition.
- B) Quantitative analysis of SRC-pY418
- C) Tumor volume, days 2 vs 0
- D) In vivo study in FVB immunocompetent mice
- E) In vivo study in CD1 immunocompromised mice
- F) Tumor volume - end of treatment
- G) In vivo study of bone metastasis inhibition
- H) Comparative analysis of bone metastasis at day 7
- I) Bioluminescence images of two representative mice at day 7 (bone metastasis experiment)

* eCF506 = NXP900

► No immunosuppression - lymphocyte infiltration observed in NXP900 treated tumors

YES1 Gene Amplification

Patient-selection strategy

YES1 gene amplification can potentially be used as a patient selection strategy in a variety of solid tumor types.

- Detection assay is a standard part of the commercially available screening panels.

Indication	Estimated Incidence (US)	Estimated Number of Patients with YES1 Gene Amplification (US)
Esophageal squamous cell carcinoma	5,778	364
Esophageal adenocarcinoma	13,482	768
Head and neck squamous cell carcinoma	65,410	3,336
Lung squamous cell carcinoma	31,584	1,421
Bladder urothelial carcinoma	75,357	3,316
Sarcoma	13,460	404
Ovarian serous cystadenocarcinoma	14,987	450

NXP900

Addresses the Shortcomings
of Other SRC/YES1 Inhibitors

NXP900 provides an opportunity to treat solid tumors with a SRC/YES1 inhibitor

SRC (overactivation) and YES1 (gene amplification) are implicated in several solid tumors.

However, the existing multi-kinase SRC/YES1 inhibitors, including dasatinib, which is approved for CML/ALL, have only shown modest activity in solid tumors.

Unique mechanism of SRC inhibition enables complete shutdown of the SRC pathway.

Avoids the immunosuppressive effects demonstrated with dasatinib and other SRC inhibitors - a major disadvantage in solid tumors.

Crosses the BBB, opportunity in brain metastasis and pediatric medulloblastoma, where SRC is implicated



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Conditions of Unmet
Medical Needs in Oncology**



Key Highlights

- **Management team** with a proven track record of clinical and regulatory success
 - 4 FDA approvals
 - 2 EU and 1 Japanese (via partner) approvals
 - Significant shareholder value creation
- **Unique pipeline** of rationally-designed precision targeted therapies
 - NXP800: A potent, clinical stage HSF1-pathway inhibitor
 - NXP900: A novel SRC/YES1 kinase inhibitor
 - Strong IP position
- **Significant news flow** expected over the next 12 months



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