Nuvectis Pharma, Inc.

Innovative Precision Medicine for Serious Conditions of Unmet Medical Need in Oncology

September 2024

NuvectisPharma, Inc.

(NASDAQ: NVCT)

Forward Looking Statements

Nuvectis Pharma, Inc.

Certain statements in this presentation constitute “forward-looking statements" within the meaning of the federal securities laws, which statements are subject to substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this press release are forward-looking statements. Forward-looking statements contained in this press release may be identified by the use of words such as "anticipate," "believe," "contemplate," "could," "estimate," "expect," "intend," "seek," "may," "might," "plan," "potential," "predict," "project," "target," "aim," "should," "will," "would," or the negative of these words or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements are based on Nuvectis Pharma, Inc.'s current expectations, estimates, and projections about future events and trends that we believe may affect our business, financial condition, results of operations, prospects, business strategy, and financial needs. The outcome of the events described in these forward-looking statements are subject to inherent uncertainties, risks, assumptions, market and other conditions, and other factors that are difficult to predict and include statements regarding the potential benefits of the Orphan Drug Designation granted to NXP800, the preclinical and the Phase 1a data generated to date for NXP800 and the clinical expectations for the NXP800 Phase 1b study, including statements regarding NXP800's mechanism of action and its potential ability to become a therapeutic option for the treatment of platinum-resistant, ARID1a-mutated ovarian carcinoma, cholangiocarcinoma, and potentially other cancer indications, and the timing for this study. Further, certain forward-looking statements are based on assumptions as to future events that may not prove to be accurate. These and other risks and uncertainties are subject to market and other conditions and described more fully in the section titled "Risk Factors" in our 2Q 2024 Form 10-Q and our other public filings with the Securities and Exchange Commission ("SEC"). However, these risks are not exhaustive and new risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward looking statements contained in this press release or other filings with the SEC. Any forward-looking statements contained in this press release speak only as of the date of this press release. 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 may be 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.

Nuvectis Pharma – Key Highlights

Our Approach to Precision Medicine

- Select and acquire novel, rationally-designed drug candidates
- Focus on drug development for serious conditions of unmet need in oncology

NXP800

- Ongoing clinical trials:
  - ARID1a-mutated, platinum resistant ovarian carcinoma (Fast Track Designation, Orphan Drug Designation)
  - Cholangiocarcinoma (Orphan Drug Designation)

NXP900

- Phase 1a dose escalation ongoing
- Potential indications: YES1/SRC-driven solid tumors, Cancers of squamous cell origin, ALK positive / EGFR-mutated NSCLC (combination)

Management Team with Strong Track Record

- 3 approved drugs in 4 indications in the US and EU and multiple strategic deals
- Cash runway into 2H2025

Management Team

Track record of success

Ron Bentsur
Chairman & Chief Executive Officer

Enrique Poradosu, PhD
Chief Scientific & Business Officer

Shay Shemesh
Chief Development & Operations Officer

Auryxia® (ferric citrate) tablets

Jelmyto® (mitomycin)

ELZONRIS® (tagraxofusp-erzs) Injection

KERYX BIOPHARMACEUTICALS, INC

UroGen Pharma

Stemline®

Nuvectis Precision Medicine Pipeline

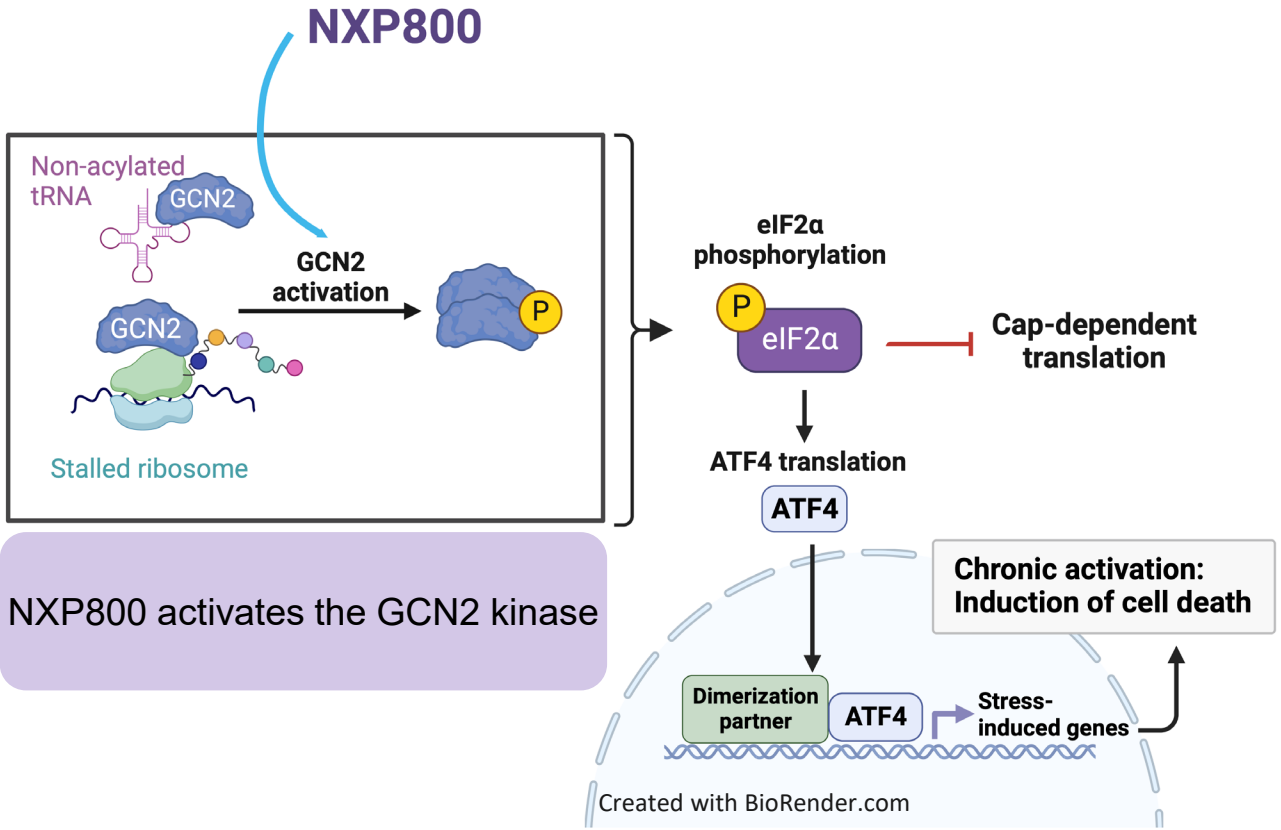
DRUG CANDIDATE	INDICATION	DISCOVERY / LEAD OPTIMIZATION	IND ENABLING	PHASE 1A	PHASE 1B	COLLABORATIONS
NXP800 [a] (GCN2 activator)	**ARID1a mutated ovarian cancer** • Ovarian clear cell carcinoma • Ovarian endometrioid carcinoma	*Fast Track Designation, Orphan Drug Designation*				GOG FOUNDATION; ENGOT European Network of Gynaecological Oncological Trial groups
	Cholangiocarcinoma (IST)	*Orphan Drug Designation*				MAYO CLINIC HEALTH SYSTEM
NXP900 [b] (SRC/YES1 inhibitor)	• **YES1 / SRC-driven solid tumors** • **Cancers of squamous cell origin** • **ALK positive / EGFR-mutated NSCLC (combination)**	*All-comer dose escalation ongoing*				

a. Exclusive worldwide rights acquired from the Institute of Cancer Research, UK.
b. Exclusive worldwide rights acquired from the University of Edinburg.

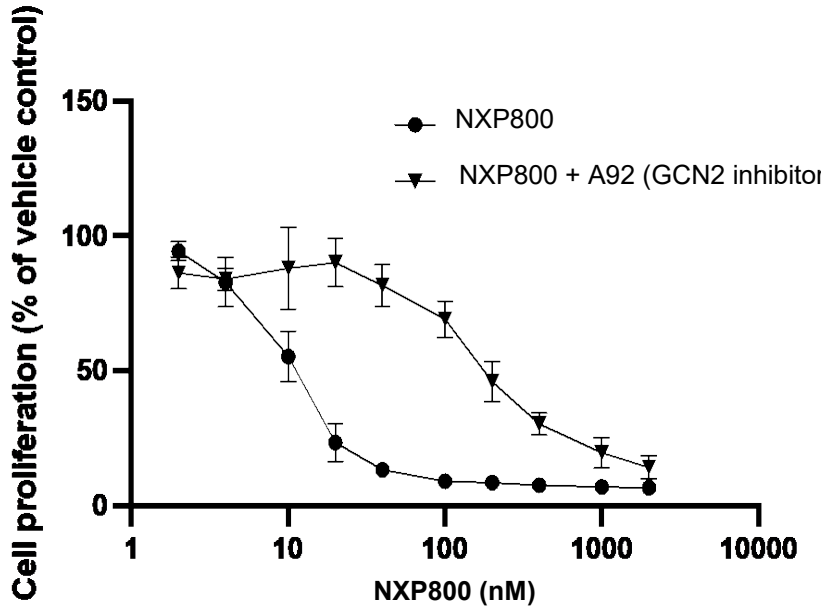
About NXP800

NXP800 Mechanism of Action

NXP800 is a GCN2 kinase activator



NXP800 activates the GCN2 kinase



- Inhibition of cap-dependent translation and chronic activation of the integrated stress response (ISR) ➔ Cancer cell death
- ARID1a-mutated tumors display an increased dependence on translation

Target validation

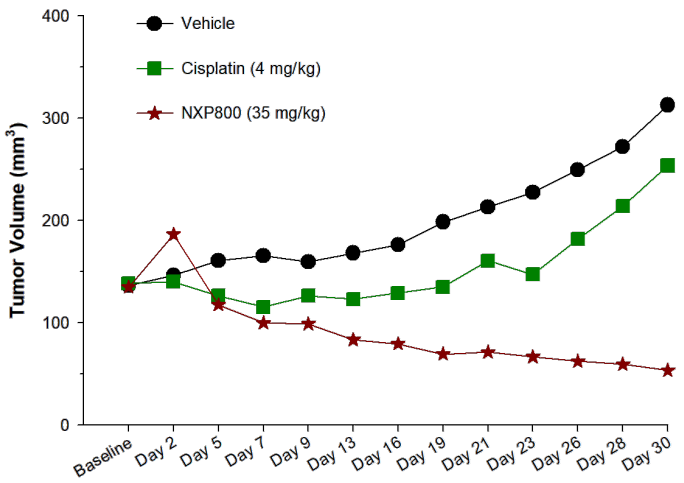
The GCN2 inhibitor A92 antagonizes the antiproliferative effect of NXP800 in ARID1a- mutated SKOV3 cells (approx. 50-fold change in GI_{50})

Powers et al., AACR 2023

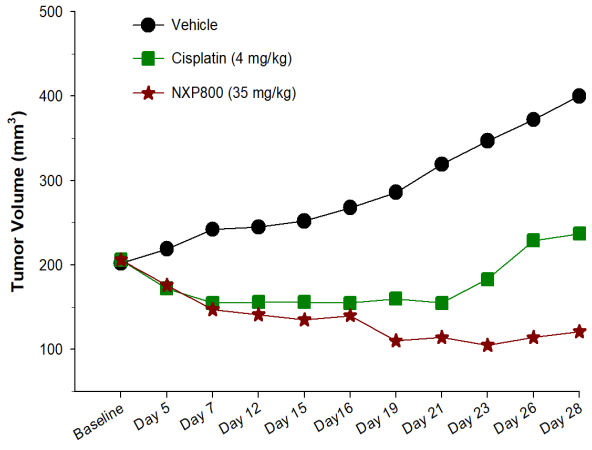
Substantial Antitumor Activity in ARID1a-Mutated Ovarian Carcinoma Xenografts (NXP800 vs. Cisplatin)

Preclinical proof of concept leading to selection of initial target indication

SKOV-3 (Cisplatin Resistant)



TOV-21G (Cisplatin Sensitive)



Disease	Est. Total Incidence (US) [a]	Est. # of Patients w/ ARID1a Deficiency
Ovarian Clear Cell Carcinoma	2,200	1,320
Ovarian Endometrioid Carcinoma	2,200	660

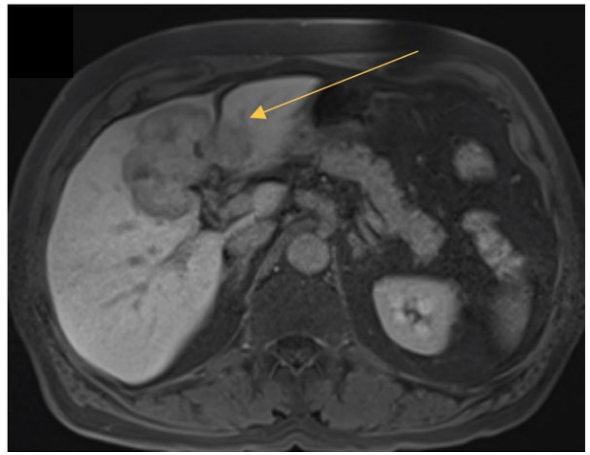
a. Based on data from the American Cancer Society, 2022

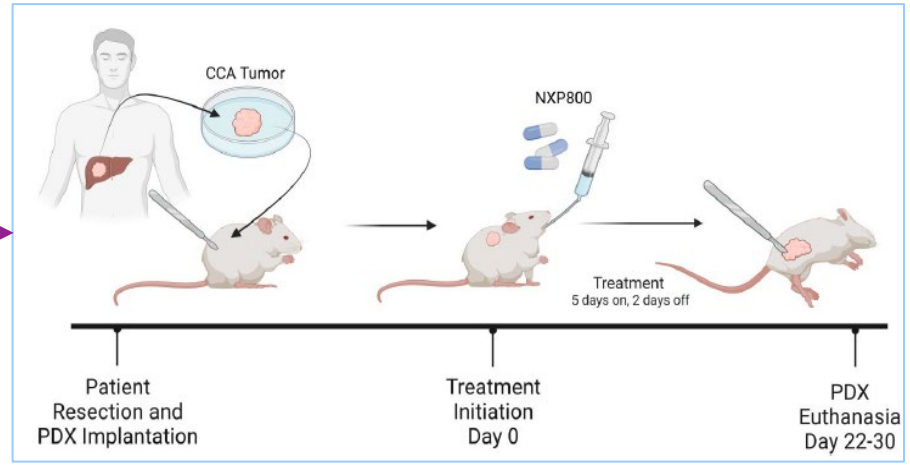
Substantial Antitumor Activity in Cholangiocarcinoma

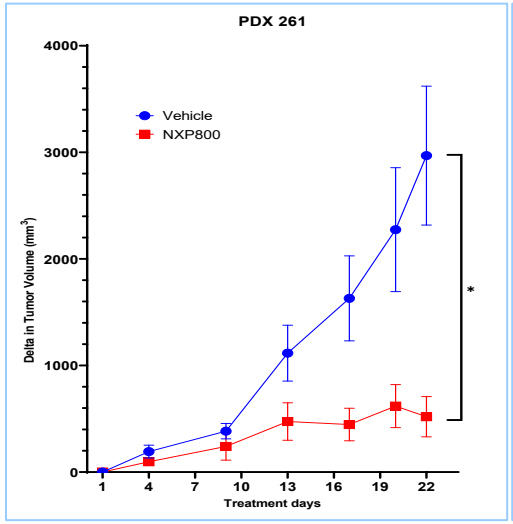
Additional potential development opportunities

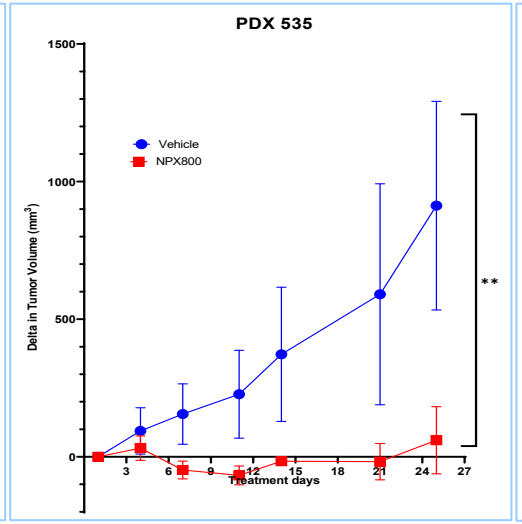
- Cholangiocarcinoma (CCA) is a lethal malignancy with poor prognosis arising from the biliary tree
- Approx. 10,000 new cases/year in the US [a]

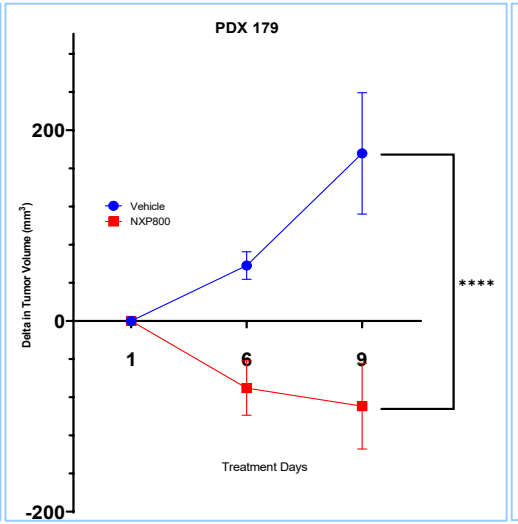
a. The cholangiocarcinoma foundation, cholangiocarcinoma.org/key-statistics

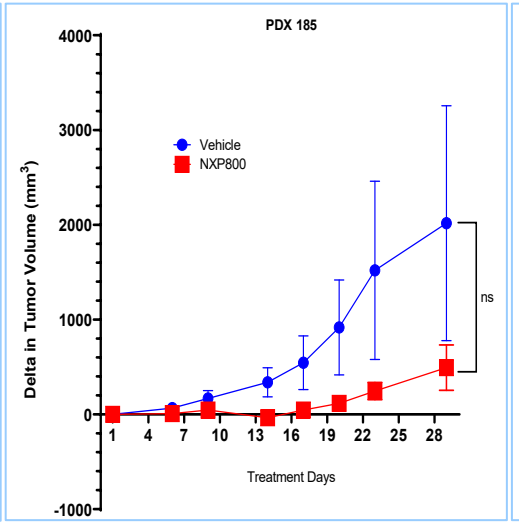


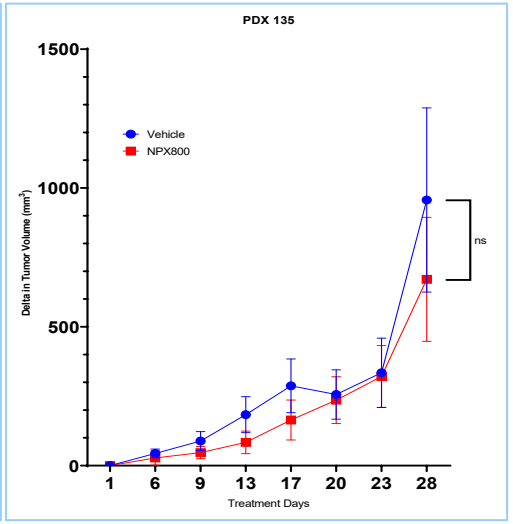










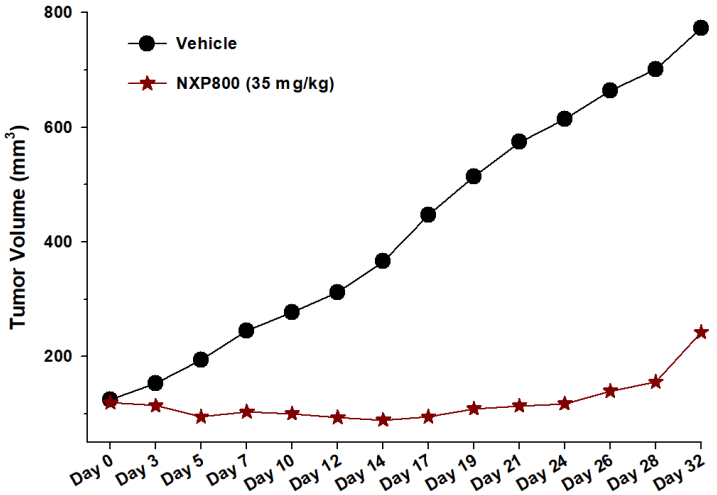


Tumor volume following NXP800 treatment in NOD SCID flank **(A)** *ARID1A* frameshift mutation **(B)** *FGFR1* and *2* overexpression **(C)** *HSF1* amplification **(D)** *PBRM1* variation **(E)** *BRAF* mutation (Carlsson et al., AACR 2024)

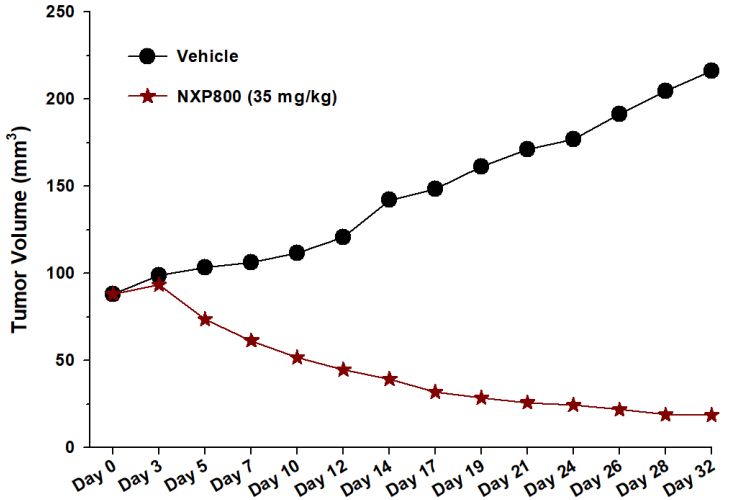
Potent Antitumor Activity in ARID1a/ARID1b Mutated Endometrial Carcinoma Xenografts

- ARID1a is the most frequently mutated SWI/SNF subunit with an estimated prevalence of 35% in endometrial carcinomas.
- Inactivation of ARID1b is highly prevalent in undifferentiated and dedifferentiated endometrial cancers (approx. 36%), often concurrent with ARID1a, and is associated with an aggressive phenotype.
- NXP800 demonstrated robust antitumor activity in ARID1a and ARID1b mutated xenografts of endometrial carcinoma, at a well-tolerated dose, including in models of poorly differentiated tumors, supporting the clinical development of NXP800 in endometrial cancer.

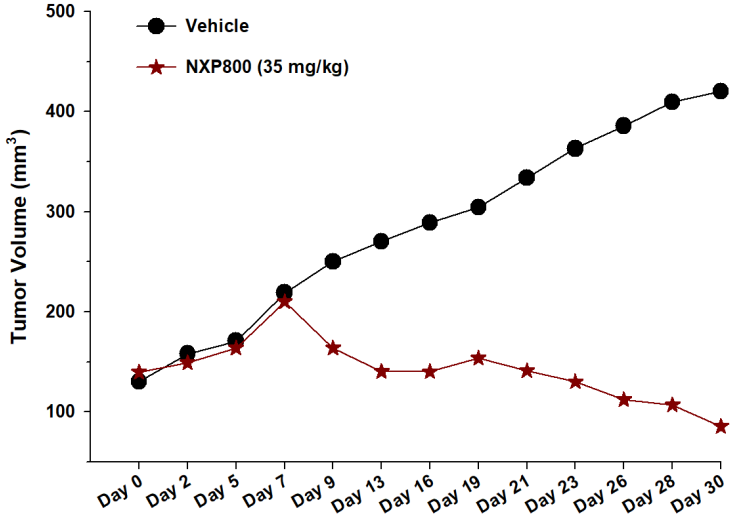
RL95-2
(ARID1a/ARID1b concurrent mutation)



KLE
(ARID1b mutation/poorly differentiated)



SNG-M
(ARID1a mutation)



NXP800 Potential Opportunity in Multiple Cancers

ARID1a is an important mutation that can be used as a patient selection strategy [a]

Indication	Estimated Incidence (US)	ARID1a mutation prevalence	Estimated Number of Patients with ARID1a protein loss (US)
Ovarian Cancer (Clear Cell and Endometrioid)	4,350	52.9%	2,300
Endometrial Carcinoma	66,200	35.6%	23,600 [b]
Cholangiocarcinoma	8,000	17.5%	1,400
Urothelial	75,350	34.0%	25,600
Hepatocellular	34,000	26.7%	9,070
Gastric	26,550	24.9%	6,600

a. The ARID1a mutation detection assay is a standard part of commercially and clinically available NGS panels.
b. Estimate based on a weighted average of the ARID1a mutation prevalence within the major endometrial histology subtypes.

NXP800: Phase 1b Underway, Fast Track Designation

Enrolling patients with platinum-resistant, ARID1a-mutated ovarian cancer (target population)

Clinicaltrials.gov NCT05226507

Phase 1a: Dose Escalation - Completed

Patients with advanced solid tumors (all comers)

Primary Objectives:

Select doses/schedules for Phase 1b

Key Endpoints:

Assess Pharmacokinetics, pharmacodynamics, lab abnormalities, dose limiting toxicities

Phase 1b: Dose Expansion - Enrolling

Patients in the target population - 2 cohorts of 20-25 patients, 2 dosing regimens (50 mg and 75 mg QD)

Primary objectives: Establish RP2D

Key Endpoints:

Preliminary Efficacy, Safety, Pharmacokinetics and Pharmacodynamics

Initial Phase 1b Clinical Data Provided in 1Q2024 Demonstrating Preliminary Activity

Preliminary Phase 1b Data

- Data reported in two patients treated with 75 mg/day and two treated with 50 mg/day.
- Prior therapies:
  - All patients failed at least two prior lines of systemic chemotherapy, including at least one prior platinum-based chemotherapy regimen.
  - Three of the patients also failed prior treatment with bevacizumab (Avastin).
- Efficacy evaluated in three of the four patients:
  - One patient treated with 75 mg/day achieved a PR, unconfirmed, that also included a CR of her non-target lymph node disease.
  - Both patients treated with 50 mg/day achieved SD.
- Safety:
- Three patients experienced Grade 4 thrombocytopenia, these events were transient in nature with no concurrent bleeding events reported.
- A management procedure for the monitoring of platelets and dose adjustments, as necessary, has been implemented. No other Grade 3 hematological toxicities were reported.
- Gastrointestinal adverse events were reported in all four patients, all Grade 1-2.

About NXP900

NXP900 Key Highlights

Precision Medicine Approach

- Discovered at the University of Edinburgh, Scotland
- A potent, novel, small molecule inhibitor of YES1/SRC signaling
- YES1-Hippo pathway alteration associated with sensitivity to NXP900 in squamous cell models

Differentiated Features

- Highly selective
- Unique mechanism of action - Complete shut-down of the SRC pathway by scaffold and catalytic domain inactivation

Strong Preclinical Proof of Concept

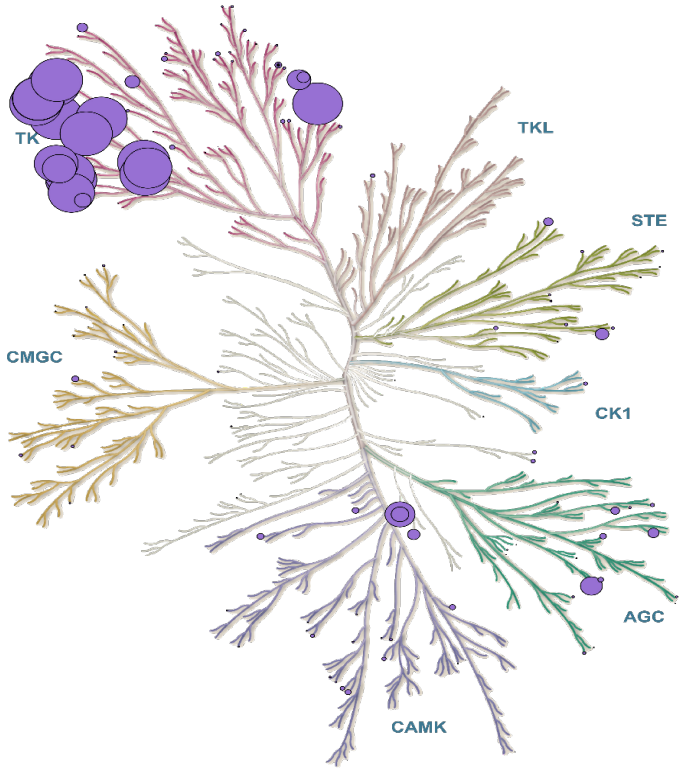
- POC in multiple xenograft models – significant single-agent activity in squamous cell cancer models
- Ability to re-sensitize resistant NSCLC cells to osimertinib
- Ability to reverse resistance to enzalutamide in vivo in mCRPC

Phase 1 Program

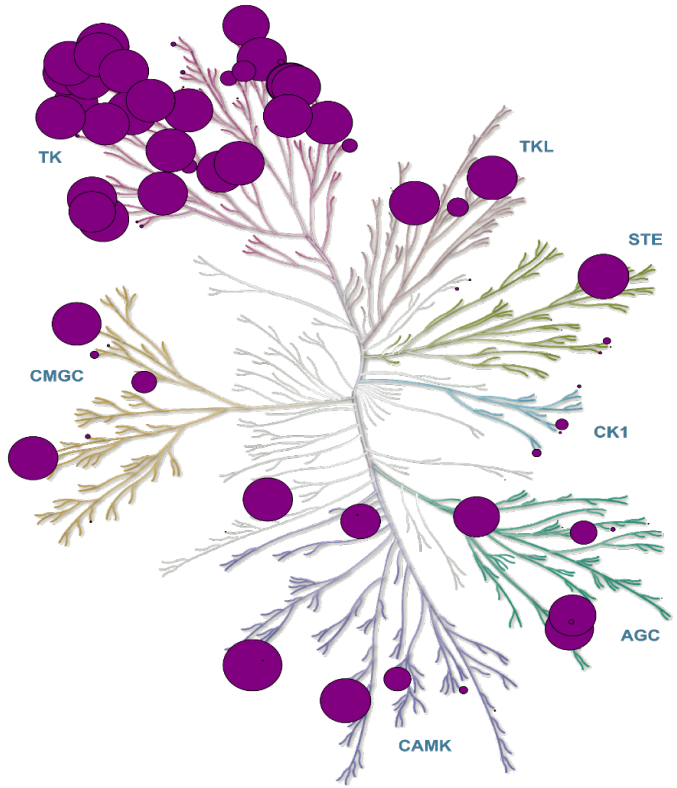
- Phase 1a dose escalation clinical trial ongoing

NXP900 Kinome Profiling Demonstrates High Selectivity

NXP900



Dasatinib

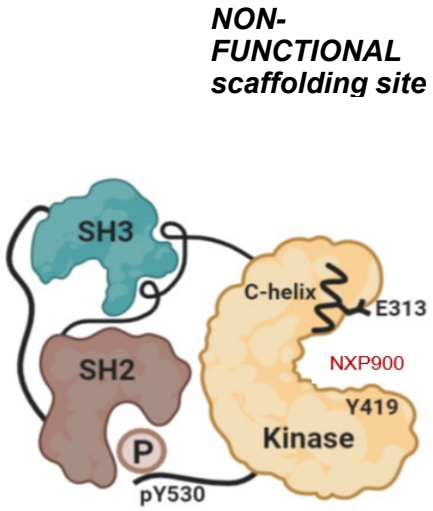


Note: Dasatinib data from Remsing Rix et al., Leukemia 23, 477–485 (2009), NXP900 data from AACR 2022.

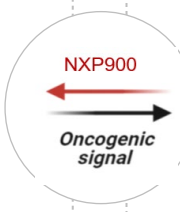
NXP900 Completely Shuts Down Signaling of Non-receptor Tyrosine Kinases of the SRC Family

Differentiated vs. other multi-kinase inhibitors that only achieve a partial SRC pathway shut down

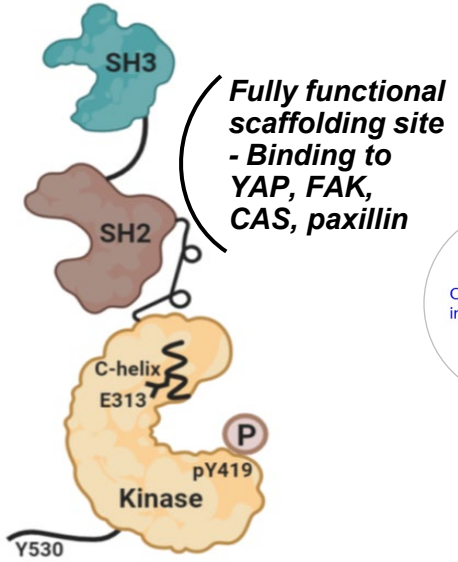
NXP900: Complete shutdown of the SRC pathway



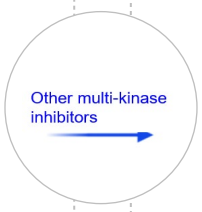
Closed, inactive conformation locked by NXP900



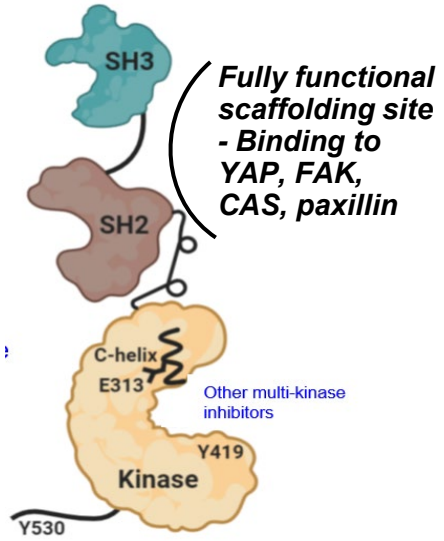
No inhibitor: Fully active SRC



Open, active conformation no inhibitor



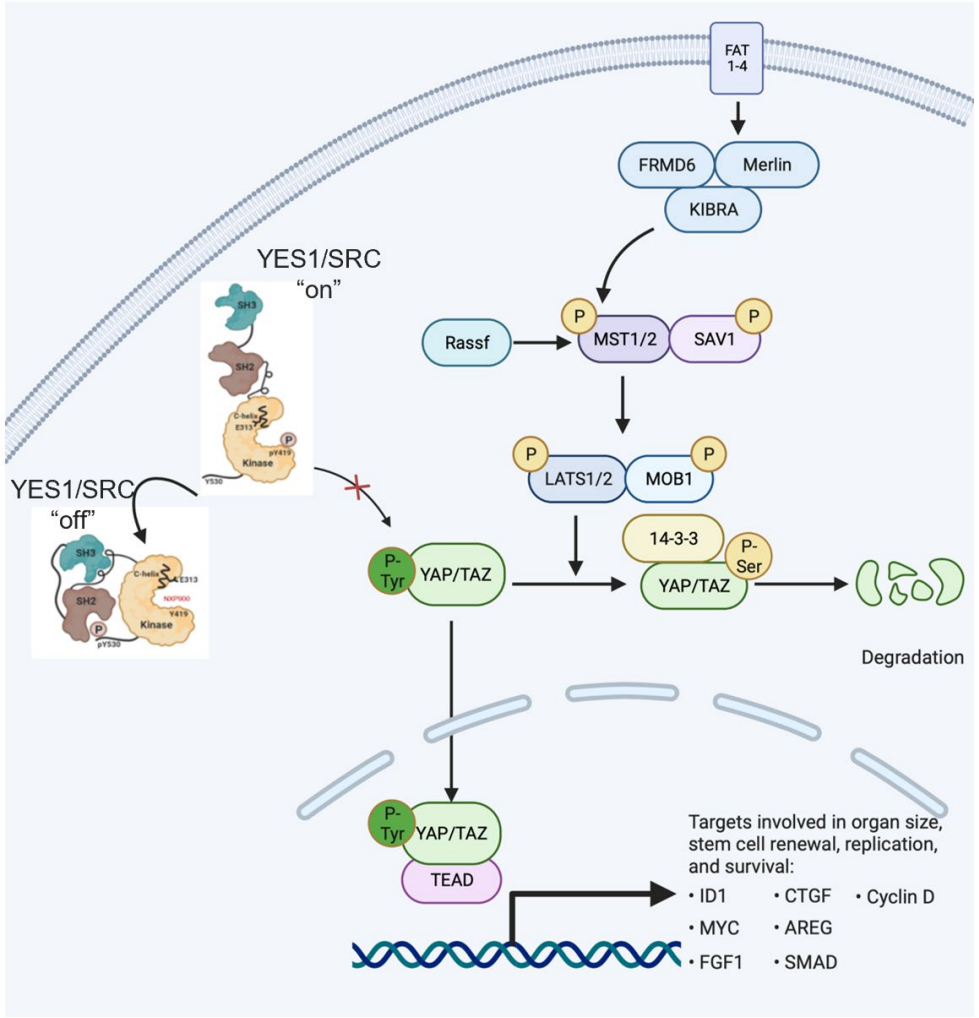
Other multi-kinase inhibitors: Partial shutdown of the SRC pathway



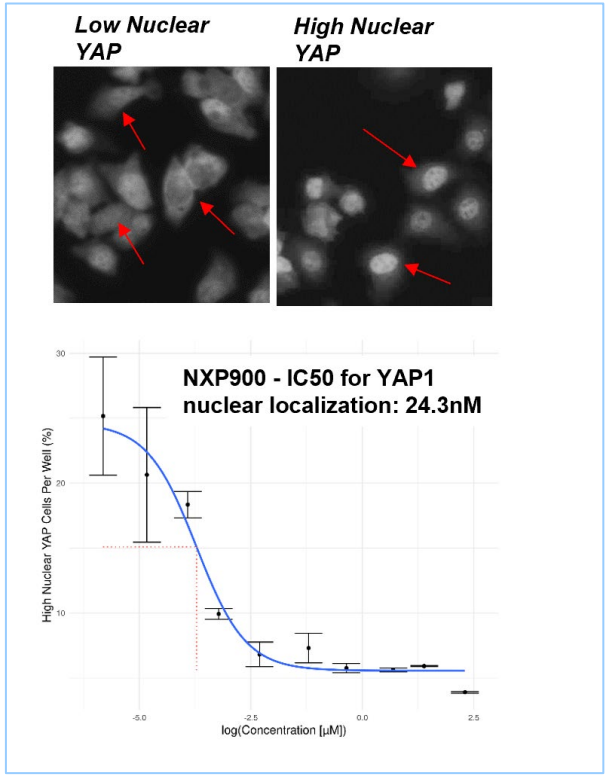
Open, active conformation stabilized by other multi-kinase inhibitors

Targeting YES1 in Cancers of Squamous Cell Origin

Single agent development strategy



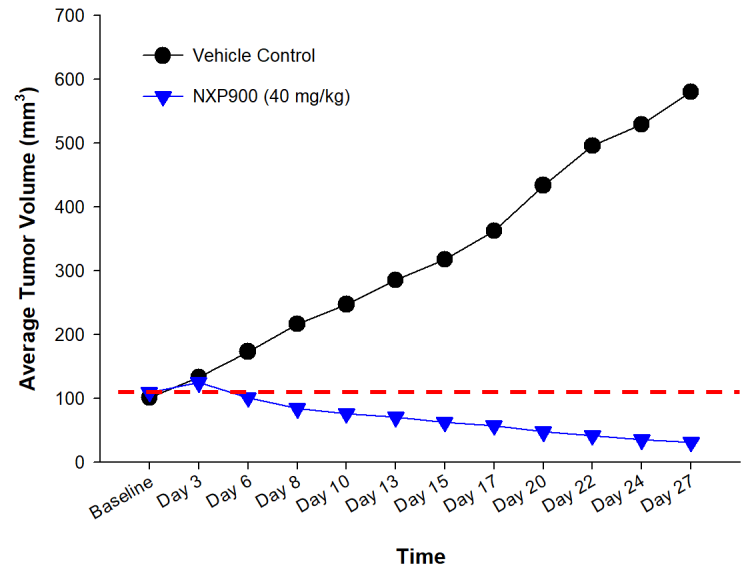
Created with BioRender.com



- Genetic alterations in the hippo pathway (FAT1-4, YAP1, TAZ) are highly prevalent in cancers of squamous cell origin and confer sensitivity to NXP900
- YES1 drives tumor growth via phosphorylation and nuclear localization of YAP1
- Significant unmet medical need opportunities within the squamous cancer universe ➔ **Regulatory opportunity**

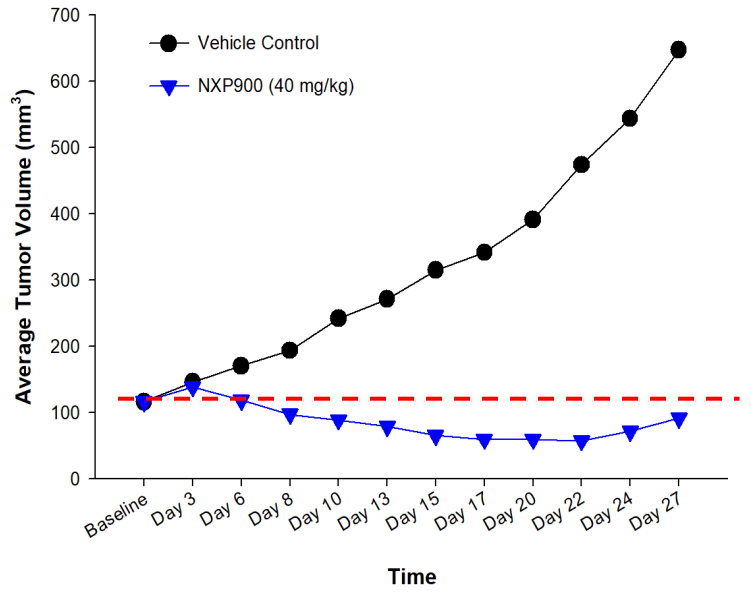
Potent Single Agent Activity in Squamous Cell Cancers

Esophageal Cancer



KYSE70 cells (YES1 gene amplification)

Head and Neck Cancer (tongue)

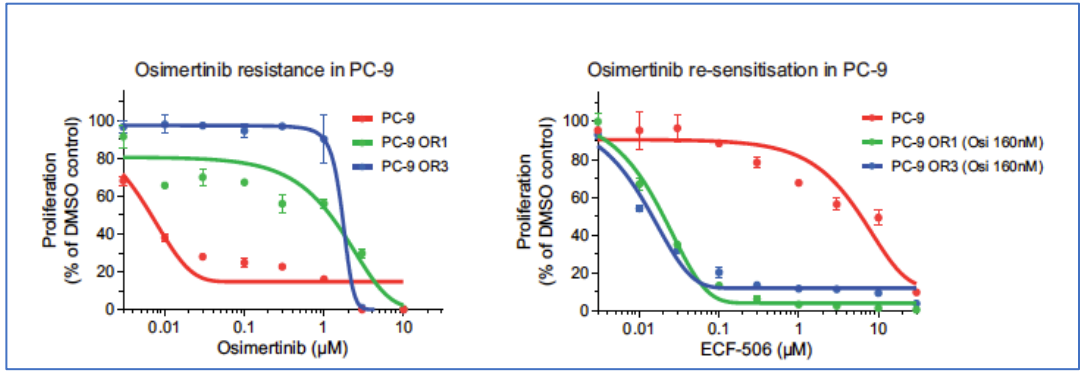


Cal27 cells (Heterozygous FAT1 copy loss)

Potential Combination Strategies

YES1 and SRC have been validated in development of resistance to osimertinib (Tagrisso) and alectinib (Alecensa) in NSCLC

NXP900 in combination with osimertinib overcomes resistance in vitro (Nature Com., AstraZeneca R&D, April 2022



NSCLC = Non-small cell lung cancer, eCF506 = NXP900

Despite the demonstrated clinical activity of alectinib and osimertinib in NSCLC, the majority of patients become resistant to treatment over time.

NXP900 demonstrates potent synergy with osimertinib and alectinib across sensitive and resistant cell lines (Carragher et al., AACR 2024)

Cell Line	NXP900 GI_{50} (nM)	Osimertinib GI_{50} (nM)	NXP900 GI_{50} (nM) + Osimertinib (160 nM)
PC9	605	62	13
PC9-OR1	4,665	1,508	121
PC9-OR3	826	1,377	43

Cell Line	NXP900 GI_{50} (nM)	Alectinib GI_{50} (nM)	NXP900 GI_{50} (nM) + Alectinib (25 nM)
NCI-H2228	48.5	76	15
NCI-H2228-ALR1	26	6,460	
NCI-H2228-ALR2	19	6,614	
NCI-H2228-ALR3	30	2,962	
NCI-H2228-ALR5	22	2,158	

NXP900 Potential Market Opportunity

Squamous cancer cells with hippo pathway alterations and NF2 mutated cells demonstrate high sensitivity to NXP900 in vitro and in vivo

Indication	Estimated Incidence (US)		Estimated Addressable Patient Population (US)
		Squamous cell prevalence	
Cervical	13,950	90%	12,500
Esophageal	21,550	30% [a]	6,500
Metastatic Anal	3,000	80%	2,400
NSCLC	202,600	25%	50,650
Head & Neck	54,000	90%	48,600
		NF2 mutation prevalence [b]	
Mesothelioma	3,000	33%	1,000
Papillary Kidney Cancer	12,000	13%	1,500

a. The prevalence of ESCC ex-US is approximately 85%.
b. The NF2 mutation is prevalent in approximately 1-3.6 % of patients in several additional solid tumors including breast, NSCLC, ovarian, bladder, melanoma and CRC

NXP900: Phase 1a Ongoing

Patients with advanced solid tumors

Clinicaltrials.gov NCT05873686

Phase 1a Dose Escalation

Starting dose of 20 mg, QD

Primary Objective:

Select doses/schedules for Phase 1b

Key Endpoints:

Assess Pharmacokinetics, pharmacodynamics, lab abnormalities, dose limiting toxicities

Financial and NVCT Stock Highlights

Cash Runway into 2H2025

Financials

Ticker	NVCT
Cash	$18.1M as of 06/30/2024

Insider Ownership

Founders and >5% holders	Approx. 65%

Research Coverage

H.C. WAINWRIGHT & CO.	Joe Pantginis
LADENBURG THALMANN ESTABLISHED 1876	Aydin Huseynov
ROTH · MKM	Jonathan Aschoff

Nuvectis Investment Highlights

Precision medicine pipeline for serious conditions of unmet medical need in oncology

2024 Milestones

- Preliminary clinical data for NXP800 (ARID1a-mutated ovarian cancer and cholangiocarcinoma) and for NXP900 (Phase 1a study)
- Presentations at medical and scientific conferences

NXP800

- ARID1a mutated, platinum resistant ovarian cancer - Phase 1b ongoing
- Cholangiocarcinoma – IST/Mayo Clinic commenced

NXP900

- Highly selective compound, differentiated from other YES1/SRC-kinase inhibitors
- Phase 1a ongoing

Management Team with Strong Track Record

- 3 approved drugs in 4 indications in the US, EU approvals and multiple strategic deals
- Generated significant shareholder value

Nuvectis Pharma, Inc.

Innovative Precision Medicine for Serious Conditions of Unmet Medical Need in Oncology

September 2024

NuvectisPharma, Inc.

(NASDAQ: NVCT)