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

September 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 preclinical studies and clinical trials, including the ongoing 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.
**Key Highlights**

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

- **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

- **Novel pipeline of rationally-designed precision targeted therapies**
  - NXP800: A potent, clinical stage HSF1-pathway inhibitor
  - NXP900: A novel preclinical SRC/YES1 kinase inhibitor
  - Strong IP position

- **In the next 12 months**
  - NXP800 - Completion of Phase 1a dose escalation and initiation of phase 1b in the targeted patient populations
  - NXP900 - Initiation of phase 1 clinical trial
  - Preclinical and clinical data updates and presentations
Leadership Team

Track Record of Success

Ron Bentsur
CHAIRMAN & CEO
• 20+ years senior leadership experience
• CEO, C-Suite roles and Board Member

Enrique Poradosu, PhD
CSO & CBO
• 20+ senior leadership experience
• Roles in Business and Scientific strategy

Shay Shemesh
CDO & COO
• 15+ years of experience in drug development
• Roles in Clinical and Regulatory Affair across a range of therapeutic areas

Auryxia®
(ferric citrate) tablets

Keryx Biopharmaceuticals, Inc.

ELZONRIS®
(tagraxofusp-erz) injection

Stemline®

Jelmyto®
(mitomycin)

UroGen Pharma
# Nuvectis Pipeline

**Unique Precision Medicine Drug Candidates**

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>IND enabling</th>
<th>Phase 1a</th>
<th>Phase 1b</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>NXP800</td>
<td></td>
<td>Ovarian Clear Cell Carcinoma</td>
<td>Endometrioid Ovarian Carcinoma</td>
<td>ARID1(^{mutation+}) Adv. Solid Tumors</td>
<td></td>
<td>Phase 1a dose escalation ongoing, Phase 1b to begin in Q1 2023</td>
</tr>
<tr>
<td>NXP900</td>
<td></td>
<td>SRC-kinase driven solid tumors</td>
<td>YES1 kinase gene amplification (solid tumors)</td>
<td></td>
<td></td>
<td>Phase 1a to begin in Q1 2023</td>
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</tbody>
</table>
About NXP800
A Novel HSF1-Pathway Inhibitor
**NXP800**

**Key Highlights**

- Discovered and optimized at the Institute of Cancer Research (ICR) in the UK. The ICR also 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 inhibition demonstrated in ARID1a-mutated ovarian clear cell and endometroid, and gastric carcinoma xenograft models.

  - These indications represent unmet medical needs, with poor prognosis and very low response rate to first line chemotherapy treatment.
  
  - ARID1a is mutated in multiple solid tumor types, potentially enabling a genetic mutation-based/tumor agnostic development opportunity.
HSF1 targets and their role in malignancies

HSF1 pathway addiction – enables cancer cells to overcome diverse stresses and promote biological activities crucial for cancer cells.

HSF1 promotes a distinct transcriptional program in cancer
- Stress resistance
- Proliferation
- Biosynthetic Demand
- Altered Metabolism
- Survival

NXP800 Demonstrated Substantial Antitumor Activity in ARID1a-Mutated OCCC Xenografts vs. Cisplatin

Model 1: SKOV-3

Model 2: TOV-21G
ARID1a-Mutated Ovarian Carcinoma

Found Almost Exclusively in OCCC and EOC

- The American Cancer Society estimates that approximately 19,880 women will receive a new diagnosis of ovarian cancer in the United States in 2022 (https://cancerstatisticscenter.cancer.org/#/cancer-site/Ovary)

Ovarian Cancer Net Incidence by Type

Endometrioid ovarian cancer (EOC) ➔

US: ~10% of ovarian cancer cases

~40% of EOC patients have an ARID1a mutation

Ovarian clear cell carcinoma (OCCC)

US: 10% of ovarian cancer cases

~2/3 of OCCC patients have an ARID1a mutation.
### NXP800 Demonstrated Substantial Antitumor Activity in an ARID1a-Mutated Gastric Carcinoma Xenograft

**SNU-1**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Day 28 Relative Tumor Volume (RTV28)</th>
<th>Tumor Growth Inhibition (TGI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle</td>
<td>2.67</td>
<td>--</td>
</tr>
<tr>
<td>NXP800 (35 mg/kg)</td>
<td>0.74</td>
<td>72%</td>
</tr>
</tbody>
</table>

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a. $RTV28 = \frac{\text{avg. tumor volume D28}}{\text{avg. tumor volume at baseline}}$; value < 1 indicates tumor regression  
b. $TGI \% = (1 - \frac{\text{RTV28 of the treated group}}{\text{RTV28 vehicle}}) \times 100$
ARID1a-Mutated Gastric Carcinoma

- The American Cancer Society estimates that approximately 26,380 people will receive a new diagnosis of gastric cancer in the United States in 2022 (https://cancerstatisticscenter.cancer.org/#/cancer-site/Stomach)

Gastric Cancer Net Incidence

ARID1a-Mutated Gastric Cancer

US: ~25% of patients with gastric cancer have an ARID1a mutation

25%
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 commercially available screening panels.

• Broad in-vivo testing program ongoing to identify additional tumor types for clinical testing.

### Indication

<table>
<thead>
<tr>
<th>Indication</th>
<th>Estimated Incidence (US)</th>
<th>Estimated Number of Patients with ARID1a protein loss (US)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian Clear Cell Carcinoma</td>
<td>1,988</td>
<td>1,325</td>
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<tr>
<td>Endometrioid Carcinoma</td>
<td>1,988</td>
<td>795</td>
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<tr>
<td>Uterine endometrioid</td>
<td>66,570</td>
<td>26,628</td>
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<tr>
<td>Urothelial</td>
<td>75,357</td>
<td>25,621</td>
</tr>
<tr>
<td>Hepatocellular</td>
<td>34,000</td>
<td>9,070</td>
</tr>
<tr>
<td>Gastric</td>
<td>26,380</td>
<td>6,595</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>60,430</td>
<td>4,230</td>
</tr>
<tr>
<td>Esophageal</td>
<td>19,260</td>
<td>2,120</td>
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**First in class HSF1-pathway inhibitor**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>HSF1 ACTIVATION</td>
<td>implicated in several solid tumors</td>
</tr>
<tr>
<td>FOCUSED</td>
<td>clinical/regulatory strategy</td>
</tr>
<tr>
<td>PHASE 1a ONGOING</td>
<td>Phase 1b expected to begin in Q1 2023</td>
</tr>
<tr>
<td>BROAD POTENTIAL</td>
<td>Arid1a mutated patients in OCCC, Endometrioid ovarian, gastric, uterine endometrioid, urothelial, hepatocellular, pancreatic and esophageal</td>
</tr>
</tbody>
</table>
About NXP900
A Novel SRC / YES1 inhibitor
NXP900

Key Highlights

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

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

- IND-enabling studies ongoing
  Phase 1 expected to begin in Q1 2023
**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 functions.
NXP900

Novel and Differentiated Mechanism of Action

NXP900: Complete shutdown of the SRC pathway

No inhibitor: Fully active SRC

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

NON-FUNCTIONAL scaffolding site

Closed, inactive conformation locked by NXP900

Open, active conformation no inhibitor

Open, active conformation stabilized by other multi-kinase inhibitors

Fully functional scaffolding site
- Binding to YAP, FAK, CAS, paxillin

Fully functional scaffolding site
- Binding to YAP, FAK, CAS, paxillin

Non-functional scaffolding site
NXP900 Selectivity

Kinome Profiling Reveals High Selectivity Compared With Dasatinib

Kinome-wide activity profile of NXP900 - enzymatic inhibition screen was performed by Carna Biosciences, against 326 wildtype and mutant kinases. Circles identify kinase targets of NXP900 (0.5μM, lilac) and dasatinib (1μM, deep purple), size represents percent inhibition. Dasatinib data from Remsing Rix et al., Leukemia 23, 477–485 (2009).
NXP900 Re-Sensitizes Resistant NSCLC Cells to Osimertinib*
Published in Nature Communications by the AstraZeneca R&D Group, April 2022

A) Osimertinib dose–response curve in PC9 NSCLC parental cells compared to two lines derived to have acquired osimertinib resistance, (96h treatment). B) ECF-506 (NXP900) dose–response curve in PC9 parental vs. resistant lines, (96 h treatment). Resistant cells were co-treated with 160 nM osimertinib. OR = osimertinib (Osi) resistant. Data are presented as mean values +/- SD (n = 3) of a typical plot, where the experiment was repeated at least three times.

- YES1/SRC gene amplification/activation has been validated as recurrent and targetable mechanism of resistance to EGFR, Alk and HER2 targeted therapies in clinical samples and models of NSCLC and Breast cancer

* Osimertinib = Tagrisso, ECF-506 = NXP900
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 (Cont.)

Eradication of TNBC-induced Bone Metastatic Lesions

No immunosuppression - lymphocyte infiltration observed in NXP900 treated tumors

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*
NXP900 is Highly Effective in a Preclinical Model of Group 4 Medulloblastoma

SRC Signaling is a Hallmark of Group 4 Medulloblastoma (Forget et al., Cancer Cell, 2018, 34, 379-395)

- SrcCA/DNp53 tumour cells (Forget et al, 2018) were cultured in vitro and transduced using lentivirus expressing Luciferase-eGFP, for tumor tracking. Mice received NXP900 (eCF506) 20mg/kg daily for 28days via IP in a citric buffer. Tumor response was monitored weekly via bioluminescence and measured by caliper.

- Data presented on June 12th, 2022 at SIOPE Brain Tumor Group in Hamburg, Germany, by the Pediatric Solid Tumor Biology and Therapeutics Team (led by Prof. Louis Chesler of The Institute of Cancer Research in London, UK), in collaboration with the Institute of Genetics & Cancer at The University of Edinburgh.
## 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.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Estimated Incidence (US)</th>
<th>Estimated Number of Patients with YES1 Gene Amplification (US)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal squamous cell carcinoma</td>
<td>5,778</td>
<td>364</td>
</tr>
<tr>
<td>Esophageal adenocarcinoma</td>
<td>13,482</td>
<td>768</td>
</tr>
<tr>
<td>Head and neck squamous cell carcinoma</td>
<td>65,410</td>
<td>3,336</td>
</tr>
<tr>
<td>Lung squamous cell carcinoma</td>
<td>31,584</td>
<td>1,421</td>
</tr>
<tr>
<td>Bladder urothelial carcinoma</td>
<td>75,357</td>
<td>3,316</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>13,460</td>
<td>404</td>
</tr>
<tr>
<td>Ovarian serous cystadenocarcinoma</td>
<td>14,987</td>
<td>450</td>
</tr>
</tbody>
</table>
NXP900 provides an opportunity to treat solid tumors with a SRC/YES1 inhibitor

SRC (OVERACTIVATION) AND YES1 (GENE AMPLIFICATION)

UNIQUE MECHANISM OF SRC INHIBITION

AVOIDS THE IMMUNOSUPPRESSIVE EFFECTS

CROSSES THE BBB

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

enables complete shutdown of the SRC pathway.

demonstrated with dasatinib - a major disadvantage in solid tumors.

opportunity in brain metastases and pediatric medulloblastoma, where SRC is implicated.
Financial Highlights

- Completed ~$16M PIPE in July 2022
- Provides cash runway into H2 2024
- IPO in February 2022 at $5 per share
- Current stock price is ~$8.40 per share, market capitalization of ~$120M

- Covering analysts include:
  - HC Wainwright & Co – Joe Pantginis
  - Roth Capital Partners – Jonathan Aschoff
  - Ladenburg Thalmann – Aydin Huseynov

Cap Table

<table>
<thead>
<tr>
<th>Shares (in millions)</th>
<th>Shares</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Shares Outstanding</td>
<td>14.6</td>
</tr>
<tr>
<td>Fully Diluted Shares</td>
<td>15.2</td>
</tr>
<tr>
<td>Management Ownership</td>
<td>~35%</td>
</tr>
</tbody>
</table>
2022 Planned Activities and Guidance
Advancing the Pipeline

- ✓ NXP800
  - Phase 1a initiation

- ✓ NXP800
  - US IND clearance

- NXP800
  - Phase 1b initiation

- NXP900
  - Phase 1a initiation

- NXP800 and NXP900
  - Data updates at medical conferences throughout the year
Key Highlights

Experienced Management Team Focused on 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

Over the next 12 months

- NXP800 - Completion of dose escalation and initiation of phase 1b in the targeted patient populations
- NXP900 - Initiation of phase 1 clinical trial
- Preclinical and clinical data presentations
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