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

July 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.
Key Highlights

Precision Medicine Innovation for Serious Conditions of Unmet Medical Need 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
Chief Scientific and Business Officer
- 20+ senior leadership experience
- Roles in Business and Scientific strategy

Shay Shemesh
Chief Development and Operations Officer
- 15+ years of experience in drug development
- Roles in Clinical and Regulatory Affairs across a range of therapeutic areas

Auryxia®
(ferric citrate) tablets

KERYX
BIOPHARMACEUTICALS, INC

ELZONRIS®
(tagraxofusp-erzys) injection

Jelmyto®
(mitomycin)

NuvectisPharma, Inc.

Corporation presentation
## 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>
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<tbody>
<tr>
<td>NXP800</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Ovarian Clear Cell Carcinoma</td>
<td>Endometrioid Ovarian Carcinoma</td>
<td>ARID1\textsuperscript{mutation+} Adv. Solid Tumors</td>
<td></td>
<td>• Phase 1a dose escalation ongoing • Phase 1b to begin in Q1 2023</td>
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<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 1 to begin in Q1 2023</td>
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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 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.
HSF1 pathway addiction enables cancer cells to overcome diverse stresses and promote pro-malignant biological activities.

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

NXP800 Demonstrated Substantial Antitumor Activity in OCCC Xenografts with the ARID1a Mutation
OCCC and Endometrioid Ovarian Cancer

Serious Conditions of Unmet Medical Need

- 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](https://cancerstatisticscenter.cancer.org/#/cancer-site/Ovary)).

**Ovarian Cancer Net Incidence by Type**

- **Endometrioid Ovarian Cancer**
  - US: ~10% of ovarian cancer cases (~2,175 new patients/year).
  - ~40% of endometrioid ovarian cancer patients have an ARID1a mutation.

- **Ovarian Clear Cell Carcinoma (OCCC)**
  - US: 10% of ovarian cancer cases (~2,175 new patients/year).
  - ~2/3 of OCCC patients have an ARID1a mutation.
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 commercially available screening panels.
- Broad in-vivo testing program ongoing to identify additional tumor types for clinical testing

<table>
<thead>
<tr>
<th>Indication</th>
<th>Estimated Incidence (US)</th>
<th>Estimated Number of Patients with ARID1a protein loss (US)</th>
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<tbody>
<tr>
<td>Ovarian Clear Cell Carcinoma</td>
<td>2,175</td>
<td>1,410</td>
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<tr>
<td>Endometrioid Carcinoma</td>
<td>2,175</td>
<td>909</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>
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<tr>
<td>Hepatocellular</td>
<td>34,000</td>
<td>9,070</td>
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<tr>
<td>Gastric</td>
<td>26,550</td>
<td>6,615</td>
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<tr>
<td>Pancreatic</td>
<td>60,430</td>
<td>4,230</td>
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<tr>
<td>Esophageal</td>
<td>19,260</td>
<td>2,120</td>
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**Arid1a mutated tumors in patients with OCCC, Endometrioid ovarian, uterine endometrioid, urothelial, hepatocellular, gastric, pancreatic and esophageal cancers**

**NXP800**
A Novel HSF1-Pathway Inhibitor

<table>
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<tr>
<th>HSF1 ACTIVATION</th>
<th>implicated in several solid tumors</th>
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<tbody>
<tr>
<td>FOCUSED</td>
<td>clinical/regulatory strategy</td>
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<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 tumors in patients with OCCC, Endometrioid ovarian, uterine endometrioid, urothelial, hepatocellular, gastric, pancreatic and esophageal cancers</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.

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

Clearly differentiated

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

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**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.

**Complete shutdown** of SRC signaling requires inhibition of both the catalytic and scaffold functions.

**Catalytic Domain**

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

Other multi-kinase inhibitors
Open, active conformation stabilized by other multi-kinase inhibitors

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

NXP900

Nuvectis Pharma, Inc.
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.

* Osimertinib = Tagrisso

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.
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

No immunosuppression - lymphocyte infiltration observed in NXP900 treated tumors
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 calliper.

- 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>
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<tbody>
<tr>
<td>Esophageal squamous cell carcinoma</td>
<td>5,778</td>
<td>364</td>
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<tr>
<td>Esophageal adenocarcinoma</td>
<td>13,482</td>
<td>768</td>
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<tr>
<td>Head and neck squamous cell carcinoma</td>
<td>65,410</td>
<td>3,336</td>
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<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>
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</table>
NXP900 addresses the shortcomings of other SRC/YES1 inhibitors. SRC (overactivation) and YES1 (gene amplification) are implicated in several solid tumors. However, the existing multi-kinase inhibitors that also inhibit SRC/YES1, which are approved for CML/ALL, including dasatinib, have only shown modest activity in solid tumors. NXP900 enables complete shutdown of the SRC pathway. This is demonstrated with dasatinib - a major disadvantage in solid tumors. NXP900 provides an opportunity to treat solid tumors with a SRC/YES1 inhibitor.

- Unique mechanism of SRC inhibition
- Avoids the immunosuppressive effects
- Crosses the BBB opportunity in brain metastases and pediatric medulloblastoma, where SRC is implicated
Financial Highlights

- Estimated cash runway to YE 2023; $17M as of March 31, 2022
- IPO: February 2022 ($5 per share)
- Included in the Russell MicroCap Index
- Covering analysts include:
  - HC Wainwright & Co - Jonathan Aschoff
  - Roth Capital Partners - Joseph Pantginis
  - Ladenburg Thalmann - Aydin Huseynov

<table>
<thead>
<tr>
<th>Cap Table</th>
<th>Shares (in millions)</th>
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<tbody>
<tr>
<td>Common Shares Outstanding</td>
<td>12.7</td>
</tr>
<tr>
<td>Fully Diluted Shares</td>
<td>13.3</td>
</tr>
<tr>
<td>Management Ownership</td>
<td>~40%</td>
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2022 Planned Activities and Guidance

Highlights advancing clinical 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

Significant news flow expected over the next 12 months
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

In the next 12 months

• NXP800 - Completion of dose escalation and initiation of phase 1b in the targeted patient populations
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