UC Irvine 趙 Chao Family Comprehensive Cancer Center

Advancing Doxorubicin/DNA Nanocomplexes from Bench to Bedside: Progress Since 2022

Young Jik Kwon, PhD

2026 Scientific Retreat

November 5, 2026

Disclosure

Co-Founder

Match the Hatch Biotechnology, Inc.

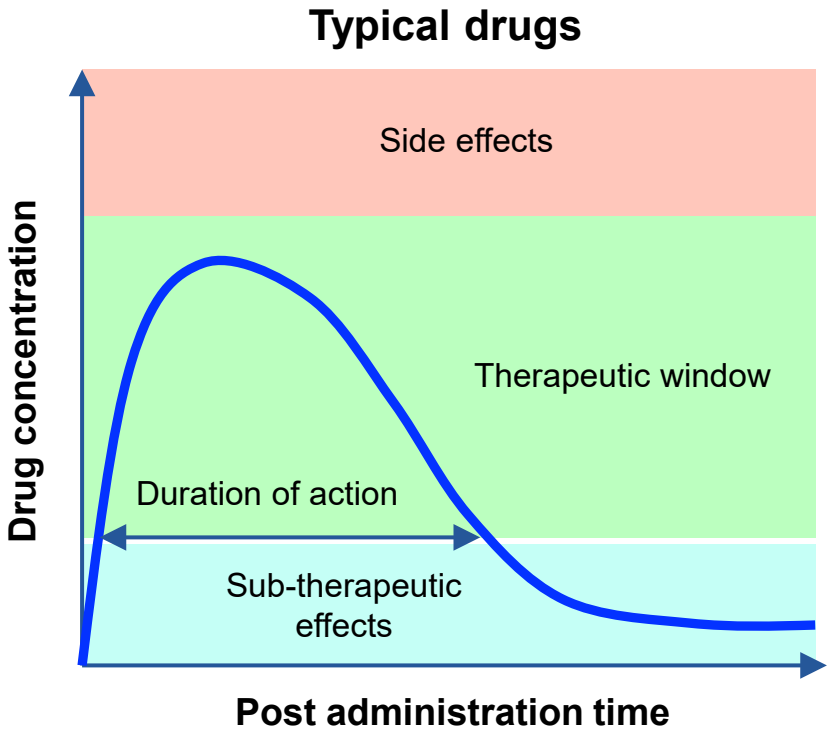
StealthGene, Inc

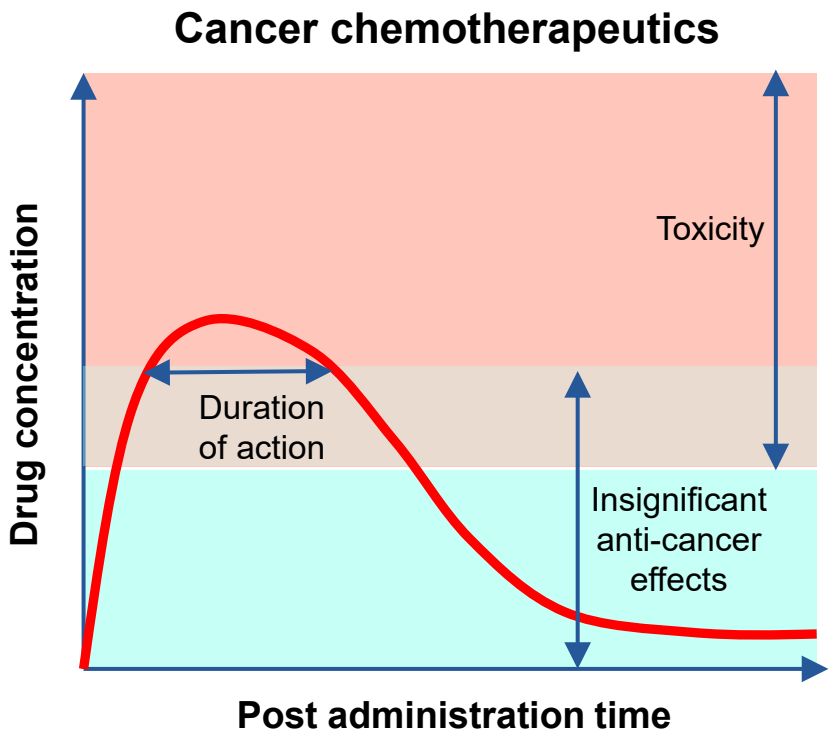
Consultant

PharmaResearch, Co., Ltd

Cancer chemotherapy

Sustained, targeted delivery is needed to widen the therapeutic window of chemotherapy





✓ Sustained/controlled drug release

✓ Targeted accumulation/action

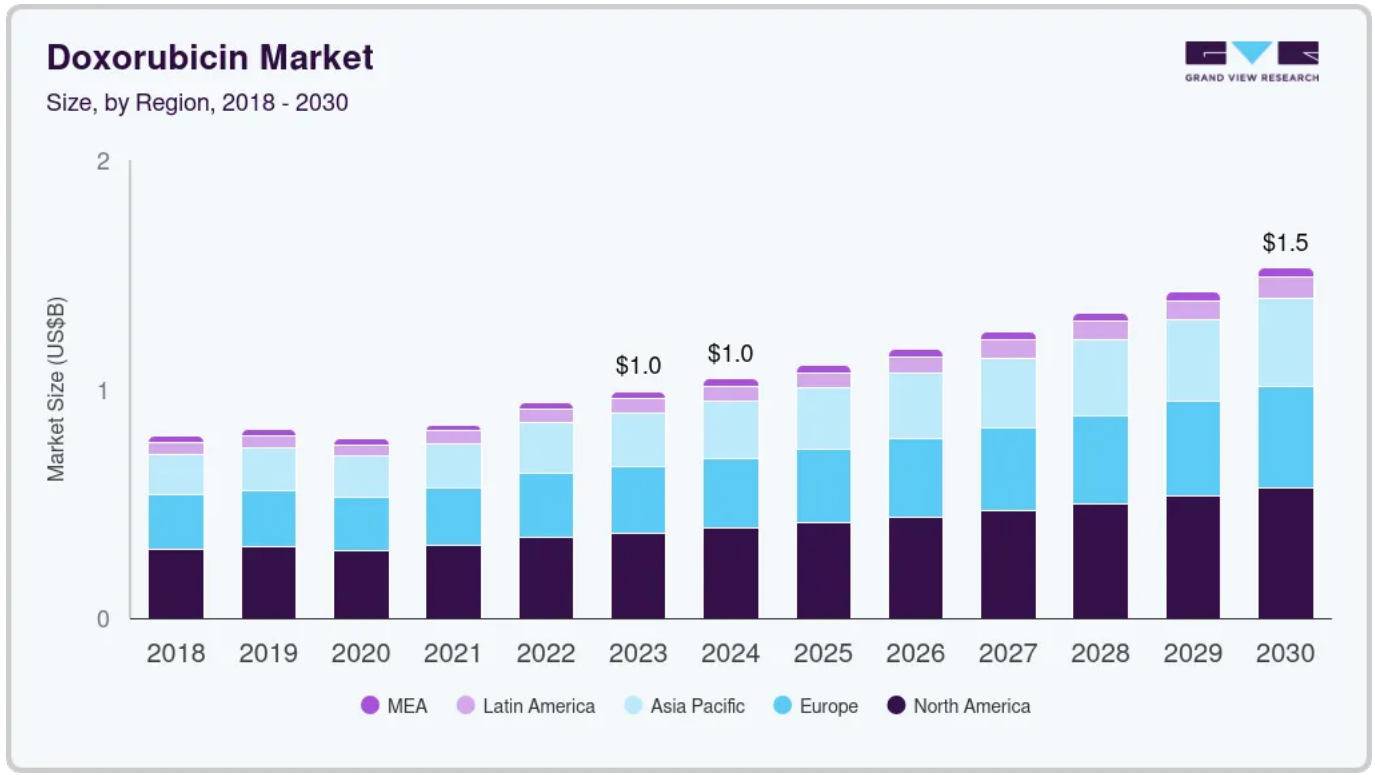
✗ Frequent administrations required

✗ Often resulting incomplete eradication

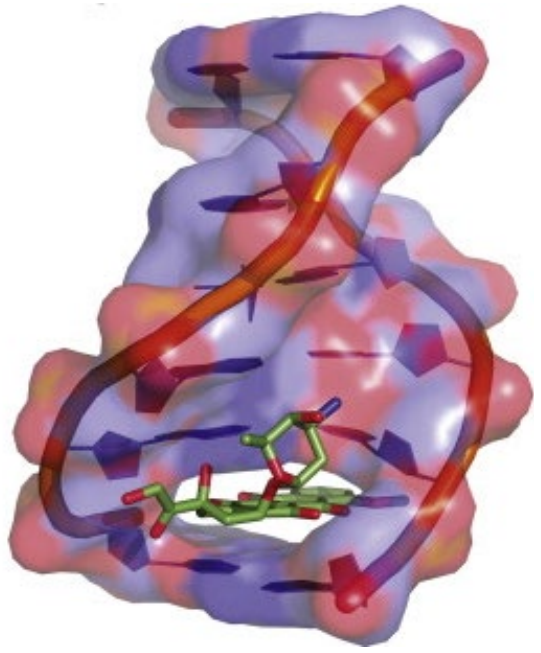
Doxorubicin (DOX)

A widely used anthracycline whose use is limited by systemic toxicity

- Stabilizes DNA-Topoisomerase II complex to prevent DNA replication
- Known as the “red devil” (systemically toxic)



DOX/DNA complex

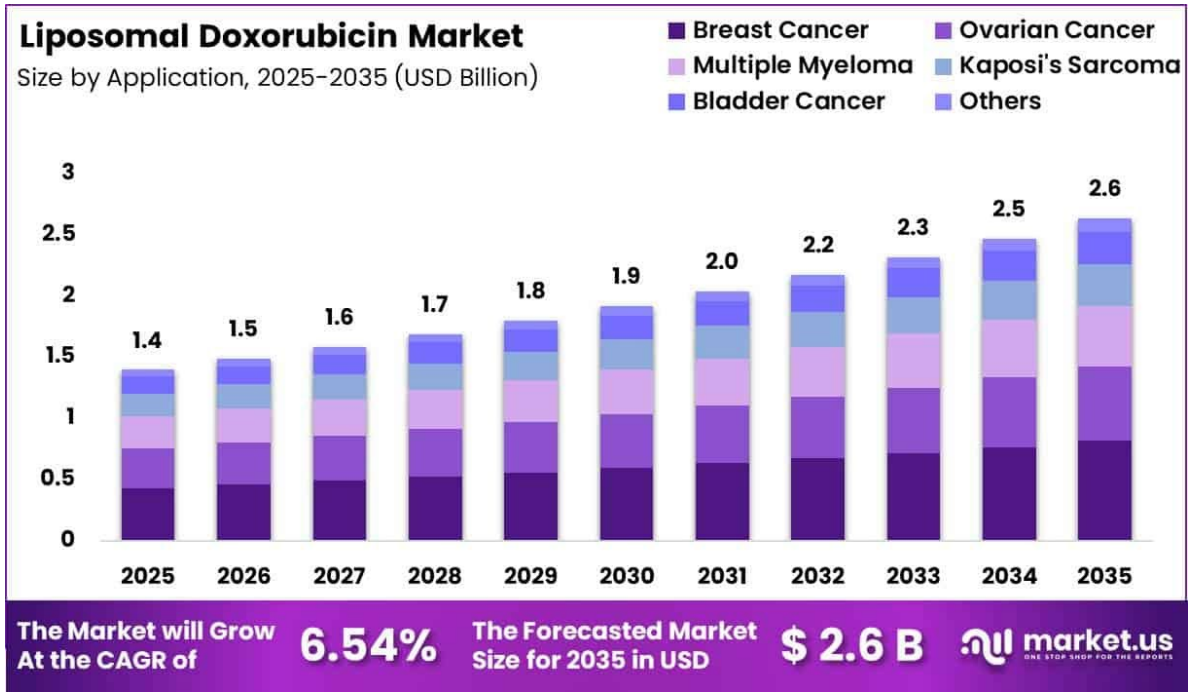


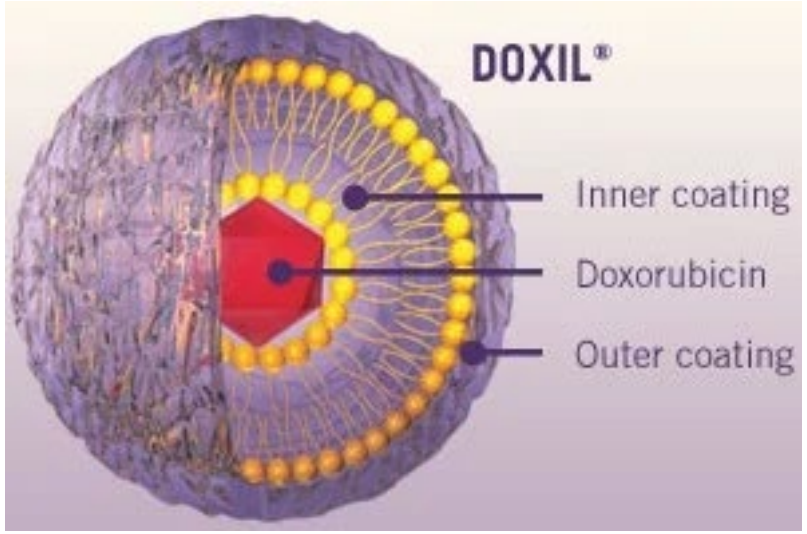
Biochimica et Biophysica Acta (2014)

Liposomal DOX

Doxil lowers toxicity, but anti-cancer efficacy is limited and cost is high

- Lowered toxicity
- Limited cancer eradication; a high price tag



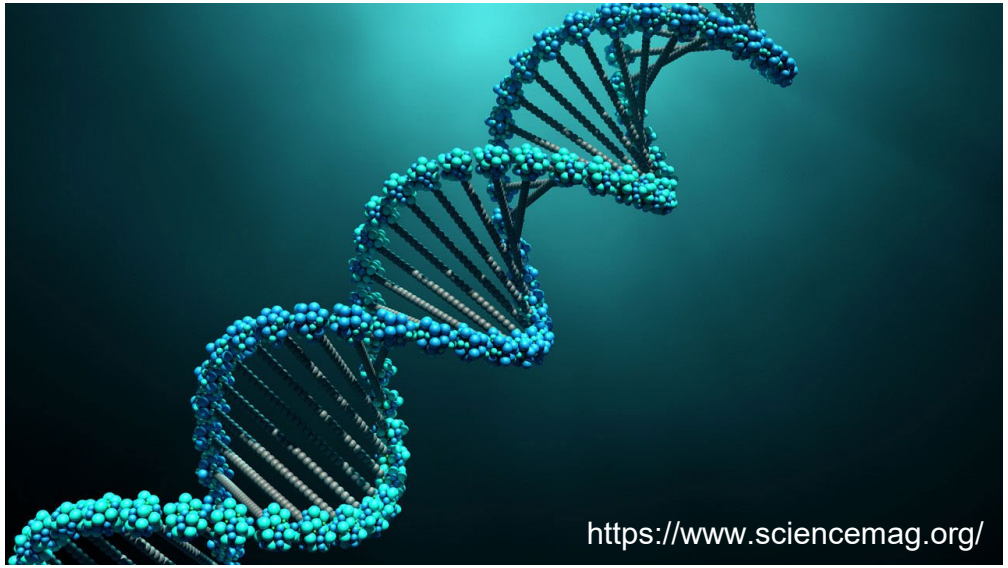


Lipids:cholesterol:DOX = 12.77:3.19:2
(**11.1%** w/w drug loading)

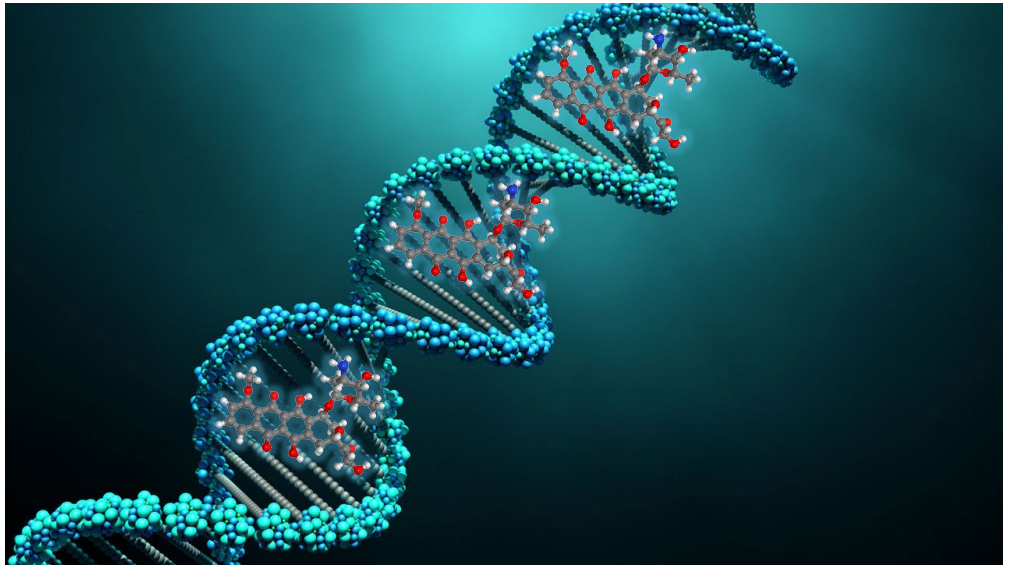
DOX/DNA complexes for drug delivery

DOX intercalates into DNA to form a simple, high-loading drug carrier

DNA



DOX/DNA



✓ **Simple** preparation ✓ **Consistent & high** drug loading

✓ **Little** impurity ✓ **Efficient/readily** drug release

Simple, scalable production

DOX/DNA nanocomplexes self-assemble in a few simple aqueous steps



DNA in DI water

DOX in DI water



Mixing with DOX

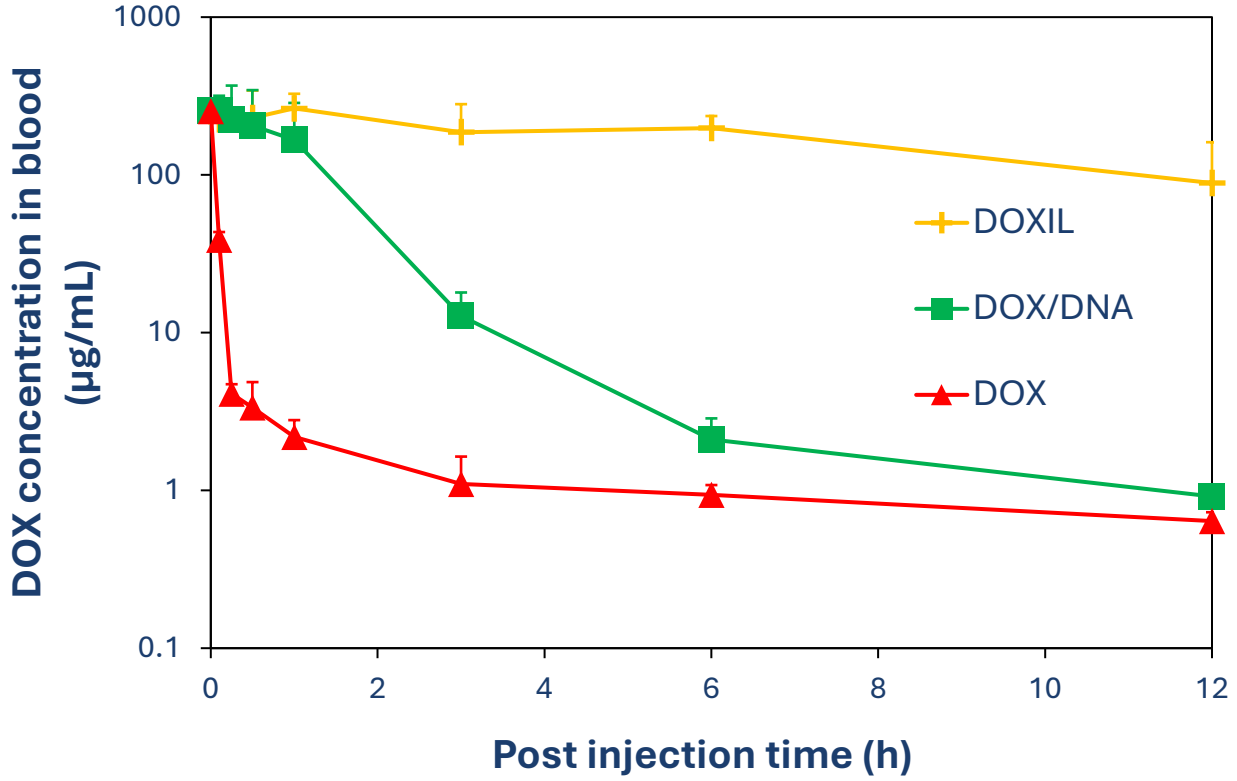


Incubation for self-assembly

Dilution in desired saline

Circulation kinetics

DOX/DNA extends circulation half-life ~19-fold over free DOX (66 vs. 3.5 min)



$t_{1/2}$ Doxil = 9.4 h

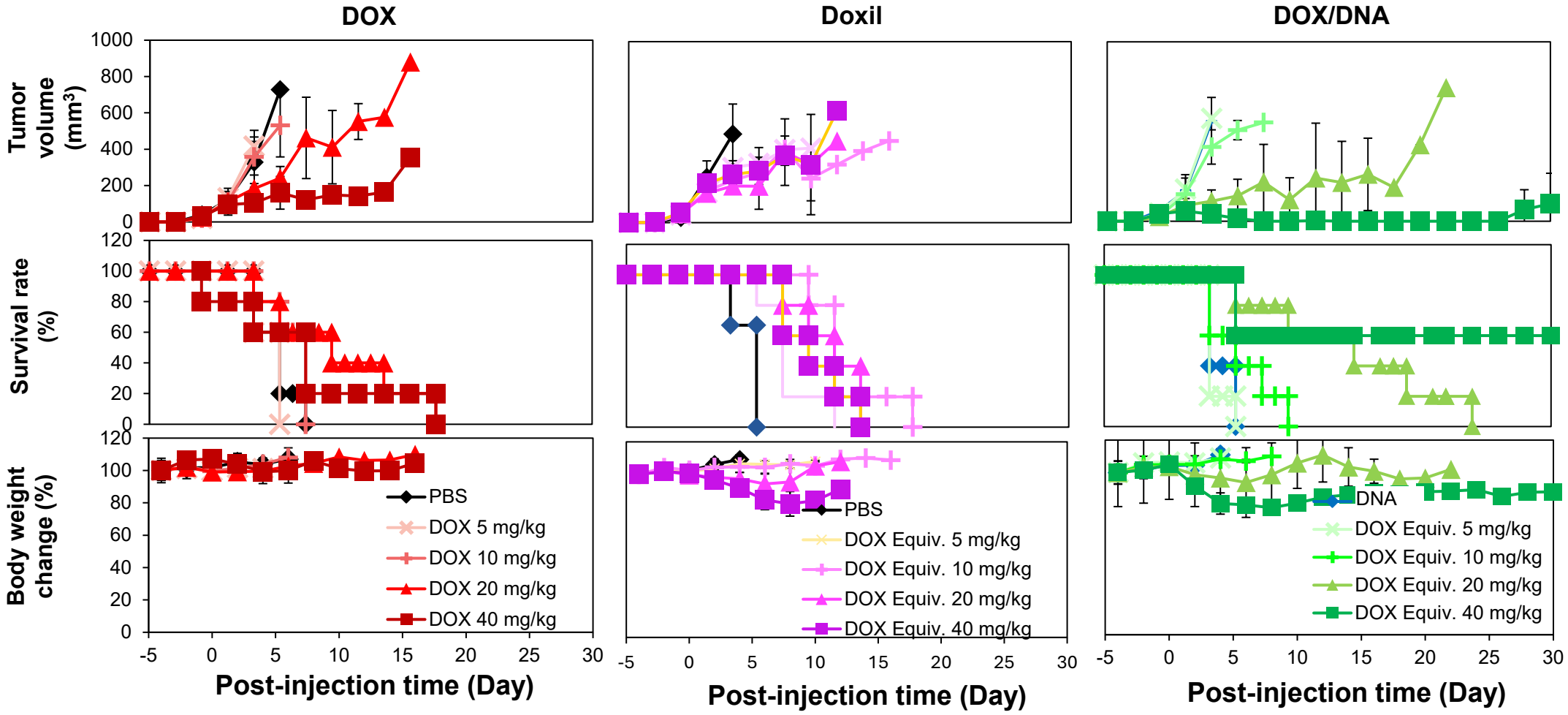
$t_{1/2}$ DOX/DNA = 66 min

$t_{1/2}$ DOX = 3.5 min

20 mg/kg DOX or DOX equiv. of DOX/DNA and Doxil given to C57BL/6 mice with a tumor (i.v. injection)

Anti-tumor activity

A single i.v. dose of DOX/DNA suppressed tumor growth and prolonged survival



EL-4 T cell lymphoma in C57BL/6 mice (syngeneic; i.v. injection)

PharmaResearch, Co., Ltd.

Licensing partner advancing DOX/DNA (NADOX) toward the clinic

PharmaResearch is dedicated to researching and developing regenerative medicine products based on natural substances, utilizing our **patented DNA Optimizing Technology.**

We aim to develop innovative pharmaceuticals incorporating **advanced biotechnologies** to improve the quality of healthy living.



Core R&D Technologies

Salmon Gametes

DOT®
DNA Optimizing Technology

High-Molecular Fragments

PN

Medical Devices

Pharmacologically Active Fragments

PDRN

Cosmetics | Health Supplements

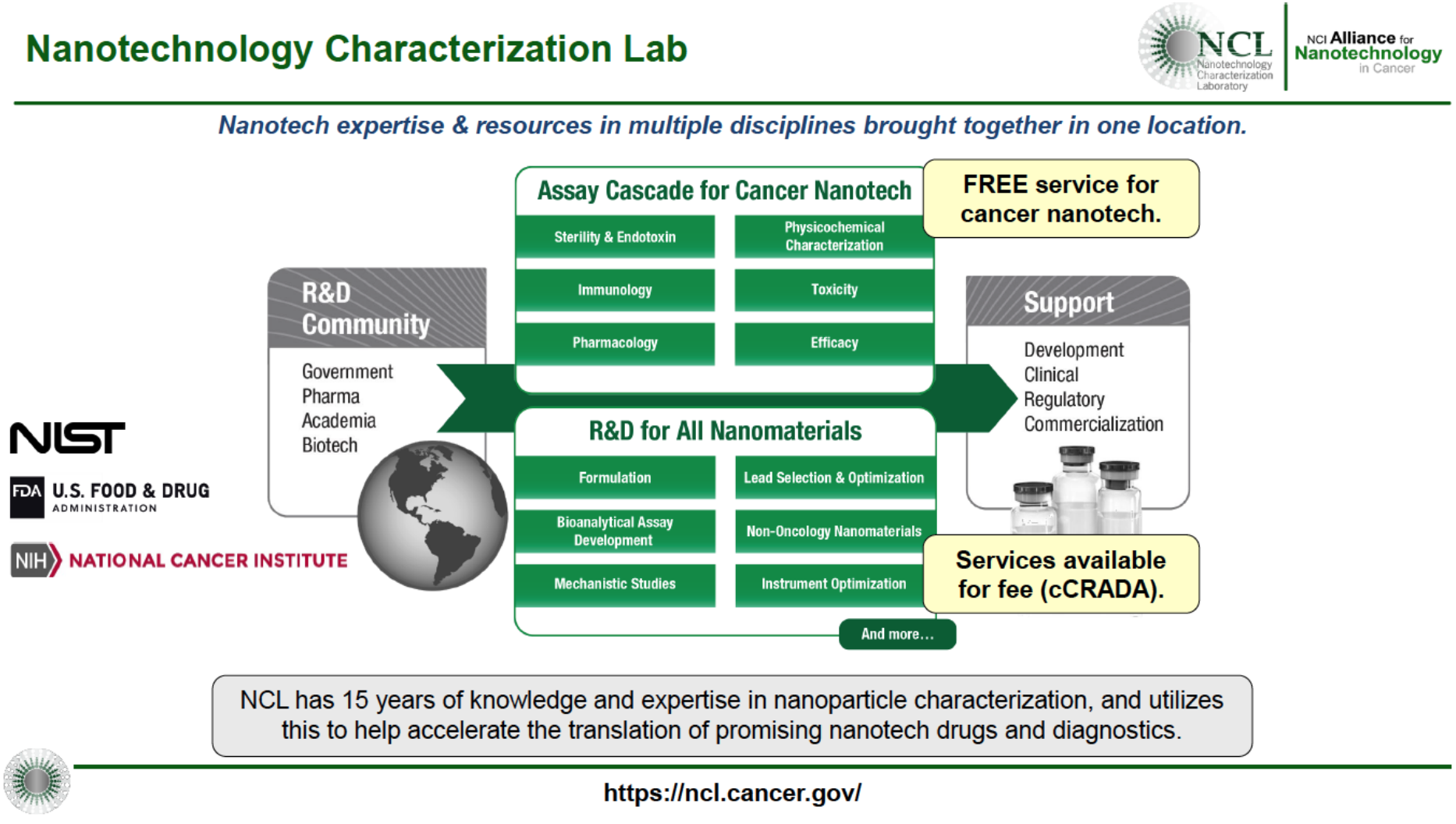
Pharmaceuticals

DOT®? DOT®, short for DNA Optimizing Technology, is PharmaResearch's proprietary technique of extracting DNA from salmon gametes and optimizing it into regenerative substances.

- Based in South Korea (Publicly traded, KOSDAQ)
- Revenue: Est. ~$500M (2026)
- US Subsidiary: PharmaResearch USA (Costa Mesa, CA)

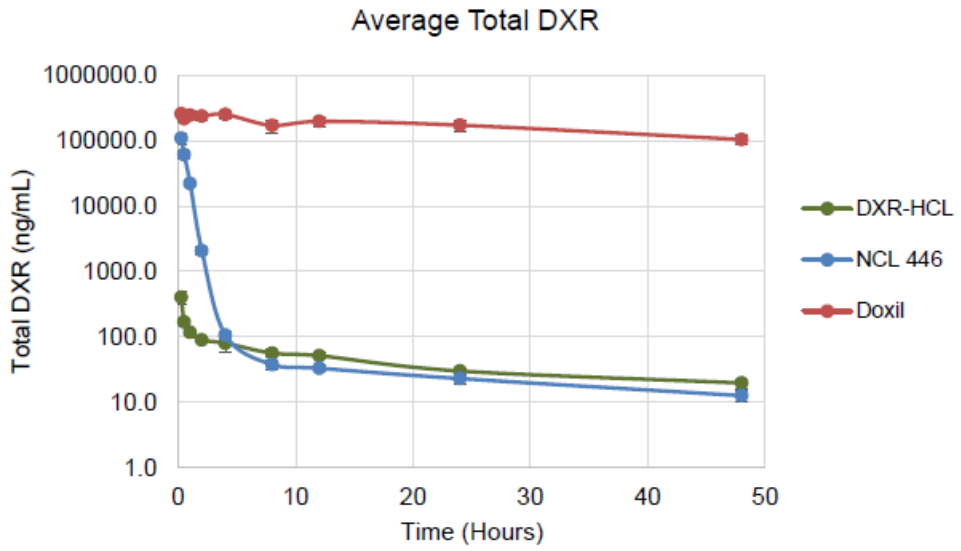
Collaboration with NCI/NCL

Independent nanomedicine characterization through the NCI Nanotechnology Characterization Lab



PK studies (NCL)

In rats, DOX/DNA increased drug exposure (AUC) 34-fold vs. free DOX



A. Total DXR Comparison

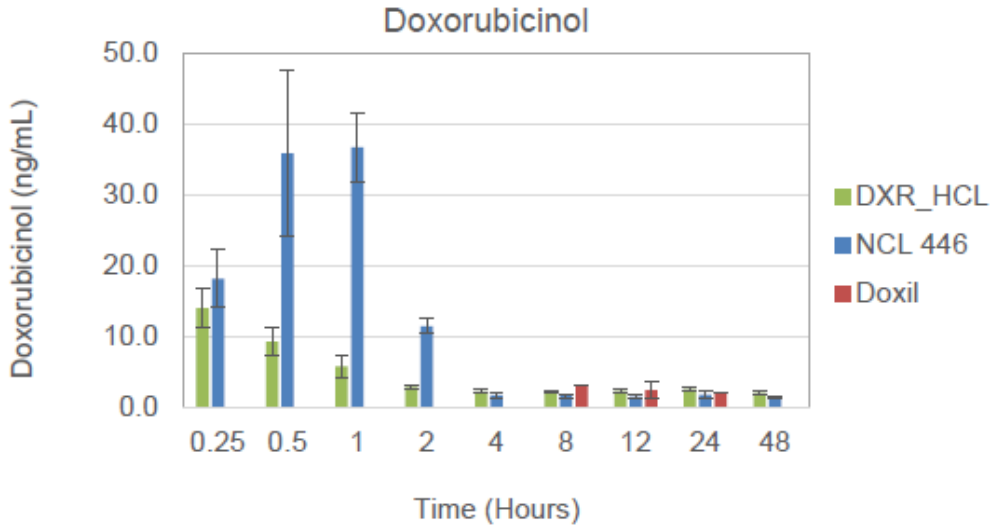
		PK Parameters									
	Animal	Tmax	Cmax	C0	AUCall	AUCinf	CLss	t1/2	lambda z	MRT	Vss
		h	ng/mL	ng/mL	ng*h/mL	ng*h/mL	mL/h*kg	h	h^{-1}	h	mL/kg
					Total DXR						
DXR HCl	1	0.25	306	517	2351	3267	3065	25	0.027	37	112064
	3	0.25	502	1299	2154	2669	3749	21	0.033	27	100349
	5	0.25	349	725	1812	2503	4000	27	0.026	36	143409
	7	0.25	480	1600	2373	2918	3429	20	0.035	26	90438
	9	0.25	375	879	2143	2793	3582	24	0.029	31	112367
	AVG	**0.25**	**402**	**1004**	**2167**	**2830**	**3565**	**23**	**0.030**	**31**	**111725**
	SD	**0.00**	**85**	**439**	**225**	**288**	**351**	**3**	**0.004**	**5**	**19918**
NCL446-1	11	0.25	124051	273780	107854	108152	92	17	0.040	0.8	75
	13	0.25	132506	265381	109737	110174	91	19	0.037	0.9	84
	15	0.25	81068	106632	79973	80325	124	17	0.040	1.2	147
	17	0.25	91264	163255	82585	82821	121	16	0.042	0.9	107
	19	0.25	111315	181857	96922	97217	103	19	0.037	0.9	90
	AVG	**0.25**	**108041**	**198181**	**95414**	**95738**	**106**	**18**	**0.039**	**0.9**	**101**
	SD	**0.00**	**21648**	**70885**	**13831**	**13866**	**16**	**1**	**0.002**	**0.1**	**29**
Doxil	21	0.25	255323	331536	7217021	14143253	0.71	47	0.015	67	48
	23	4	261884	291479	8490296	17213958	0.58	51	0.014	71	41
	25	4	298159	279352	9530746	15838850	0.63	39	0.018	52	33
	29	0.25	255863	322544	6828409	10280051	0.97	31	0.023	44	43
	AVG	**2.13**	**267807**	**306228**	**8016618**	**14369028**	**0.72**	**42**	**0.017**	**59**	**41**
	SD	**2.17**	**20452**	**24809**	**1233984**	**3001373**	**0.17**	**9**	**0.004**	**13**	**6**

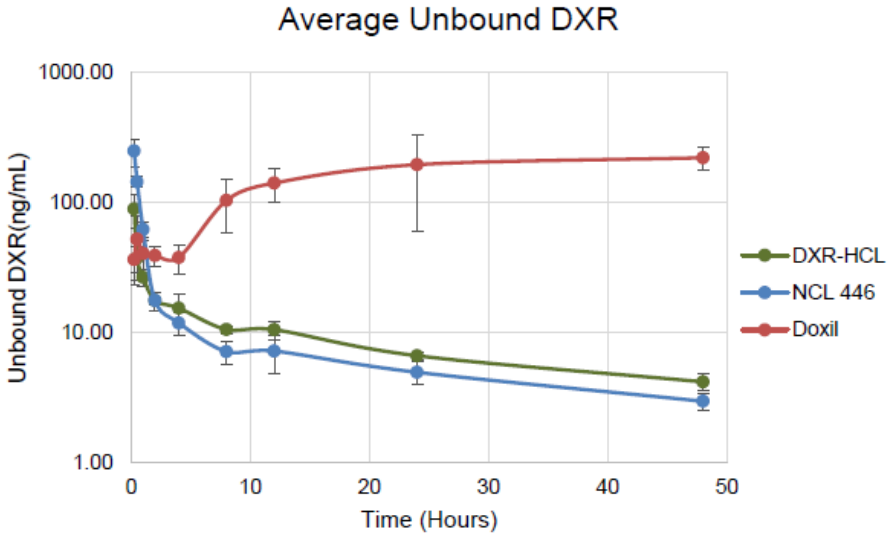
- Male Sprague-Dawley rats; IV injection, once; 10 mg/kg DOX equivalent
- Half-life: similar to DOX (13 times longer compared to the fixed initial concentration)
- AUCinf: 34 times higher than DOX

NCL Nanotechnology Characterization Laboratory

Drug metabolism and clearance (NCL)

Metabolism and clearance match free DOX, with no concern for accumulation





- Identical metabolism and clearance (DOX vs DOX/DNA)
- Unbound drug concentrations/profiles were nearly identical
- No concern for accumulation
- Dramatically different PK from Doxil

NCL Nanotechnology Characterization Laboratory

In vitro immunological profiles (NCL)

Favorable immunological profile, with heparin-like activity and RANTES induction

Test items	Results	Note
Hemolysis	Not hemolytic	-
Platelet aggregation	No induction	-
Plasma coagulation	Prolongation of APTT and thrombin time	Heparin-like activity
Complement activation	No activation	-
Cytokine induction	Not proinflammatory Induction of RANTES	Absence of IL-1, TNF, IL-6
CFU-GM	Suppression of CFU-GM formation	Common for cytotoxic oncology drugs
Leukocyte proliferation	No induction Inhibition of PHA-M induced proliferation	Common for cytotoxic oncology drugs

"DOX is known to promote consumptive coagulopathy. DOX/DNA demonstrated heparin-like activity, likely due to polyanionic nature of the DNA component.
This may provide a collateral benefit for cancer therapy"

"Induction of the chemokine RANTES, which suggests potential utility of NADOX in cancer immunotherapy when combined with immune checkpoint inhibitors"

NCL Nanotechnology Characterization Laboratory

Highlighted in the NCL 2025 Annual Report

DOX/DNA featured among the regulatory successes of NCL assay cascade collaborators





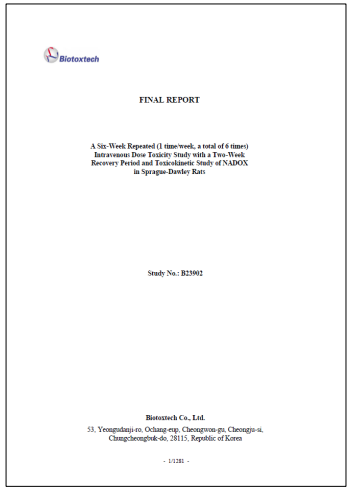
Comprehensive GLP toxicology package: improved safety vs. DOX

Toxicity was less severe than DOX at equivalent doses in rats and dogs

Criteria	Study items	Compliance	Species / Route of Administration
Formulation analysis	Formulation analytical method validation (Full validation)	GLP	
Repeat-dose Toxicity study	3-week repeated Dose Range Finding (DRF) study	Non-GLP	Rat / IV infusion
	Formulation analysis: Drug content	GLP	
	6-week repeat-dose toxicity		Rat / IV infusion
	+ 2-week recovery study		Rat / IV infusion
	+ 6-week repeat-dose toxicokinetics (TK) Study		Rat / IV infusion
	3-week repeated Dose Range Finding (DRF) study	Non-GLP	Dog / IV infusion
	Formulation analysis: Drug content	GLP	
	6-week repeat-dose toxicity		Dog / IV infusion
	+ 2-week recovery study		Dog / IV infusion
	+ 6-week repeat-dose toxicokinetics (TK) Study		Dog / IV infusion
TK Analyses	TK method development, feasibility	Non-GLP	-
	TK method validation	GLP	Rat / IV infusion
	TK analysis	GLP	Rat / IV infusion
	TK method validation	GLP	Dog / IV infusion
	TK analysis	GLP	Dog / IV infusion
Safety pharmacology	Cardiovascular safety pharmacology (Telemetry)	GLP	Dog / IV infusion

"NADOX showed improved safety vs. DOX across all GLP toxicology studies"

Rodent


Biotoxtech

FINAL REPORT

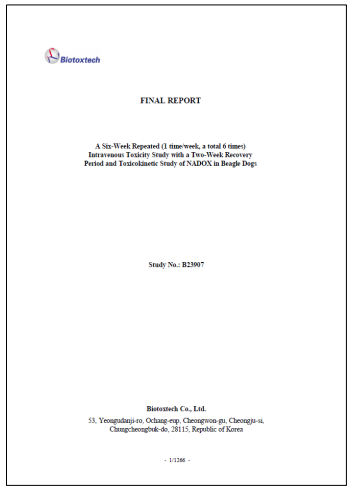
A Six-Week Repeated (1 time/week, a total of 6 times) Intravenous Dose Toxicity Study with a Two-Week Recovery Period and Toxicokinetic Study of NADOX in Sprague-Dawley Rats

Study No.: B25902

Biotoxtech Co., Ltd.
53, Yeongudanji-ro, Ochang-eup, Cheongwon-gu, Cheongju-si, Chungcheongbuk-do, 28115, Republic of Korea

- 1/1281 -

Non-Rodent


Biotoxtech

FINAL REPORT

A Six-Week Repeated (1 time/week, a total of 6 times) Intravenous Toxicity Study with a Two-Week Recovery Period and Toxicokinetic Study of NADOX in Beagle Dogs

Study No.: B23907

Biotoxtech Co., Ltd.
53, Yeongudanji-ro, Ochang-eup, Cheongwon-gu, Cheongju-si, Chungcheongbuk-do, 28115, Republic of Korea

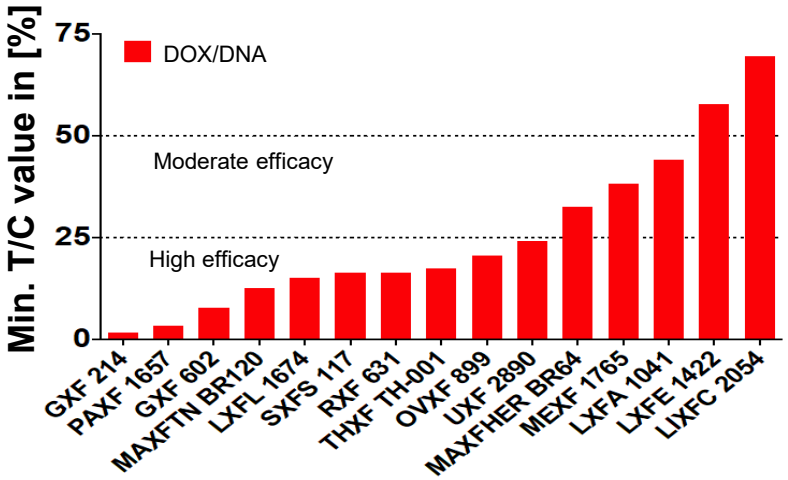
- 1/1266 -

"The toxicological effects of the test substance were significantly less severe than those of the comparative substance at the same dose level of doxorubicin."

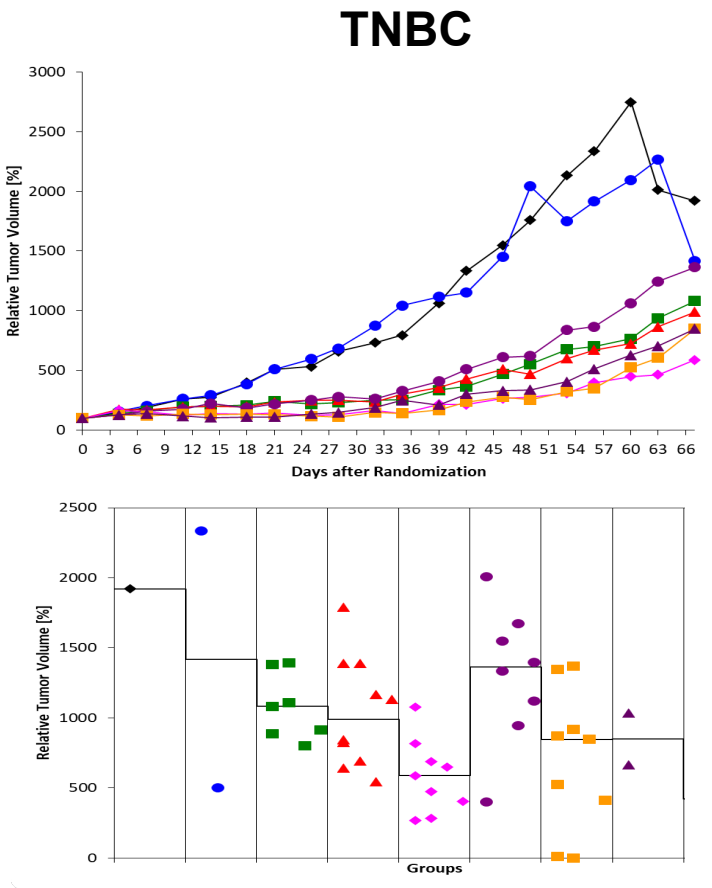
→ Novel excipient (NF) confirmed to be non-toxic, supporting a clean regulatory pathway

PDX studies (mini-screen, CRL)

Mini-screen across PDX models: optimal efficacy vs. side effects at 12 mg/kg



charles river



Optimal efficacy vs side effects at 12 mg/kg

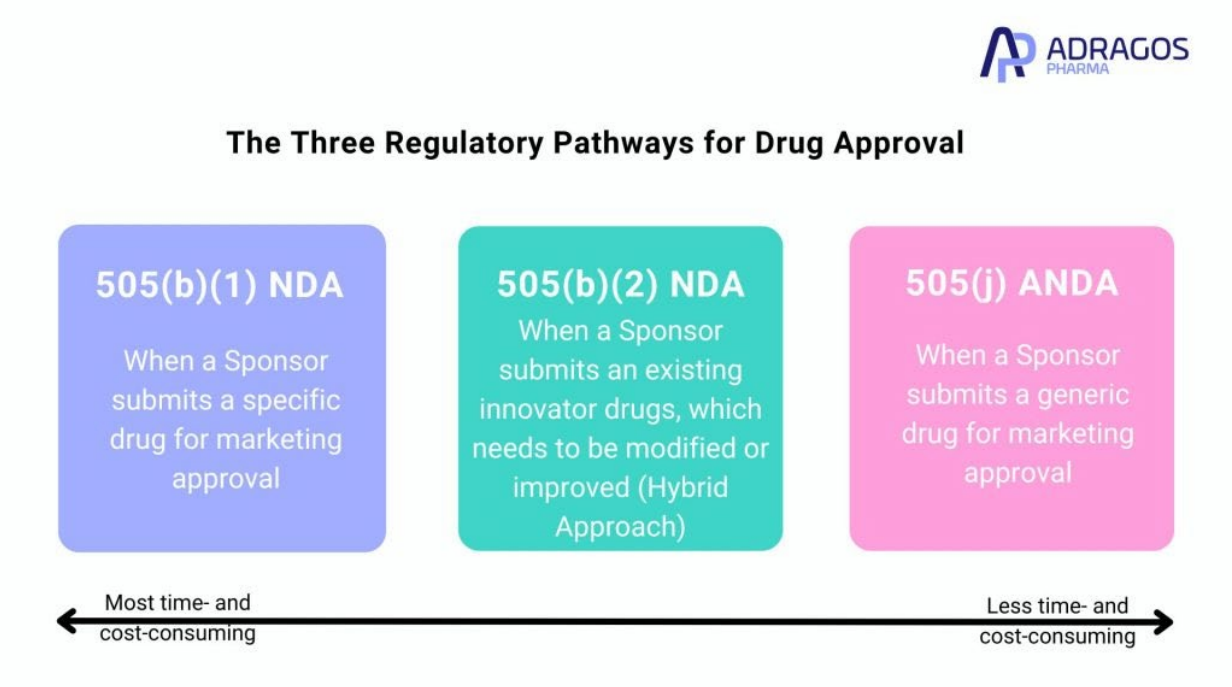
DOX/DNA vs. DOX vs. liposomal DOX

DOX/DNA pairs DOX's broad indications with low cardiotoxicity and no hand-foot syndrome

	DOX/DNA	DOX	Liposomal Doxorubicin
Delivery technology	Nucleotide fragment carrier	Free drug : no carrier	STEALTH® : PEGylated liposome
Cardiotoxicity	Low	High	Low
Hand-foot syndrome	None	None	High
Half-life	Moderate (balanced PK)	Short	Long
Manufacturing Cost	-	Low	High
Indication Coverage	Inherits Dox's broad label via 505(b)(2)	10+ approved (ovarian, breast, leukemia, lymphoma, etc.)	3 indications (Ovarian, Kaposi’s sarcoma, multiple myeloma)

Regulatory strategy

The 505(b)(2) pathway leverages existing DOX data to shorten development



EXPLORING THE 505(b)(2) PATHWAY

WHAT?

Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (The "Hatch-Waxman" act) was created to simplify and speed up the approval process for drugs incorporating pharmacological agents which have already received approval. In such cases, the FDA application relies on clinical data previously submitted by others.

WHY?

The intent of the 505(b)(2) pathway was to speed up the FDA application & review process and encourage further innovation with already-approved chemical entities by eliminating the need to duplicate, previously performed work.

HOW?

Using a 505(b)(2) filing, companies and organizations can reference existing data and studies. This is done in consultation with the FDA. The 505(b)(2) approval process can lower risks (e.g., clinical and regulatory) while accelerating development and commercialization.

Pre-IND consulting

FDA pre-IND feedback confirmed the 505(b)(2) route and supported the development plan



U.S. FOOD & DRUG ADMINISTRATION

PIND 174651

MEETING REQUEST-
WRITTEN RESPONSES

PharmaResearch Co., Ltd.
Attention: Diane Chambers
Regulatory and Submissions Specialist
101 Federal Street
Boston, MA 02110

Dear Diane Chambers:

Please refer to your pre-investigational new
(doxorubicin hydrochloride).

We also refer to your submission dated No
request. The purpose of the requested mee
of the development program, including regu
the study protocol for the initial clinical trial
metastatic solid tumors, in support of the 5

Further reference is made to our Meeting C
wherein we stated that written responses to
a meeting.

The enclosed document constitutes our wri
your December 20, 2024, background pack

If you have any questions, contact me at 30
Craig.Long@fda.hhs.gov.

Sincerely,

{See appended elec

Craig Long
Regulatory Health P
Division of Regulato
Office of Regulatory
Office of New Drugs
Center for Drug Eva

Reference ID: 5514515

U.S. FOOD & DRUG ADMINISTRATION

WRITTEN RESPONSES

Meeting Type: B
Meeting Category: Pre-IND

Application Number: 174651

Product Name: NADOX (doxorubicin hydrochloride)

Indication: Locally advanced or metastatic solid tumors including but not limited to triple negative breast cancer and soft tissue sarcoma

Sponsor Name: PharmaResearch Co., Ltd.

Regulatory Pathway: 505(b)(2) of the Federal Food, Drug, and Cosmetic Act

BACKGROUND

Regulatory
On November 22, 2024, PharmaResearch Co., Ltd. (PharmaResearch) submitted a request for a Type B Pre-Investigational New Drug (pIND) meeting to gain feedback on the adequacy of the development program, including regulatory requirements, nonclinical studies, and the study protocol for NADOX for the initial clinical trial for the treatment of locally advanced or metastatic solid tumors, in support of the 505(b)(2) pathway. FDA granted this meeting request on December 1, 2024.

Nonclinical
PharmaResearch states NADOX is a formulation of doxorubicin hydrochloride (DOX) with a nucleotide fragments (NF) excipient. The proposed nonclinical package includes pharmacology, pharmacokinetics, safety pharmacology of NADOX and the excipient alone in dogs, and 6-week repeat-dose toxicology studies in rats and dogs with doxorubicin and excipient only groups.

CMC
NF is a naturally sourced (from wild-caught salmon), fragmented polynucleotide excipient that self-assembles into nanocomplexes by DOX intercalating between the base pairs through planar π-π stacking, a noncovalent interaction, in both intra- and intermolecular manners. The loading of DOX to NF was adjusted by a fluorescence quenching study, where the change in fluorescence of DOX (Excitation 490 nm and Emission 520–700 nm) was measured with varying NF to DOX ratios in the range of 1–12 (w/w), at a fixed DOX concentration of 11 mg/mL, and a final volume of 100 mL. The NF-to-DOX ratio of 6:1 (w/w) was used to prepare NADOX particles.

Reference ID: 5514515

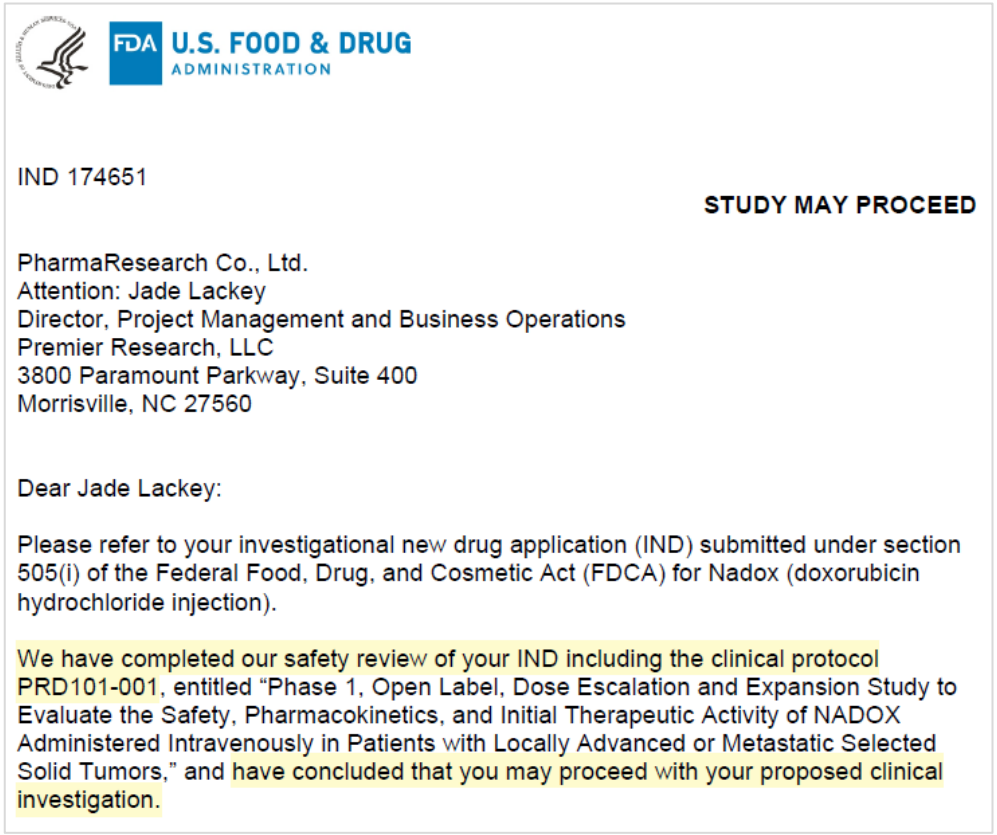
Question	Answers
Suitability for 505(b)(2)	Appropriate
DOX/DNA quality control data	Satisfactory, recommending supplementary data
DNA as excipient	Assessed to be acceptable
Manufacturing preparation plans	Plans for manufacturing clinical materials are required
Pre-clinical data package	Assessed to be sufficient
Suitability for Phase I studies	Assessed to be appropriate but final decision to be made on IND

IND submission and outcome

IND submitted in December 2025; FDA 'Study May Proceed' received in January 2026

IND package	
CTD Module	**Content**
Module 1 (Regional admin information)	• Admin (Form 1571, US Agent etc.) • Pre-IND meeting minutes • Investigator's Brochure • Investigational drug label • General investigational plan
Module 2 (Overview and summary)	• Nonclinical overview / summary • Clinical overview / summary
Module 3 (Quality)	• Drug Substance • Drug Product • Novel Excipient • Adventitious agents (virus, TSE/BSE risk)
Module 4 (Non-clinical study reports)	• Nonclinical study reports • GLP Toxicology SEND data sets
Module 5 (Clinical study reports)	• Protocol • Informed Consent Form • Form 1572, Principal Investigator's CV

Submitted in December 2025



FDA U.S. FOOD & DRUG ADMINISTRATION

IND 174651

STUDY MAY PROCEED

PharmaResearch Co., Ltd.
Attention: Jade Lackey
Director, Project Management and Business Operations
Premier Research, LLC
3800 Paramount Parkway, Suite 400
Morrisville, NC 27560

Dear Jade Lackey:

Please refer to your investigational new drug application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Nadox (doxorubicin hydrochloride injection).

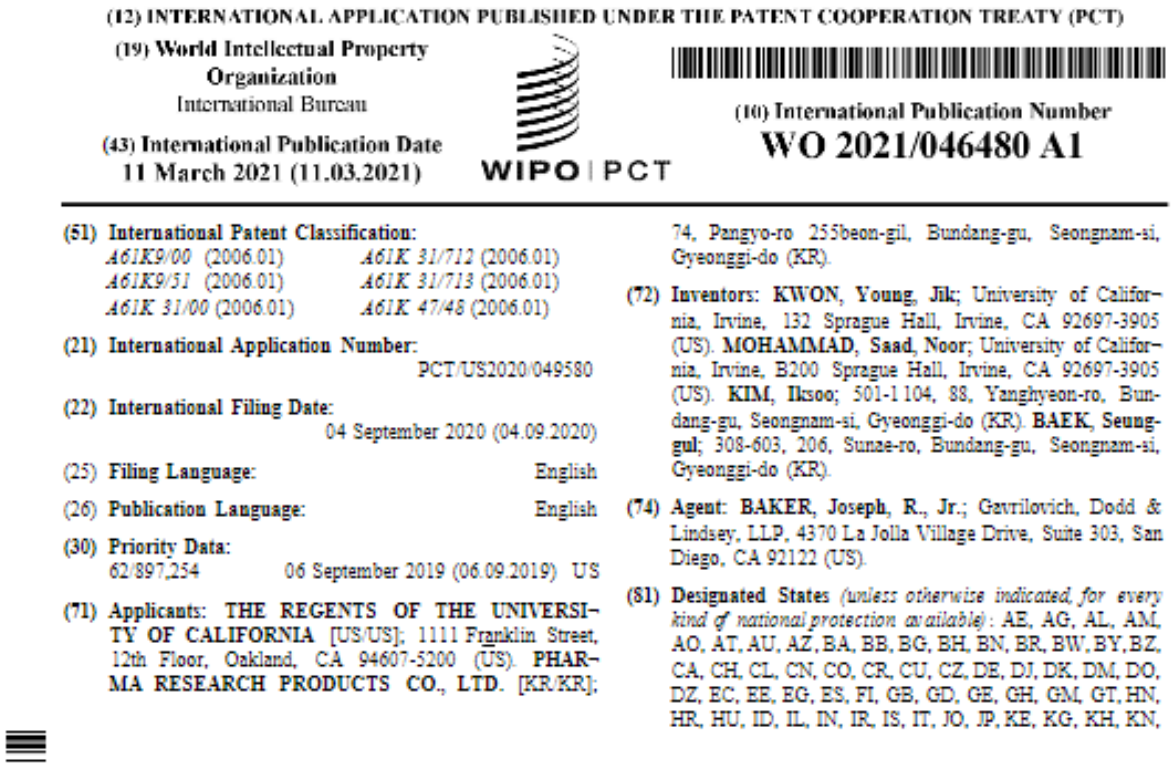
We have completed our safety review of your IND including the clinical protocol PRD101-001, entitled "Phase 1, Open Label, Dose Escalation and Expansion Study to Evaluate the Safety, Pharmacokinetics, and Initial Therapeutic Activity of NADOX Administered Intravenously in Patients with Locally Advanced or Metastatic Selected Solid Tumors," and have concluded that you may proceed with your proposed clinical investigation.

Received in January 2026

Intellectual property status

PCT application filed; patents granted in Canada, Korea, Japan and Australia

PCT international patent application filed for global protection



(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
11 March 2021 (11.03.2021)

WIPO | PCT

(10) International Publication Number
WO 2021/046480 A1

(51) International Patent Classification:
A61K9/00 (2006.01) *A61K 31/712* (2006.01)
A61K9/51 (2006.01) *A61K 31/713* (2006.01)
A61K 31/00 (2006.01) *A61K 47/48* (2006.01)

(21) International Application Number:
PCT/US2020/049580

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04 September 2020 (04.09.2020)

(25) Filing Language: English

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(30) Priority Data:
62/897,254 06 September 2019 (06.09.2019) US

(71) Applicants: **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** [US/US]; 1111 Franklin Street, 12th Floor, Oakland, CA 94607-5200 (US). **PHARMA RESEARCH PRODUCTS CO., LTD.** [KR/KR]; 74, Pangyo-ro 255beon-gil, Bundang-gu, Seongnam-si, Gyeonggi-do (KR).

(72) Inventors: **KWON, Young, Jik**; University of California, Irvine, 132 Sprague Hall, Irvine, CA 92697-3905 (US). **MOHAMMAD, Saad, Noor**; University of California, Irvine, B200 Sprague Hall, Irvine, CA 92697-3905 (US). **KIM, Iksoo**; 501-1104, 88, Yanghyeon-ro, Bundang-gu, Seongnam-si, Gyeonggi-do (KR). **BAEK, Seung-gul**; 308-603, 206, Sunae-ro, Bundang-gu, Seongnam-si, Gyeonggi-do (KR).

(74) Agent: **BAKER, Joseph, R., Jr.**; Gavrilovich, Dodd & Lindsey, LLP, 4370 La Jolla Village Drive, Suite 303, San Diego, CA 92122 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN,

	Status
PCT	Filed
US[1]	Under examination
China[1]	Under examination
EU[1]	Under examination
Canada	Granted
India	Under examination
Korea[1]	Granted
Japan[1]	Granted
Australia	Granted
Hong Kong	Under examination

[1]IP5 (Intellectual Property 5): A forum of the five largest intellectual property offices in the world

ARDENA cGMP site

cGMP manufacturing of clinical supply by ARDENA (the Netherlands)

Pivot Park (Development)



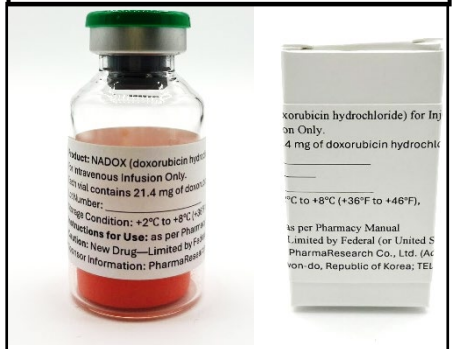
Prasfarma (Drug Product)



Kantsingel (Bulk Solution)

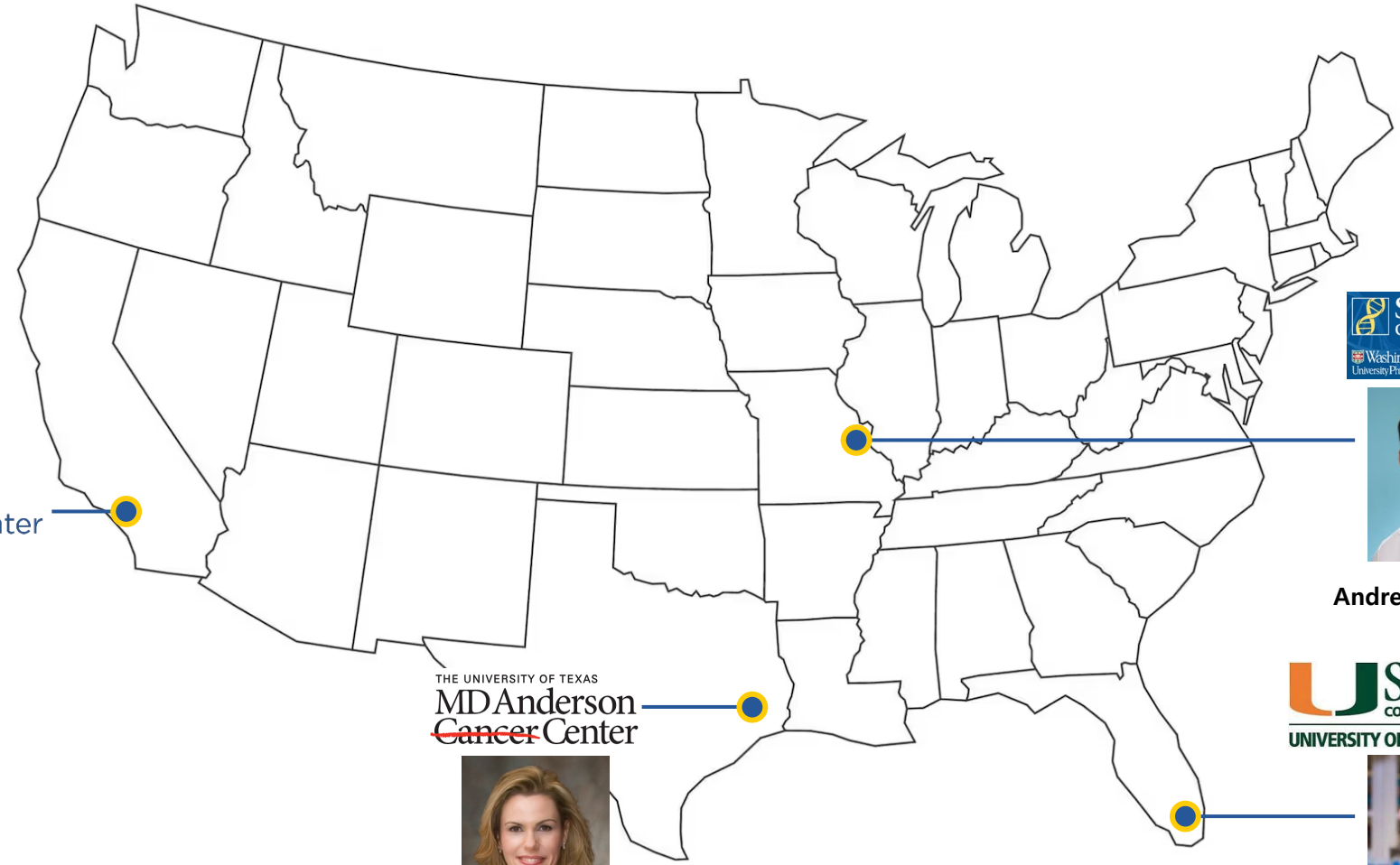


DOX/DNA clinical sample



Selected sites

Four NCI-designated comprehensive cancer centers selected for the Phase I study

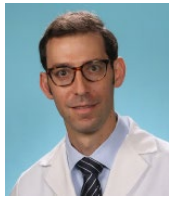


UC Irvine Chao Family Comprehensive Cancer Center



Farshid Dayyani, MD, PhD

SITEMAN CANCER CENTER
Washington University Physicians | BJC HealthCare

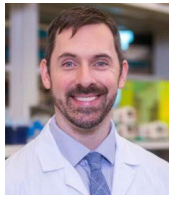


Andrew Davis, MD

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Apostolia Tsimberidou, MD, PhD

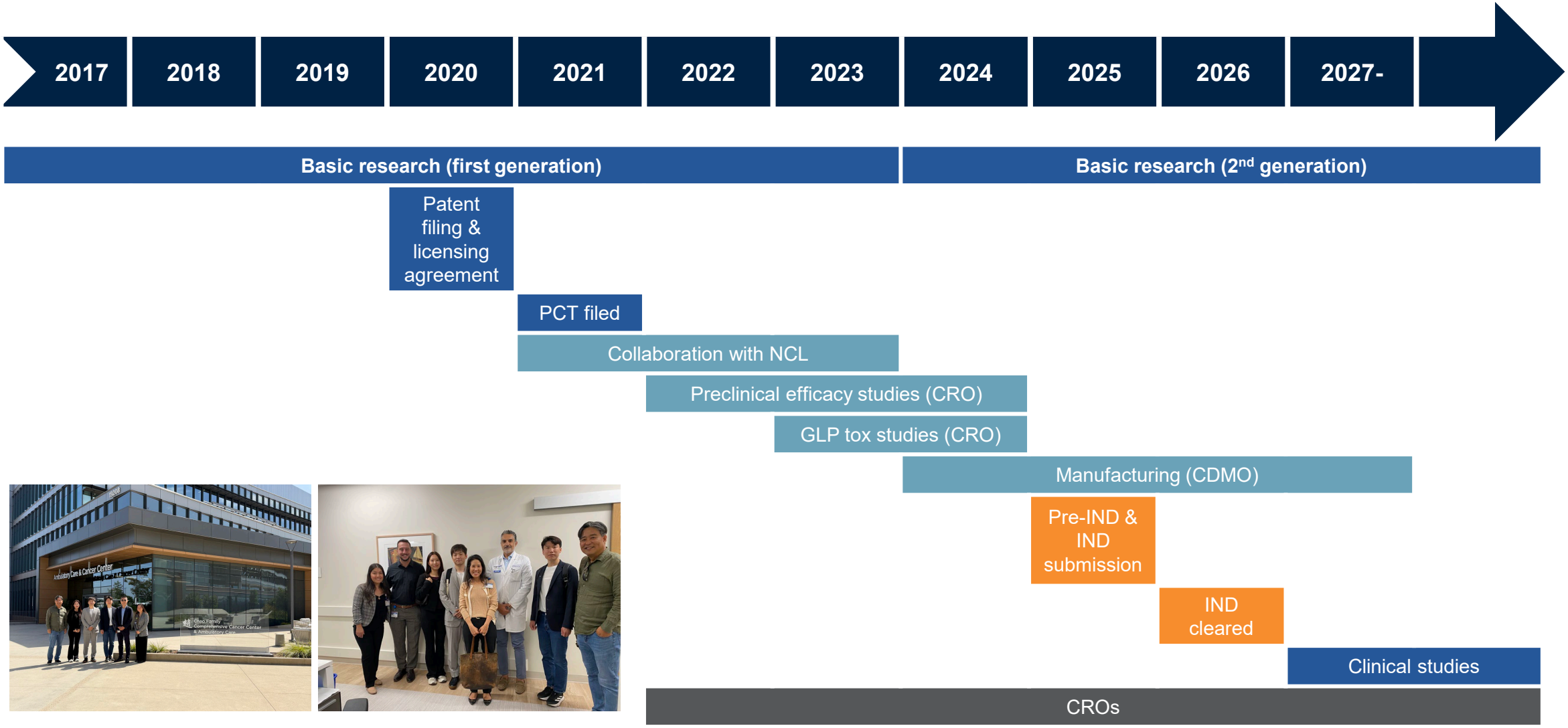
SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM



Matthew P. Schlumbrecht MD, MPH

Overview timeline

From first-generation research in 2017 to IND clearance and clinical studies in 2026



Consulting progress summary

Specialist consultants supported each regulatory and clinical planning step

Company Name	Key Activities
Ahn Bio Consulting	Regulatory Review on FDA Requirements for Early-Stage 505(b)(2) Drugs
Parexel	Nonclinical Data Review & Development Guidance
Biologics Consulting	Review of CMC & Nonclinical Data, and Preparation of Early-Phase Clinical Study Design
OPIS	Preparation of Pre-IND Meeting Package (Briefing Document)
Premier Consulting	IND Dossier Preparation and In-depth Clinical Design & Strategy Discussions
AIMS	PK Modeling & Clinical Operational Strategy Support
IQVIA (DDRS)	IND Transfer & maintenance, Supplementary Nonclinical Study Plan for Introducing Additional Clinical Regimens, Clinical Study Synopsis/Protocol Review

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ARDENA

Biotoxtech

premier research

IQVIA BIOTECH

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Questions?