SCOPUS BIOPHARMA

Launch of Duet Therapeutics, a wholly-owned immuno-oncology subsidiary of Scopus BioPharma

September 2021

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SCOPUS BIOPHARMA AT A GLANCE

Scopus is a clinical-stage biopharmaceutical company developing transformational therapeutics for serious diseases with significant unmet medical need

COMPANY	EXCHANGE	SYMBOL	SHARE PRICE	MARKET CAP	10-DAY AVG VOLUME	SHARES OUTSTANDING
Scopus BioPharma	NASDAQ Global Market	"SCPS"	$5.77	$104.4M	1,331,365	18,094,265

*Share information as of 4 PM close on September 9, 2021

SCOPUS BIOPHARMA

DUET THERAPEUTICS, A SCOPUS BIOPHARMA COMPANY

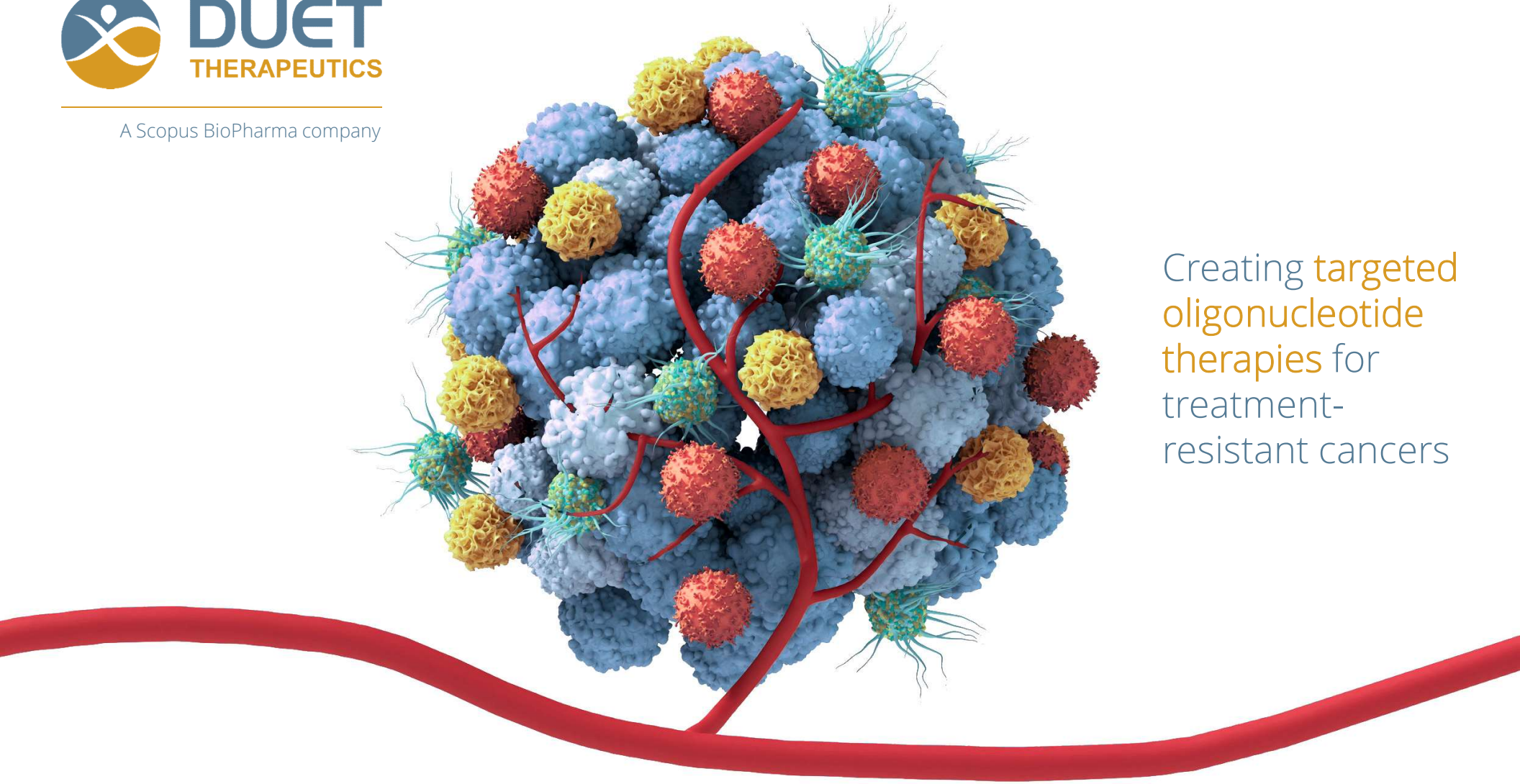
On September 2, 2021, Scopus announced the launch of Duet Therapeutics to integrate the management and clinical development of the immuno-oncology assets of Scopus and Olimmune, acquired by Scopus in June 2021

DUET THERAPEUTICS

A Scopus BioPharma company

DUET THERAPEUTICS

A Scopus BioPharma company



Creating targeted oligonucleotide therapies for treatment-resistant cancers

Duet's platform provides a unique approach to treating hematological malignancies and solid tumor cancers

Bi-functional mode of action

Duet's platform stimulates the immune activation and releases immunosuppression, both of which are required for durable therapeutic responses.

Targeted delivery platform

Duet's method of targeted delivery works by activating specific immune cells in the tumor microenvironment against the cancer.

World-class team & partners

Duet is working with world class researchers and clinicians to bring the technology through the clinic and to patients.

Addresses solid tumors

Duet's platform targets a fundamental mechanism that underlies hematological malignancies and solid tumor cancers.

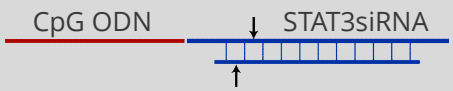
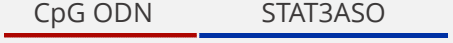
Clinical stage

Duet has a Phase 1 clinical trial that is actively recruiting patients for B-cell non-Hodgkin Lymphoma, and two additional Phase 1 trials targeted to begin in Q1 2023.

Strong IP position

Duet has 4 issued patents and 4 submitted PCT applications that cover the technologies that make up Duet's platform.

The Duet technologies create a powerful portfolio of bi-functional molecules that hold broad potential across multiple tumor types

Molecule name	CpG-STAT3siRNA (DUET-01)	CpG-STAT3ASO (DUET-02)	CpG-STAT3decoy (DUET-03)
Structure			
STAT3 mechanism of action	Bi-functional effect resulting from synergy of CpG-mediated immunostimulation and STAT3 inhibition through **RNA silencing**	Bi-functional effect resulting from synergy of CpG-mediated immunostimulation and STAT3 inhibition through **antisense**	Bi-functional effect resulting from synergy of CpG-mediated immunostimulation and **DNA-binding inhibition**
Optimal delivery / targets	**Local delivery**	**Systemic or local delivery**	**Systemic or local delivery**
Publications	Nature Biotechnology, 2009; Blood, 2013, 2014; Cancer Research, 2010, 2013; Clinical Cancer Research, 2015	Clinical Cancer Research (2018) Journal of Clinical Investigation (2021)	Blood, 2015; Journal of Leukemia Biology, 2017; Molecular Therapy, 2018
Patents	US 9,688,982	US 10,758,624: broad coverage for all STATs (STAT1/2/3/4/5/6) for cancer/inflammation	US 9,976,147 US 10,829,765
Clinical trials initiation / indication	Q3 2021 / B-cell non-Hodgkin lymphoma	Q1 2023 / Genitourinary and Head & Neck cancers	Acute Myeloid Leukemia

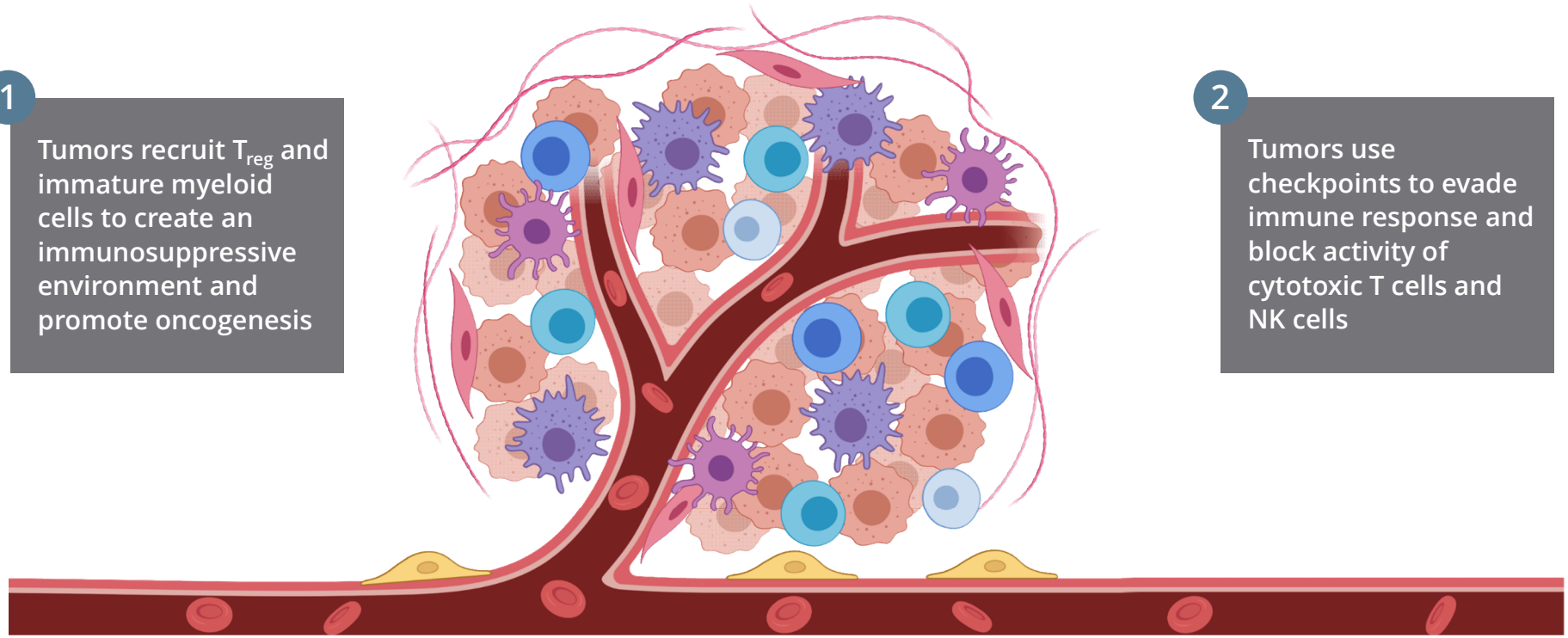
Duet's pipeline of STAT3 inhibitors includes a suite of technologies and several expansion indications in immuno-oncology

	Candidate	Program / indication	Discovery / optimization	IND enabling	Phase 1
Development	DUET-01	B-cell non-Hodgkin lymphoma	Target milestone: Dosing first patient Q4 2021		
	DUET-01 + ICI	B-cell non-Hodgkin lymphoma	Target milestone: Dosing first patient Q3 2022		
	DUET-02	Genitourinary cancers	Target milestone: IND Q4 2022		
	DUET-02	Head & neck cancers	Target milestone: IND Q4 2022		
Research	DUET-01 + ICI	Cutaneous T-cell lymphoma	Discovery		
	DUET-03	Acute myeloid leukemia	Discovery		

Tumor cells co-opt the immune system to evade adaptive immunity and promote oncogenesis in the TME

Tumor Microenvironment (TME)

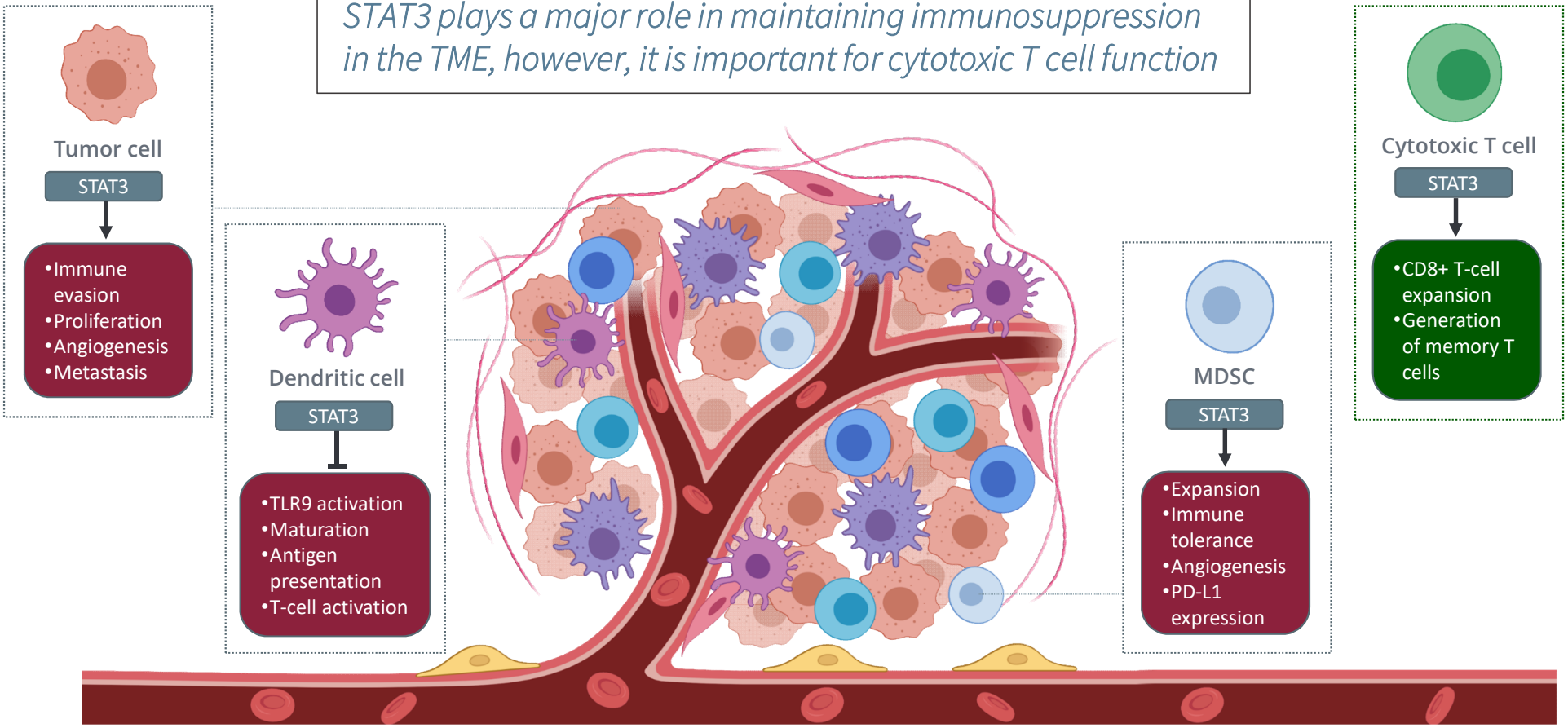
1 Tumors recruit T_{reg} and immature myeloid cells to create an immunosuppressive environment and promote oncogenesis



2 Tumors use checkpoints to evade immune response and block activity of cytotoxic T cells and NK cells

STAT3 is a master regulator of the immune system and a high-value immuno-oncology target, but requires cell-specific modulation

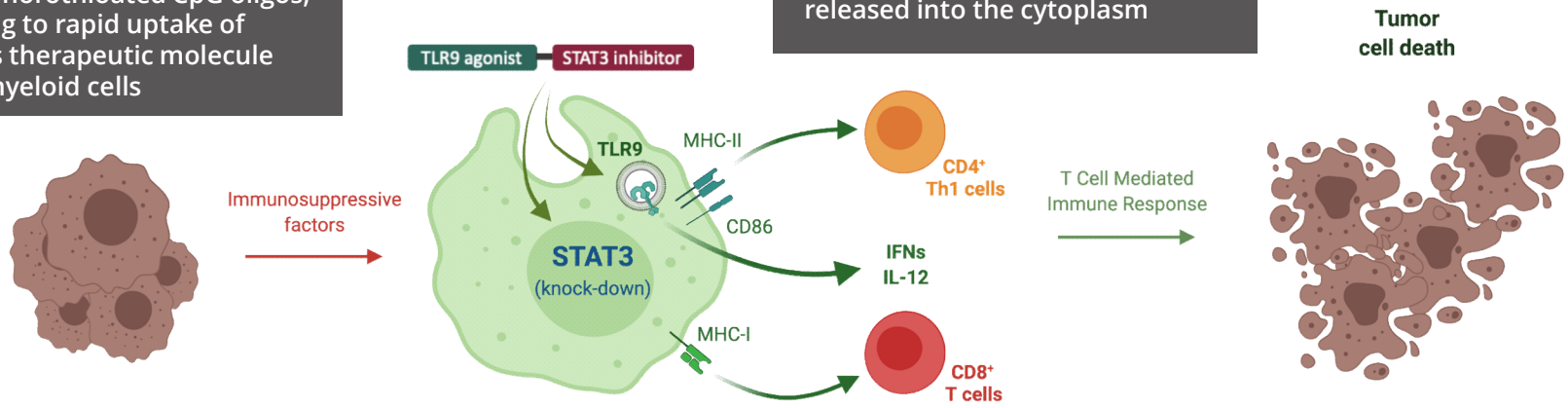
STAT3 plays a major role in maintaining immunosuppression in the TME, however, it is important for cytotoxic T cell function



Duet strategy: bi-functional oligonucleotide activates immune system (TLR9) and turns off master checkpoint (STAT3)

1 Scavenger receptors, highly expressed in antigen-presenting cells, have a natural affinity for phosphorothioated CpG oligos, leading to rapid uptake of Duet's therapeutic molecule into myeloid cells

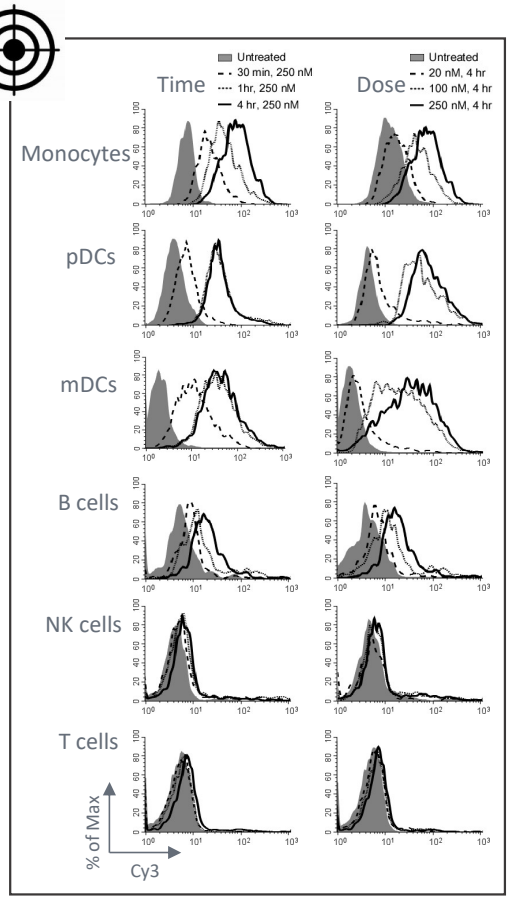
2 The bi-functional oligonucleotide is internalized into early endosomes, where it binds to TLR9 and is released into the cytoplasm



3 **The activated TLR9 triggers the signalling cascade that results in enhanced antigen presentation, pro-inflammatory cytokine release, and T-cell stimulation**

4 STAT3 inhibition releases the brakes on immune activation, allowing for the full potential of TLR9-driven innate and adaptive immune responses

DUET-01 targets TLR9+ immune cells and results in complete response in A20 model of B-cell non-Hodgkin lymphoma

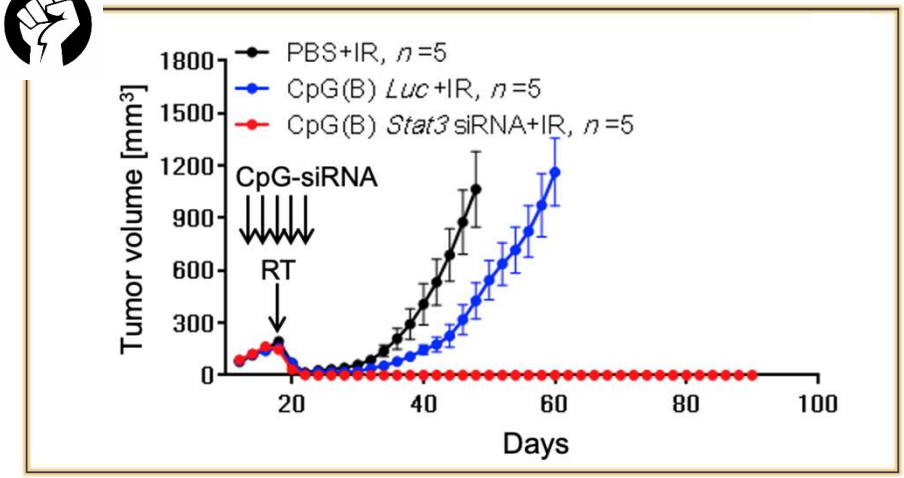


DUET-01

CpG — STAT3 siRNA

Targeted uptake of DUET-01 by TLR9+ immune cells and avoiding uptake by NK or T cells

The DUET-01 oligonucleotide results in **complete response in A20 mice** compared to radiation alone or radiation in combination with CpG only



Zhang *et al.*, TLR9-mediated siRNA delivery for targeting of normal and malignant human hematopoietic cells in vivo, *Blood* (2013)[1]

A Phase I study of intratumoral injections of DUET-01 with local radiation in patients with relapsed/refractory B-cell NHL

ELIZABETH BUDDE, MD, PHD

Associate Professor, Division of Lymphoma, Department of Hematology & Hematopoietic Cell Transplantation at City of Hope

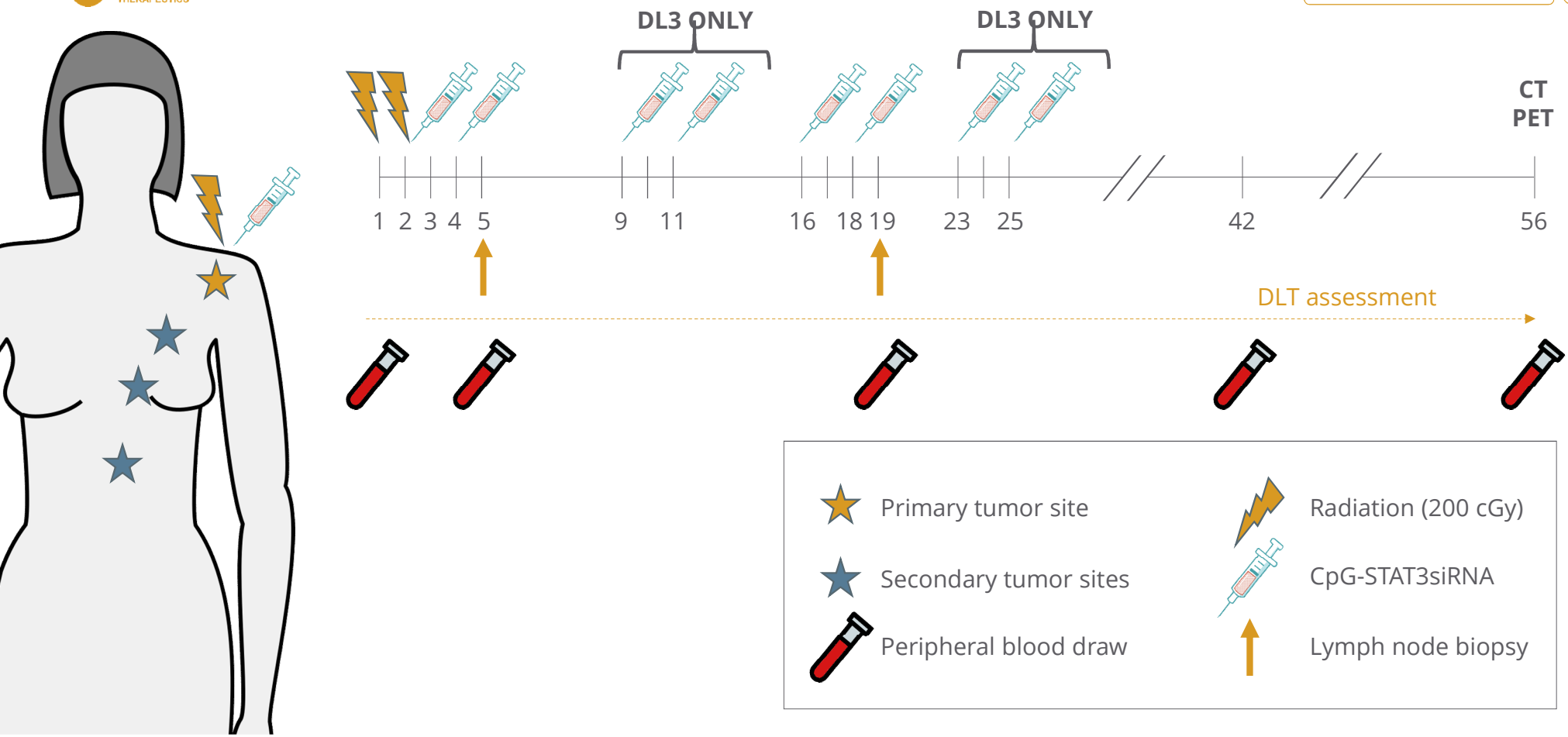
PRIMARY OBJECTIVES:

- **Determine the recommended Phase 2 dose** of DUET-01 when given in combination with local radiation therapy.
- **Evaluate safety and feasibility** of intratumoral injections when combined with radiation, by evaluation of toxicities.

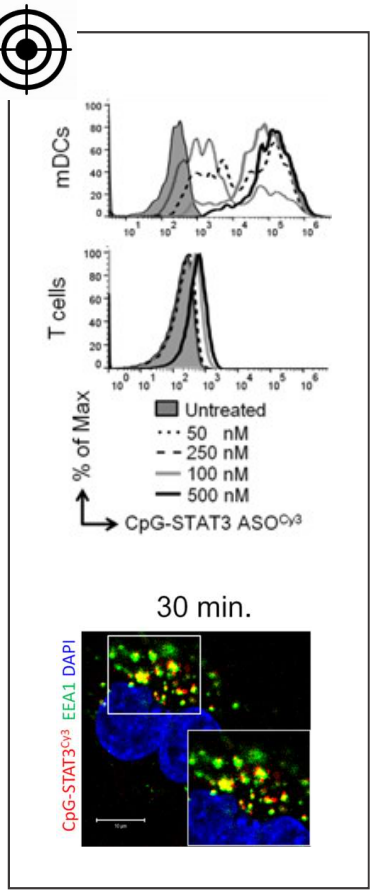
SECONDARY OBJECTIVES:

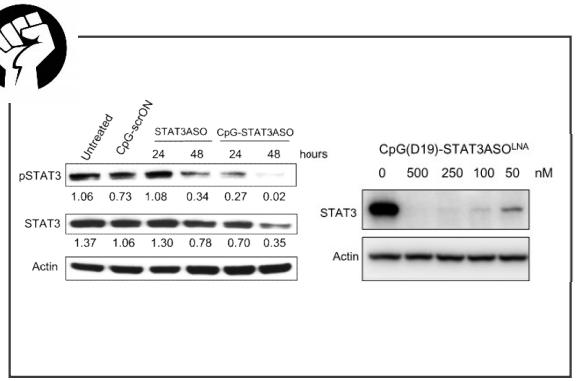
- **Characterize the clinical activity** of DUET-01 through the assessment of disease response, and response duration. (Clinical)
- Characterize the biologic activity when combined with radiation by assessing through immunologic correlative studies. (Biologic)
- **Characterize silencing of the STAT3** gene and its key downstream genes through correlative studies. (Biologic)
- **Characterize local and systemic immune responses**, including evidence/extent of immune cell intratumoral infiltration, immune cell activation within the tumor and in the peripheral blood, and changes in proinflammatory mediators in plasma.

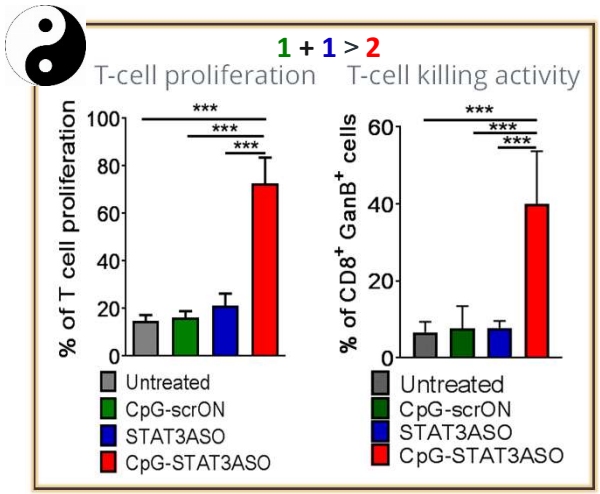
The Phase 1 clinical trial is evaluating three different dose levels of DUET-01 in combination with radiation therapy for B cell NHL



DUET-02 restores human T-cell proliferation and activity in the prostate tumor microenvironment







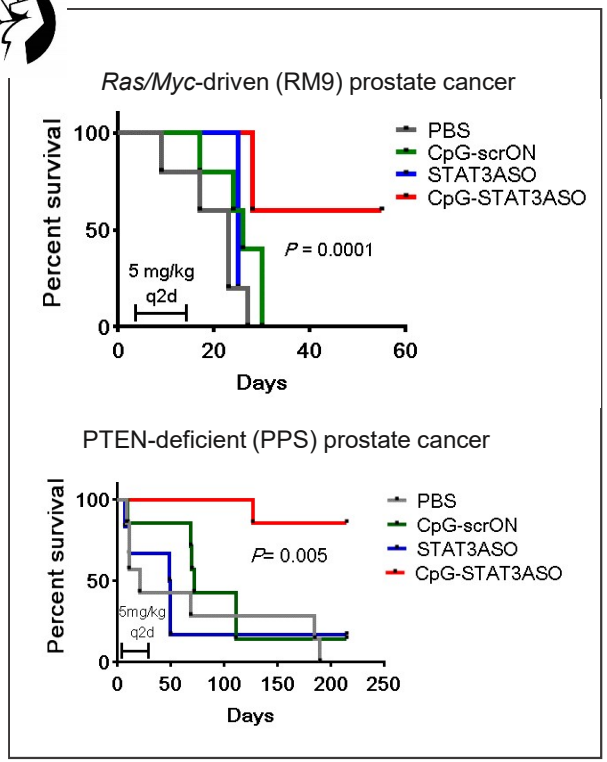
Efficient and rapid (within 30 min of dosing) DUET-02 uptake specifically by TLR9$^+$ immune cells controlled by CpG-ODN[1]

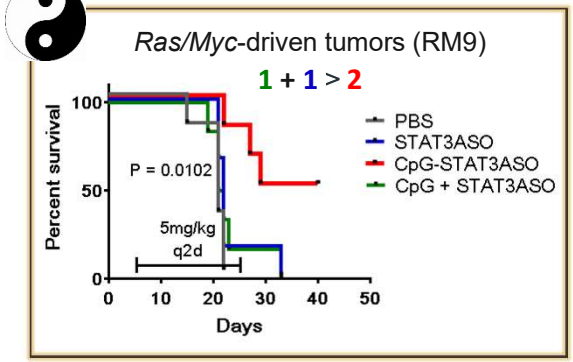
The DUET-02 oligonucleotide results in **significant and dose-dependent inhibition of STAT3** levels and activity[1]

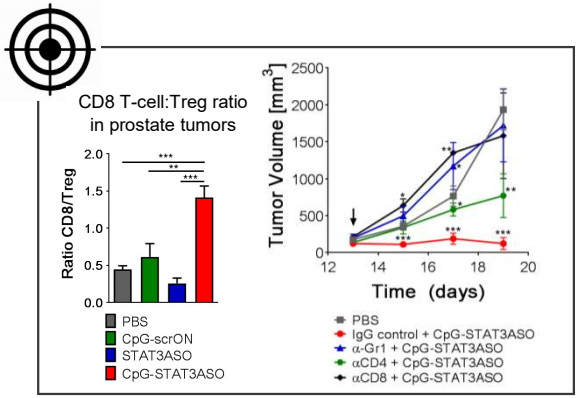
The bi-functional CpG-STAT3 inhibitor (1 + 1 > 2) – neither CpG nor STAT3 antisense alone can restore activity of human T cells in the prostate tumor microenvironment[1]

Moreira *et al.*, STAT3 inhibition combined with CpG immunostimulation activates antitumor immunity to eradicate genetically distinct castration-resistant prostate cancers, *Clinical Cancer Research* (2018)[1]

DUET-02 induces T-cell mediated rejection of bone-localized and ICI-resistant prostate cancers in mice







Six intravenous injections of DUET-02 are sufficient to unleash potent antitumor effects and increase animal survival in genetically different prostate tumor models

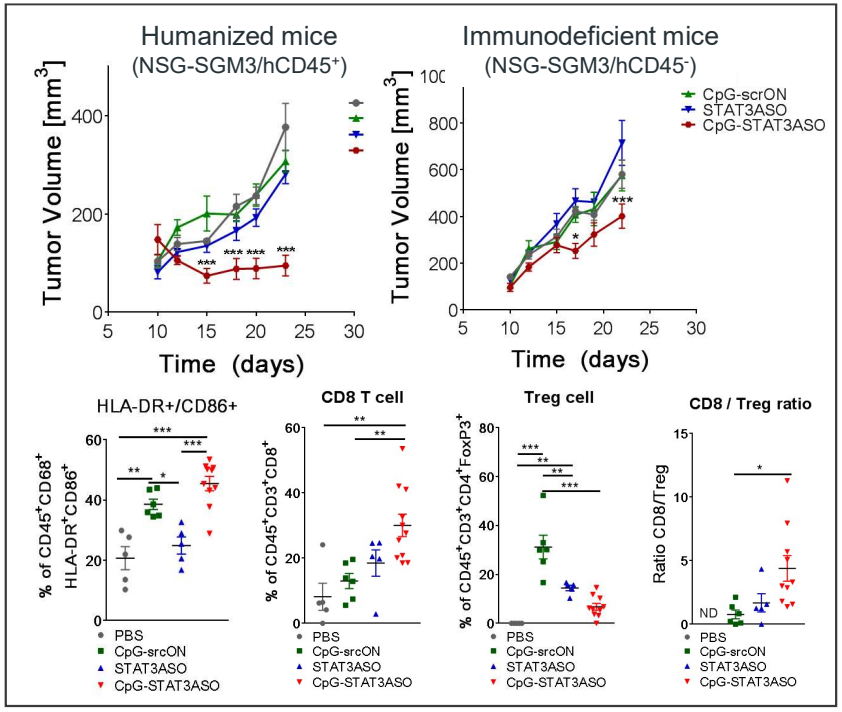
The bi-functionality of DUET-02 is key for efficacy (CpG and STAT3ASO co-injected as unconjugated oligonucleotides fail to improve the survival)

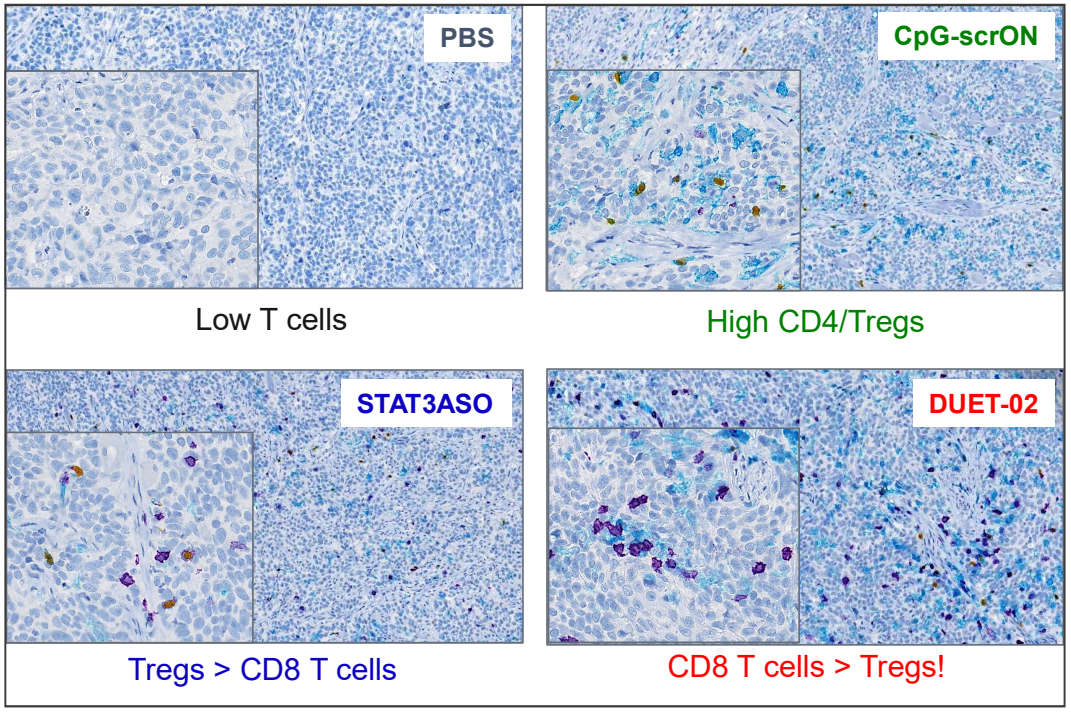
DUET-02 breaks tumor immune tolerance and generates cancer-specific $CD8^+$ and $CD4^+$ T cell-mediated immune responses

Moreira *et al.*, STAT3 inhibition combined with CpG immunostimulation activates antitumor immunity to eradicate genetically distinct castration-resistant prostate cancers, *Clinical Cancer Research* (2018)[1]

DUET-02 generates effective CD8⁺ T-cell immune responses against human HPV⁻ head and neck cancer (HNC) in humanized mice

CpG-STAT3ASO (DUET-02) results in regression of xenotransplanted **human head and neck tumors (SCC1) in humanized mice,** with evidence of immune activation, **CD8⁺ T-cell recruitment and reduction of regulatory T cells in tumors.**





Moreira *et al.*, Myeloid cell-targeted STAT3 inhibition sensitizes head and neck cancers to radiotherapy and T cell-mediated immunity, *The Journal of Clinical Investigation* (2021)[2]

Duet is planning two clinical Phase 1 trials to begin in Q1 2023 for Genitourinary and Head & Neck Cancers

Genitourinary Cancers

Systemic intravenous infusions of DUET-02 as a monotherapy for treatment of metastatic prostate, kidney, and bladder cancers

Sumanta Pal MD

Clinical Professor, Medical Oncology & Therapeutics Research; Director of the Kidney Cancer Program at City of Hope

Tanya Dorff MD

Associate Clinical Professor, Medical Oncology & Therapeutics Research, Head of the Genitourinary Cancers Program at City of Hope

Head & Neck Cancers

Intratumoral injection of DUET-02 in combination with radiotherapy for squamous cell carcinoma of head & neck cancers

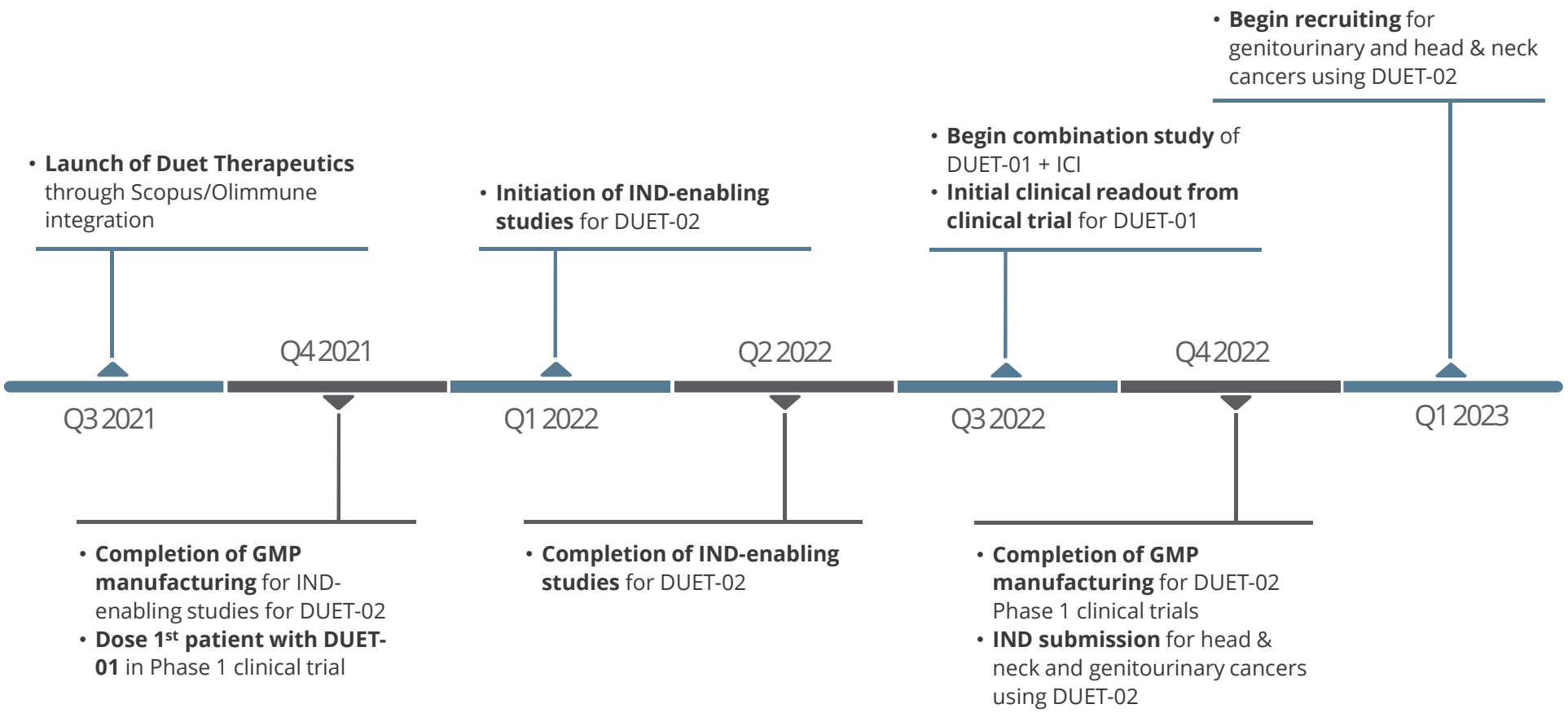
Sagus Sampath MD

Associate Clinical Professor, Radiation Oncology, specializing in head and neck, lung, skin, bladder cancers

Ermina Massarelli, MD, PhD

Associate Clinical Professor, Medical Oncology & Therapeutics Research, specializing in lung and head and neck cancers

Target milestones that will culminate in Phase 1 clinical trials in three unique clinical indications



Duet is building a leadership team that has extensive company building and clinical development experience

ALAN HORSAGER, PH.D.
President, CEO & Director

MARCIN KORTYLEWSKI, PH.D.
Senior Scientific Advisor

Other team members to be announced in the coming weeks

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