Anchiano therapeutics

INODIFTAGENE

Gene Therapy for Bladder Cancer

September 2019

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Inodiftagene: Gene Therapy for Bladder Cancer

INODIFTAGENE

First-in-class gene therapy in registrational development in early stage bladder cancer

Data from six clinical trials show activity in pancreatic, ovarian and bladder cancer, with complete and durable responses in NMIBC

First pivotal clinical trial is open to enrollment, the second planned for late 2019

NON-MUSCLE INVASIVE BLADDER CANCER (NMIBC)

A large and underserved population

Current standard-of-care is a therapy introduced in the 1970s; patients who relapse go on to radical surgery or distant metastasis

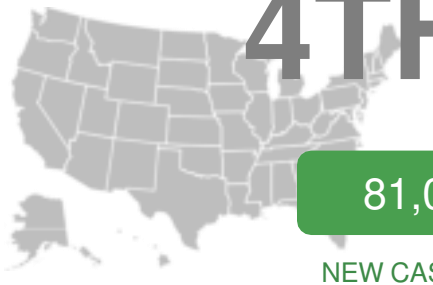
FDA guidance to industry and path to approval is clear

Potential market of

$1.5 billion

Non-Muscle Invasive Bladder Cancer: NMIBC

NMIBC is a common cancer in need of new therapies



4TH MOST COMMON CANCER IN MALES BEHIND ONLY LUNG, COLON, PROSTATE

In the United States[1]

81,000	708,000
NEW CASES IN 2018	PREVALENT CASES IN 2015

5TH MOST COMMON CANCER OVERALL IN EU

EU and Worldwide[2,3]

141,000	550,000
EU EXPECTED NEW CASES IN 2020	WORLDWIDE NEW CASES/YEAR

Quality of Life Issues

Repeated recurrence
Repeated cystoscopy, surgery and drug treatment cycles
Lifelong cystoscopy follow-up
Most expensive cancer to treat

No New Drugs in 20 Years

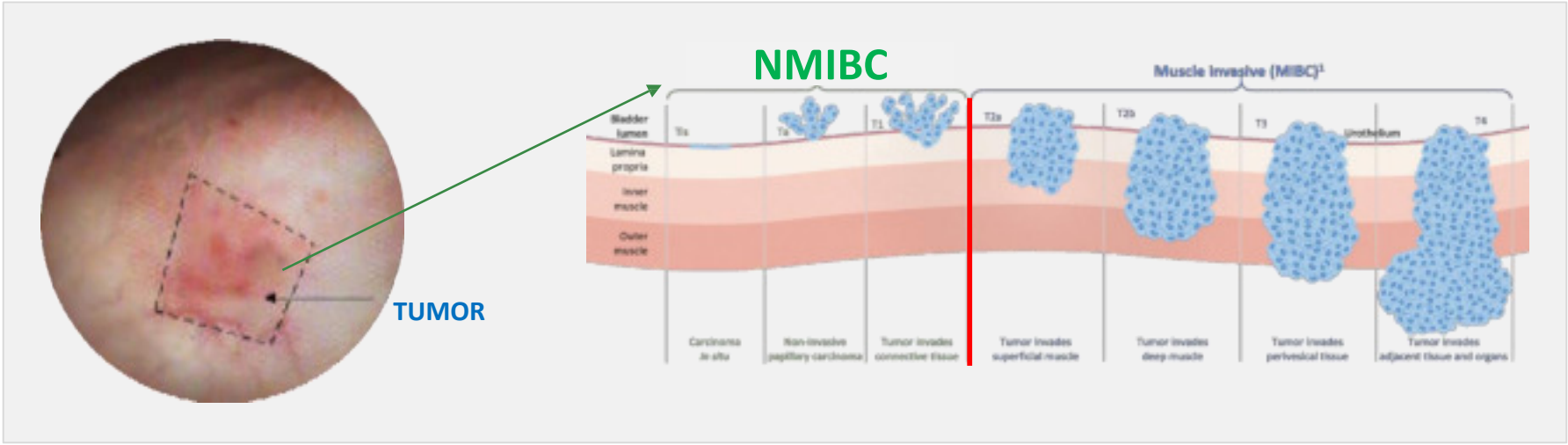
0

Drugs approved by FDA since 1998 for NMIBC

1. ACS Cancer Facts and Figures 2018, www.cancer.org; 2. https://ec.europa.eu/jrc/en/publication/epidemiology-bladder-cancer-Europe; 3.https://wcrf.org/dietandcancer/cancer-trends/bladder-cancer-statistics

NMIBC Classification and Treatment

Recurrence leads to progression and metastasis

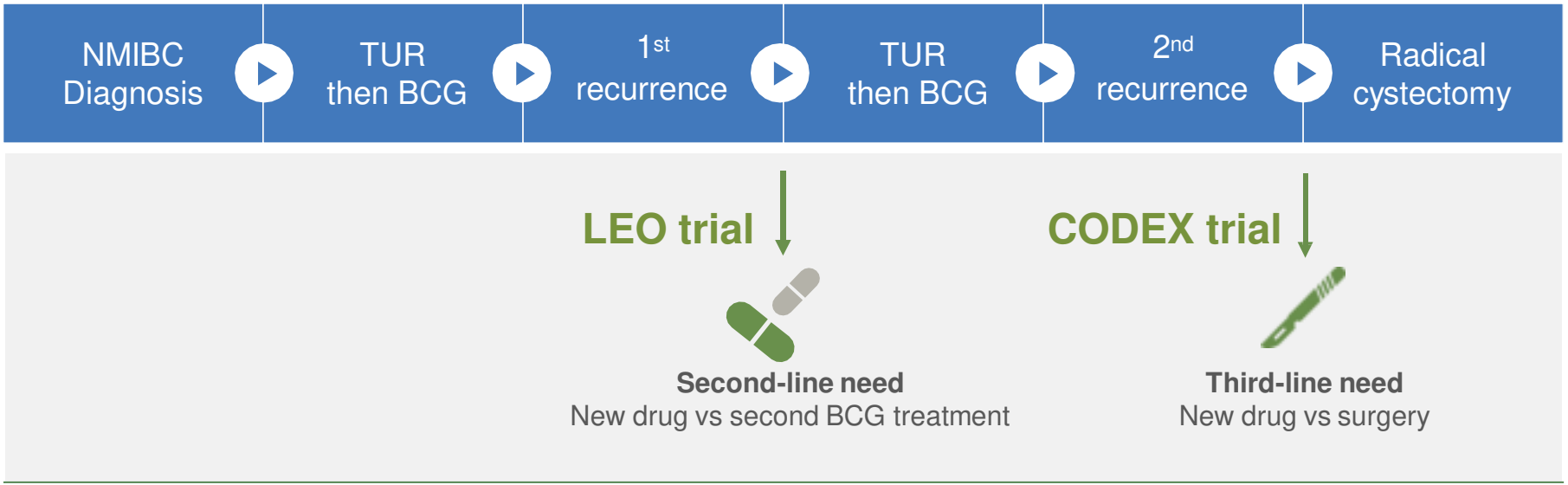


DIAGNOSIS	LOCALIZATION	THERAPY
Patients are diagnosed and evaluated via cystoscope	Tumors are identified on the inner surface of the bladder, resected and classified by depth	NMIBC patients initially receive Bacillus Calmette Guerin (BCG) and are the focus of inodiftagene therapy

Sources: Knowles MA and CD Hurst, 2015. *Nature Rev Cancer*, 15: 25-41, Link. : NCCN Bladder Cancer Guidelines, v. 1.2017.

Two Unmet Needs in NMIBC Therapy

Inodiftagene addresses both



90,000 patients whose tumors recur after one or two courses of BCG are eligible for inodiftagene annually in the US, EU and Japan

Inodiftagene Uses H19 to Target Cancer Cells and Avoid Normal Cells

PLoS one

The H19 Non-Coding RNA Is Essential for Human Tumor Growth

SCIENTIFIC REPORTS

Hypoxia induces H19 expression through direct and indirect Hif-1α activity, promoting oncogenic effects in glioblastoma

www.impactjournals.com/oncotarget/ Oncotarget, 2016, Vol. 7, (No. 50), pp: 83177-83186

Research Paper

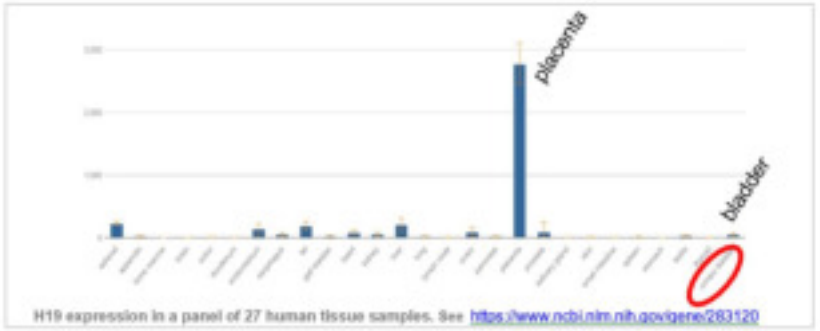
Prognostic and clinicopathological significance of long noncoding RNA H19 overexpression in human solid tumors: evidence from a meta-analysis

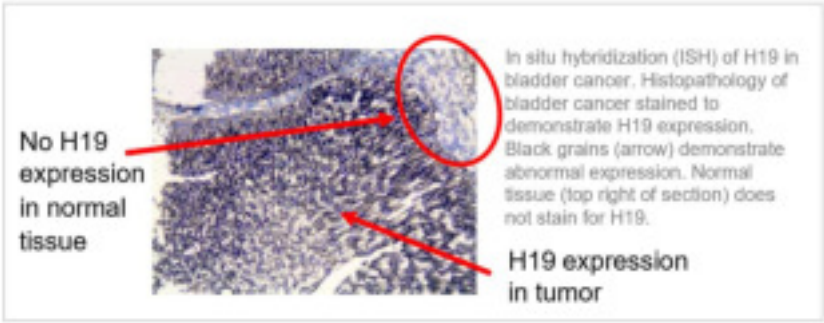
Fang-teng Liu[1], Hua Pan[1], Guang-feng Xia[1], Cheng Qiu[1], Zheng-ming Zhu[1]

FEBS Journal

Upregulated H19 contributes to bladder cancer cell proliferation by regulating ID2 expression

Ming Luo[1], Zuowei Li[2], Wei Wang[2], Yigang Zeng[2], Zhihong Liu[2] and Jianxin Qiu[2]



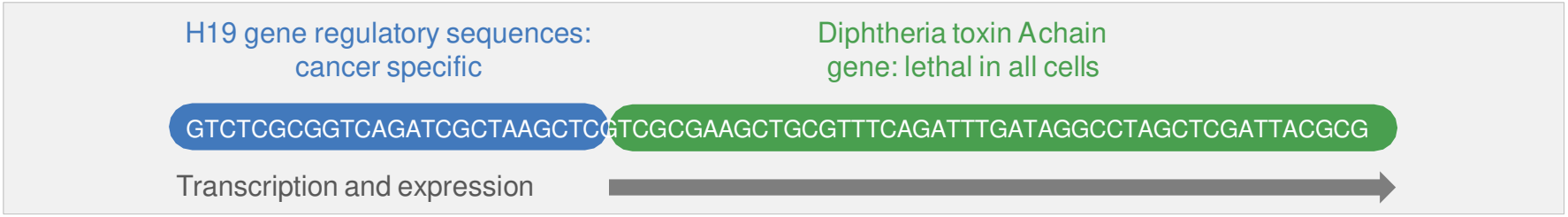


First-in-Class, First-of-its-Kind Treatment

Inodiftagene vixteplasmid gene therapy

Targeted gene therapy

Inodiftagene is a recombinant DNA molecule containing regulatory sequences from the H19 gene driving expression of diphtheria toxin A chain gene **only in malignant cells**



Diphtheria toxin gene: efficient delivery

Plasmid facilitates high transfection efficiency. In vitro uptake demonstrable in 85% of cells after a single exposure; in clinic detectable in bladder more than 48 hours after instillation, and administered weekly to every third week for up to 3 years

Well-understood and validated mechanism-of-action

Lethal inhibition of protein synthesis

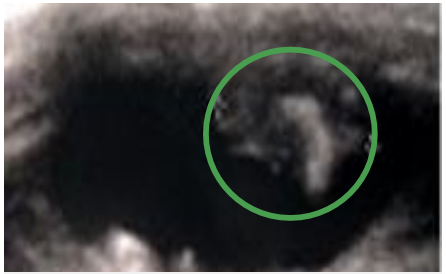
Effective in Eliminating Experimental Bladder Cancer

Inodiftagene in vivo

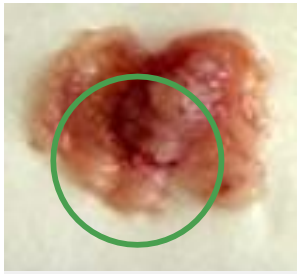
Animal model data demonstrate that intravesical instillation of inodiftagene eliminates rat bladder cancers

Analysis of inodiftagene-treated rat bladders by ultrasound and at necropsy shows progression of experimentally induced tumor when treated with control vector (left) but absence of tumor when treated with inodiftagene (right)

Superficial Tumor

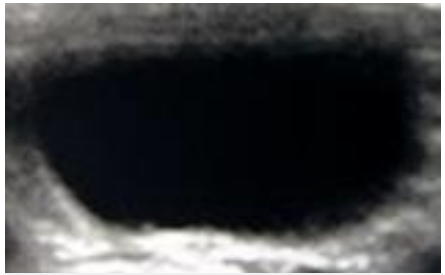


Ultrasound



Resected Bladder

Tumor Response



Ultrasound

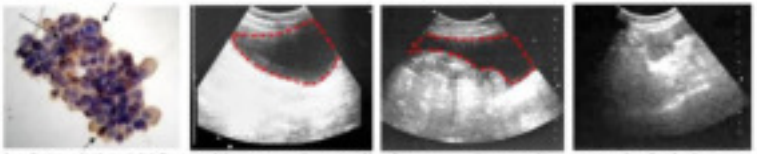
Resected Bladder

Wistar rats received N-butyl-N(4-hydroxybutyl) nitrosamine (BBN), a potent carcinogenic alkylating agent, in drinking water for 5-30 weeks. Tumors were evident by 10 weeks, with superficial invasion evident by 15 weeks and typically deep invasion by 20 weeks. At 19 weeks 100 ug of control luciferase vector (left) or inodiftagene (right) was instilled weekly for 5 weeks intravesically.

Responses in Advanced Ovarian and Pancreatic Cancer

Inodiftagene activity in solid tumors validates mechanism of action

Complete resolution of ascites following instillation of inodiftagene



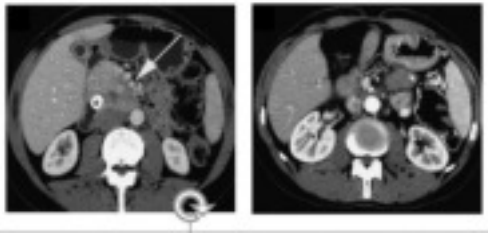
Left to right: H19-positive ovarian cells from ascites; ultrasound of abdomen at baseline, prior to 5th treatment, and after 10th treatment. Red border demarcates ascites, resolved at right

Advanced pancreatic cancer responses to monotherapy: 2 partial responses with inodiftagene alone

Table 5. Subject status at 3 months follow-up

Cohort #	Subject ID	End of study at 4 weeks	3 Months	Other treatments
1	201	PD	PD	None
1	202	PD	SD	Chemotherapy
1	602	SD	[illegible]	[illegible]
2	204	PD[a]	PR[a]	None
2	205	SD	[illegible]	[illegible]
2	301	PD	SD	Chemotherapy
2	501	SD	[illegible]	[illegible]
2	604	SD[b]	PR[b]	None
2	1102	SD	SD	[illegible] - Complete Resection at 3 months

Complete resection of advanced pancreatic cancer following inodiftagene, chemoradiation and surgery



Left baseline tumor; right complete resection of tumor following inodiftagene and multimodality therapy

1. Mizrahi et al., J. Med. Case Reports 2:228, 2010 http://www.jmedicalcasereports.com/content/4/1/228; 2. Ohana et al., Cancer Gene Therapy 19:374, 2012.

Three Studies Support Path to Potential Approvability

Inodiftagene Clinical Data in NMIBC

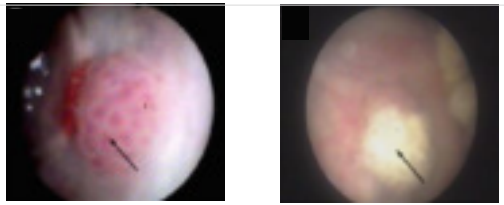
Inodiftagene results in 33% complete responses in marker papillary tumors, 86% CRs in CIS alone and with BCG

Safety observations: no DLT or MTD in phase 1 study, 23% related AEs in phase 2, 3/47 patients with SAEs

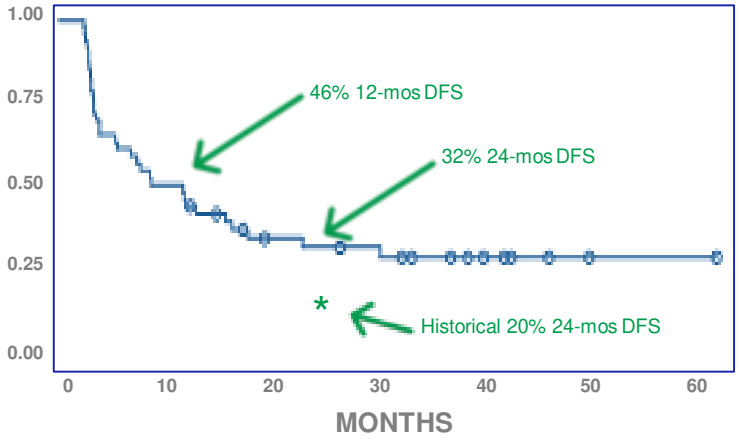
Monotherapy durability surpasses historical experience:

- FDA specified in CIS 30% recurrence-free rate at 18-24 months, excluding 20%, as being an approvable endpoint enpoint[1]
- Phase 2 study demonstrates 18- and 24- month rates are >30% (right)

Inodiftagene in combination with BCG shows 3-mo and 6-mo DFS of 95% and 74%



L: Baseline: papillary tumor
R: 3 weeks following 6th instillation of inodiftagene: necrosis

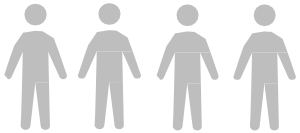


1. Jarow et al., J. Urology, 2014

Pathway to Registration in Two Discrete Indications

Inodiftagene registrational program

Codex



Codex phase 2 pivotal study
trial is a single-arm path with FDA concurrence designed for approval in **third line** patients

Monotherapy, 140 patients, single arm

Open label, interim analysis at 35 patients essentially allows repeat of phase 2 experience in US

Open to enrollment in US

Leo

Leo phase 3 pivotal study
trial is approved under SPA and will support indication in **second line** patients

Combination therapy, 500 patients, randomized

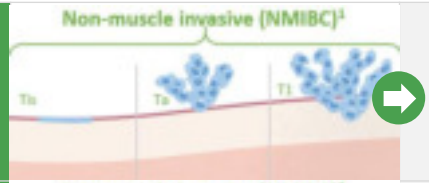
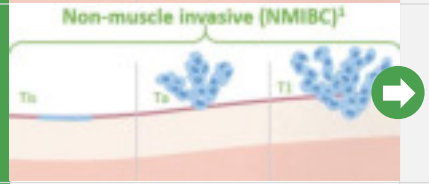
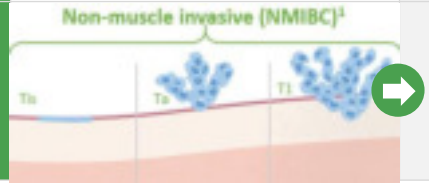
Trial has been granted an SPA by the FDA

This trial is complementary to the phase 2

These two trials provide independent routes to potential approval in two separate (but related) indications

Unique Strategy for Inodiftagene Approval in Two Indications

Inodiftagene clinical development strategy

Standard of care		**TUR BCG 1L**	**Recurrence TUR, BCG 2L**	**Recurrence Cystectomy**
Codex		TUR BCG	Recurrence TUR, BCG	Recurrence **Inodiftagene 3L**
Leo		TUR BCG	Recurrence TUR, BCG **Inodiftagene 2L**	Recurrence Cystectomy

Development plan in second-line patients, the Leo patient population, addresses the majority of the market potential of NMIBC therapy

Experienced Management Team

US-based clinical development team with record of US approvals with FDA

	**Frank G. Haluska, MD, PhD** President and Chief Executive Officer	Former Harvard Medical faculty, ARIAD CMO, led global research team and two oncology drug approvals
	**Jonathan Burgin, MBA, CPA** Chief Financial Officer and Chief Operating Officer	Former Anchiano CEO, CFO of TASE and Nasdaq companies
	**David Kerstein, MD** Chief Medical Officer	Former Takeda Lung Cancer Clinical Portfolio Strategy Lead
	**Ron Knickerbocker, PhD** Senior Vice President of Clinical Development and Data Sciences	Designed and analyzed clinical trials for two successful NDAs
	**Sean Daly** Vice President of Clinical Operations	Successfully conducted clinical trials supporting two approvals
	**Salar Roshan, MBA, MSF** Head of Business Development	Extensive experience in biopharmaceutical business development

Funding Plans and Upcoming Milestones

Clinical trial timelines

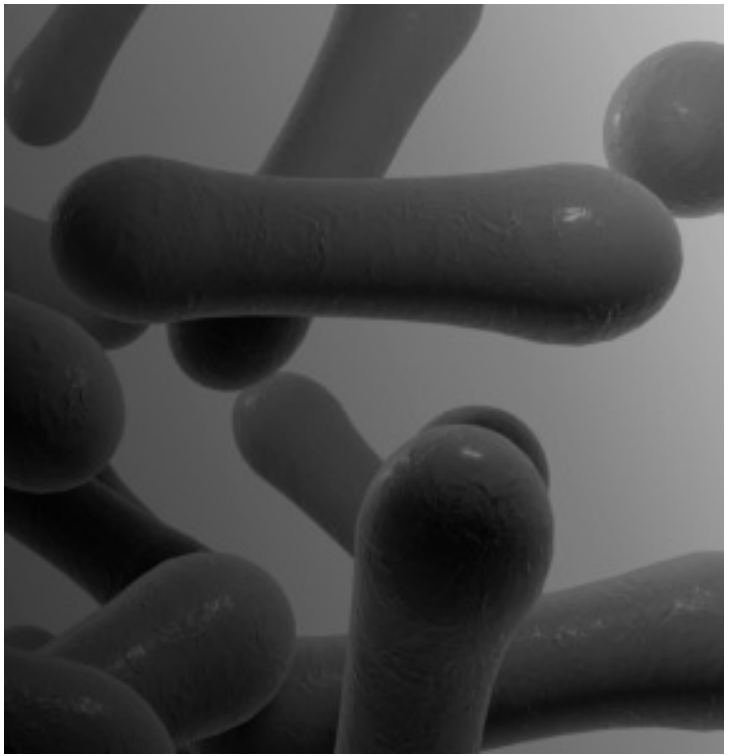
4Q 2018: Codex trial initiated for registration of inodiftagene

1Q 2019: $30.5M IPO on Nasdaq (ANCN)

3Q 2019: Open label Codex data becoming available

4Q 2019: Final Codex interim analysis

1H2020: Initiation and first patient enrolled in Leo



Key Takeaways

Inodiftagene vixteplasmid is a first-of-its-kind gene therapy for NMIBC

Over $1.5 billion commercial potential

Preliminary data from development program and FDA SPA path to potential approval

Strong balance sheet: $30.5M US IPO (Nasdaq: ANCN) in Q1, $27M cash end Q2

Codex pivotal trial underway, with data coming soon

Experienced management team with history of successful commercialization and expanding global organization