Prospective Open-Label Study to Evaluate the Safety and Efficacy of Intravesical Sustained-Release Gemcitabine Docetaxel Combination (NDV-01) in High-Risk NMIBC: Update with 12-month Complete Response Data

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Introduction

Conventional intravesical gemcitabine and docetaxel (Gem/Doce) represents a promising treatment option for patients with high-risk NMIBC – including those who are BCG-naïve, BCG-exposed and BCG-unresponsive. Gem/Doce is not available in a sustained-release formulation, limiting intravesical exposure. NDV-01 is an investigational intravesical agent designed for sustained release of Gem/Doce continuously over a 10-day period. NDV-01 may also help overcome the patient and provider burden (e.g. time toxicity) of traditional Gem/Doce. NDV-01 can be administered in <5 minutes and does not require a specialized pharmacy or hood.

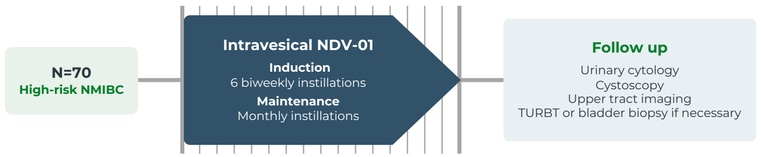
Objective

Evaluate the safety and efficacy of NDV-01 (sustained-release Gem/Doce) in high-risk NMIBC.

Methods

The study is a single-arm, open-label trial of NDV-01 in subjects with high-risk NMIBC. Subjects were given 6 bi-weekly instillations of NDV-01 followed by monthly maintenance instillations through month 12. Complete response (CR) was defined as a negative cystoscopy, cytology, and biopsy (if indicated). The first assessment for CR was evaluated at 3 months. Subjects with a non-CR at 3 months, were eligible to be reinduced with an additional 6 bi-weekly course of therapy. Disease assessments for CR were also performed at 6, 9, and 12 months. Thirty-eight patients have reached the first disease assessment (3-months follow-up) and are included in the per-protocol efficacy analysis (10 patients are pending their first response assessment). Forty-eight patients have received ≥1 dose of NDV-01 and are included in the safety analysis.

TRCG-011 Study Design



Inclusion Criteria

High-risk disease with CIS, Ta, T 1 tumors[1,2]

BCG-naive, BCG-unresponsive, intolerant and experienced patients

Purpose

Evaluate the potential of NDV-01 as a safe and effective treatment for patients with high-risk NMIBC

Primary Endpoint

Safety

CR Rate at 12 months

Secondary Endpoint

DOR

EFS

Exploratory

PK

Results

Baseline characteristics of the 48 enrolled subject are shown in Table 1. All patients were ECOG 0-1. Of the 48 patients who received ≥1 dose of NDV-01, 30 (63%) had a TRAE (54% dysuria, 8% asymptomatic positive urine culture, 8% hematuria). No patient had ≥ Grade 3 TRAE and no patients discontinued treatment due to AEs. Response rates in the 38 patients who received ≥ 3-month disease assessment are shown in table 2 – including 25 patients who have reached the 12-month assessment. No patient had progression to muscle invasive disease. No patient underwent a radical cystectomy.

Table 1: Baseline Characteristics (n=48)

Characteristics	N=48	%
Age		
Median (range)	75 (52-93) yr	
Sex		
Male	42	87.5%
Female	6	12.5%
BCG doses		
Median BCG doses (range)	9 (3-23)	
BCG-status		
BCG-naive	23	47.9%
BCG-exposed	5	10.4%
BCG-unresponsive	20	41.7%
Stage		
CIS +/- Ta/T1	12	25.0%
Ta HG	29	60.4%
T1 HG	7	14.6%

Table 2: Efficacy Results (Complete Response)

Efficacy Evaluable Patients	n/N	%
Anytime	36/38	95%
3-month	33/38	87%
6-month	25/29	86%
9-month	22/26	85%*
12-month	19/25	76%*
12-month KM analysis	-	83%

BCG-UR Subpopulation	n/N	%
Anytime	16/17	94%
3-month	14/17	82%
6-month	12/14	86%
9-month	10/11	91%
12-month	8/10	80%
12-month KM analysis	-	84%

*Includes patients with CR after re-induction. 80% CR rate after re-induction; BCG-UR defined by FDA definition.

Conclusions

NDV-01 is a novel sustained-release Intravesical formulation of Gem/Doce.

NDV-01 provides Durable 76% CR rate at 12 months with 95% CR rate at anytime in high-risk NMIBC.

Tolerability profile remains favorable – no ≥ Grade 3 TRAEs and no treatment-related discontinuations.

Next steps:

- Initiate Phase 3 RESCUE Trial in Mid-2026
- Targeting two independent registrational pathways: 2L BCG-Unresponsive NMIBC and adjuvant intermediate-risk NMIBC

Disclosures

This research was sponsored by Relmada Therapeutics, Inc. and was managed by Trigone Pharma Ltd at 1 site in Israel. Dr. Lotan and Dr. Kates are paid consultants of Relmada Therapeutics. Dr. Pruthi, , Scott White, Tiffany Sepp, and Leo Watson are employees of Relmada Therapeutics. Drs. Chertin and Abbas are employees of Shaare Zadek Medical Center, Jerusalem, Israel. Dan Touitou, Avigdor Gordon, Hila Kfir are employees of Trigone Pharma Ltd.

1. The American Cancer Society. Bladder Cancer Stages. American Cancer Society, 12, Mar, 2024. https://www.cancer.org/cancer/types/bladder-cancer/detection-diagnosis-staging/staging.html; **2.** Holzbeierlein, Jeffrey M., et al. "Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline: 2024 Amendment." The Journal of Urology, vol. 211, no. 4, Jan. 2024, pp. 533–38, doi:10.1097/ju.0000000000003846. **CIS:** Carcinoma In Situ; **Ta:** Noninvasive papillary carcinoma; **TI:** Tumor invades lamina propria; **HG:** High grade; **CR Rate:** Complete Response Rate; **DOR:** Duration of Response. **EFS:** Event Free Survival; **PK:** Pharmacokinetics; **TURBT:** Transurethral resection of bladder tumor; **CR:** Complete response; **BCG:** Bacillus Calmette-Guérin; **BCG-UR:** BCG-unresponsive; **KM:** Kaplan-Meier analysis; **TRAE:** Treatment-related adverse events; **AE:** Adverse events

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