# QUILT 3.032

# Phase 2 / 3 Clinical Results: IL-15RαFc Superagonist N-803 with BCG in BCG-Unresponsive Non-Muscle Invasive Bladder Cancer (NMIBC) Carcinoma in Situ (CIS) Patients (Cohort A)

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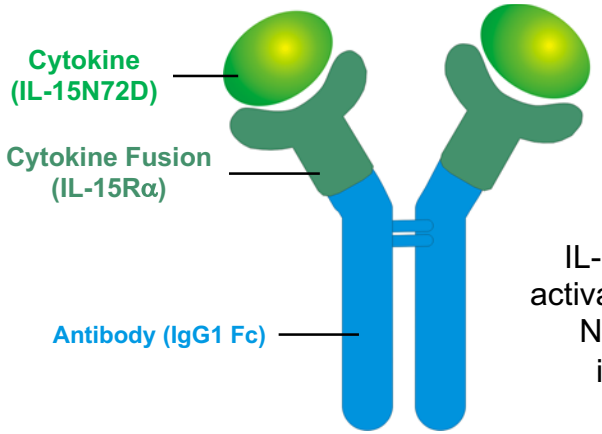
UCLA Health

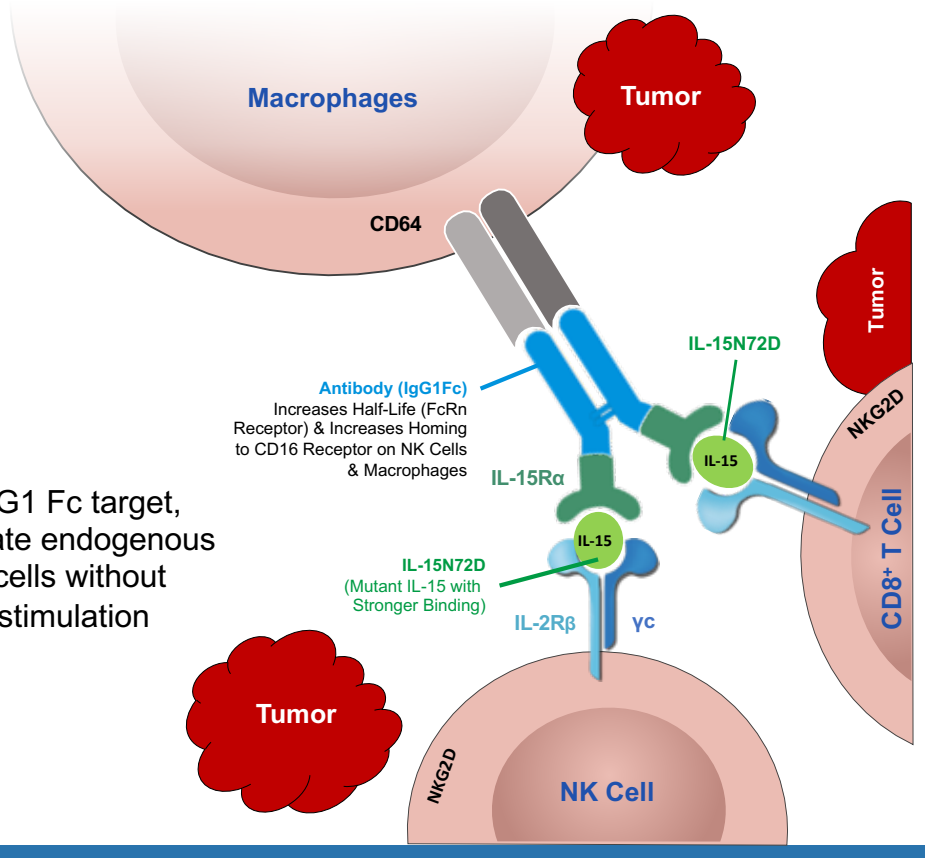
# Novel IL-15 Superagonist Fusion Protein Upregulates Natural Killer (NK) and T Cells

## N-803 Mechanism of Action

N-803 IL-15 Superagonist Antibody Cytokine Fusion Protein




IL-15N72D and IgG1 Fc target, activate and proliferate endogenous NK and CD8+ T cells without inducing T Reg stimulation



# QUILT 3.032
# Phase 2 / 3: IL-15RαFc Superagonist N-803 with BCG in BCG-Unresponsive Non-Muscle Invasive Bladder Cancer (CIS)

## BCG Unresponsive Disease

- Histologically Confirmed
- Persistent or recurrent CIS (+/- recurrent Ta/T1 disease) within 12 months of receiving adequate BCG

## Treatment

50 mg BCG **plus** 400 µg N-803 intravesically weekly x 6 induction or re-induction x 6 + maintenance for up to three years

CR at 3 Months

Rescue, Reinduction, CR at 6 Months

N = 81

## Efficacy Endpoints

**Primary Endpoint:**
- Biopsy confirmed complete response (CR) at 3 or 6 months, with lower bound 95% CI of ≥ 20%

**Secondary Endpoints:**
- Duration of CR
- Cystectomy Avoidance
- Time to Cystectomy

## Safety Endpoints

**Serious Adverse Events**

**Immune Adverse Events**

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# Demographics: Heavily Pre-Treated NMIBC Subjects

| Number of Prior TURBT | |
|---|---|
| Median | **5.0** |
| Mean | **5.3** |

| Number of Prior BCG Instillations | |
|---|---|
| Median | **12.0** |
| Mean | **16.4** |

| Subjects with Therapy in Addition to BCG | | |
|---|---|---|
| Checkpoint, Vicinium, Interferon* | **N=14** | **17%** |
| Chemotherapy | **N=34** | **42%** |

*includes nadofaragene firadenovec

# QUILT 3.032 CIS (+/- Ta/T1)

# N-803 + BCG: Well Tolerated Safety Profile

**Treatment-Related SAE's**

**0%**

**Immune-Related SAE's**

**0%**

**Treatment Related Grade 4 & 5**

**0%**

**Treatment-Related Adverse Events**

| Adverse Events (AE) | Grade 1-2 % | Grade 3 % | Grade 4 % |
|---|---|---|---|
| Dysuria | 22 | 0 | 0 |
| Hematuria | 16 | 0 | 0 |
| Pollakiuria | 19 | 0 | 0 |
| Urgency | 11 | 0 | 0 |
| Bladder Spasm | 5 | 0 | 0 |
| Fatigue | 9 | 0 | 0 |
| Chills | 7 | 0 | 0 |
| Pyrexia | 7 | 0 | 0 |
| Non-Infective Cystitis | 6 | 0 | 0 |
| UTI | 5 | 1 | 0 |
| Arthralgia | 4 | 1 | 0 |

Grade 3 TRAEs all seen in 2 patients,
AE seen in ≥ 5% listed

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# N-803 + BCG: Primary Endpoint Met

- Complete Response (CR) at 3 or 6 months, biopsy confirmed
- 81 patients enrolled
- **58 out of 81** patients have achieved a CR at any time
- CR rate at any time of **72%** (95% CI: 61%, 81%)
- **Primary endpoint met**

# QUILT 3.032
# N-803 + BCG: Duration of Complete Response (CR) in All Subjects

**Median Follow Up**

**20.4 Months**

As of May 19, 2021

**Median Duration of CR in All Responders**

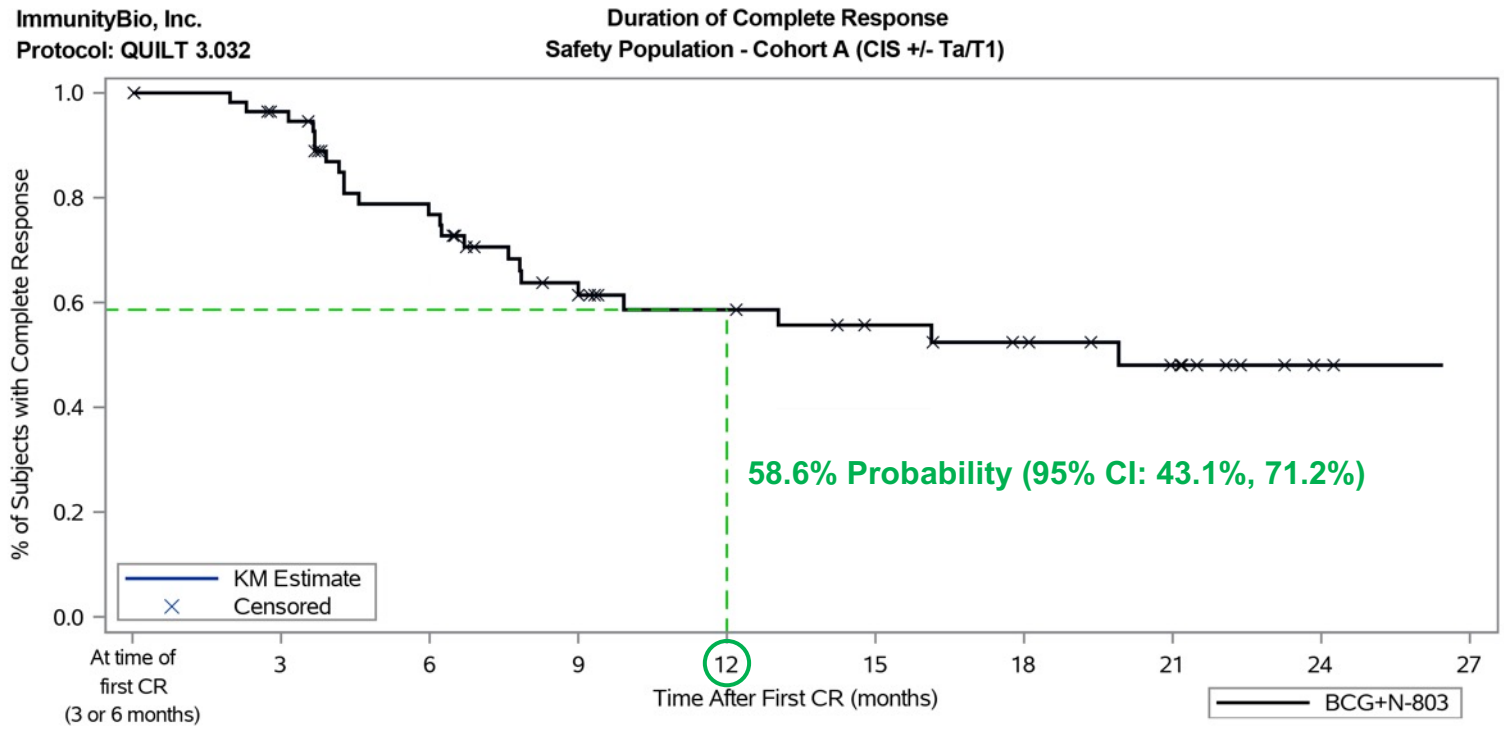
**19.9 Months***

95% CI (7.8, Not Reached)

*Kaplan-Meier Estimate

Data cutoff May 19, 2021

**58.6% Probability (95% CI: 43.1%, 71.2%) of Duration of CR Greater than 12 Months**



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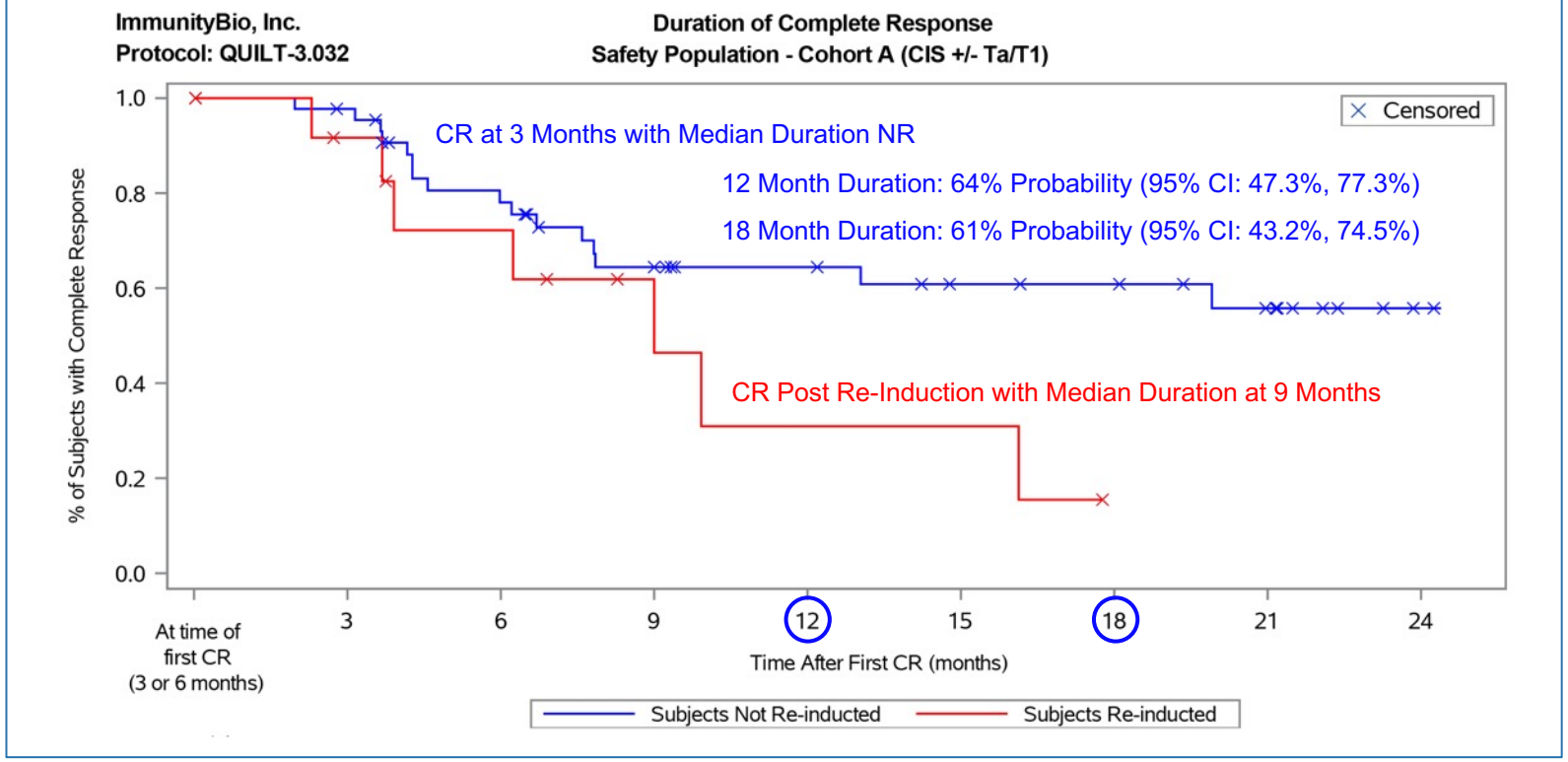
## N-803 + BCG: Durability Stratified by Initial Complete Responses Versus Re-Induction

**64% Probability (95% CI: 47.3%, 77.3%) of Duration of CR Greater than 12 Months in Patients with Initial CR at 3 Months**

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# N-803 + BCG: Cystectomy Avoidance

**85% Cystectomy Avoidance**

- **69 of 81** **(85%)** patients have not progressed to radical cystectomy through a data analysis as of May 2021

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# Comparison with Approved Therapies

| Drug | N | CR Rate at Anytime | Median Duration of CR in all responders | Median follow up (months) | Cystectomy Free Rate to date | Immune Related Adverse Events |
|---|---|---|---|---|---|---|
| N-803 + BCG | 81 | 72% | 19.9 Months* | 20.4 As of May 19, 2021 | 85% | 0% |
| Pembrolizumab[1] | 97 | 41% | 16.2 Months | 24.1 | 63% | 21% |
| Valrubicin | 78 | 18% | < 6 months | - | 76% (1 year) | 0% |

***Kaplan-Meier estimate, as of May 19, 2021. Median duration of response not met in patients with CR at 3 months**

1. ODAC: https://www.fda.gov/media/133542/download, ASCO 2020

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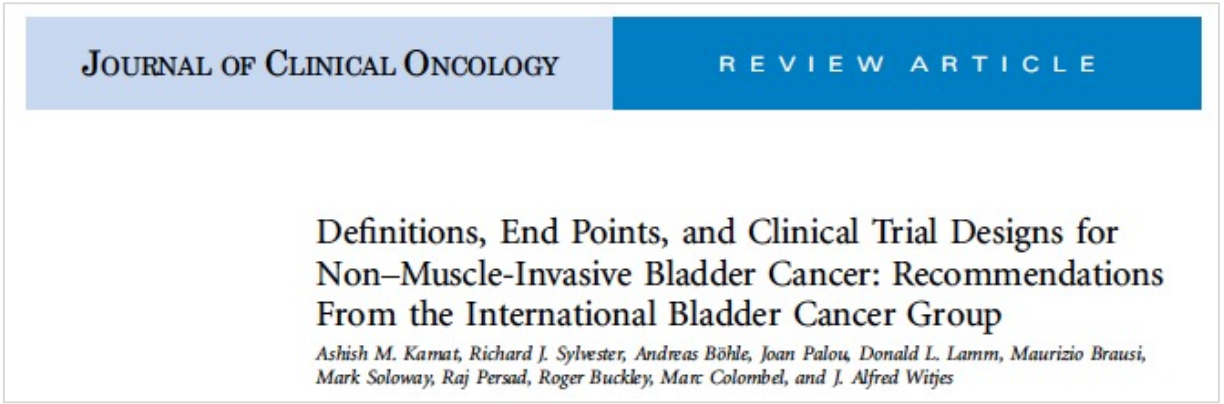
# Durability of Response at 12 Months

*"Clinically meaningful magnitude of effect*

*In a recent FDA–AUA public workshop, some panel members felt that an* ***initial CR rate of 40% to 50% at 6 months and a durable response rate of at least 30% for 18 to 24 months, with the lower bound of the 95% CI excluding 20%, could be clinically meaningful*** *in the BCG-refractory CIS population*

*We are in partial agreement with these recommendations but feel that the 30% durable response at 18 to 24 months criterion is likely too high and may not be realistically achievable."*


JOURNAL OF CLINICAL ONCOLOGY | REVIEW ARTICLE

Definitions, End Points, and Clinical Trial Designs for Non–Muscle-Invasive Bladder Cancer: Recommendations From the International Bladder Cancer Group

Ashish M. Kamat, Richard J. Sylwester, Andreas Böhle, Joan Palou, Donald L. Lamm, Maurizio Brausi, Mark Soloway, Raj Persad, Roger Buckley, Marc Colombel, and J. Alfred Witjes

**As of May 19, 2021, 30% Durable Response at 18 Months**

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# Conclusion

- **Safety & Tolerability:** Excellent safety and tolerability profile of N-803 + BCG with:
  - **0%** treatment related SAE's
  - **0%** immune related AE
  - **0%** grade 4 and 5 treatment related AE.
- **Complete Response: 72%** CR rate at anytime with primary endpoint met
- **Duration of Response: 58.6%** probability of maintaining CR at least 12 months based on Kaplan-Meier analysis with median follow up 20.4 months and median duration of CR of 19.9 months.
- **Among CR Responders at 3 Months**: **61% probability of maintaining CR at 18 months**
- **Cystectomy Avoidance: 85%** cystectomy free rate
- **Intravesical Administration:** Favorable intravesical administration profile

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