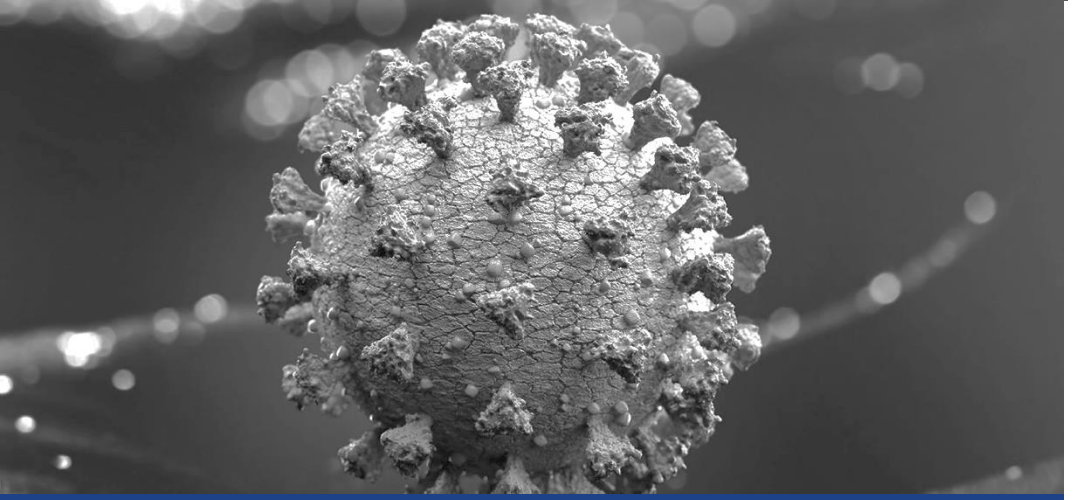
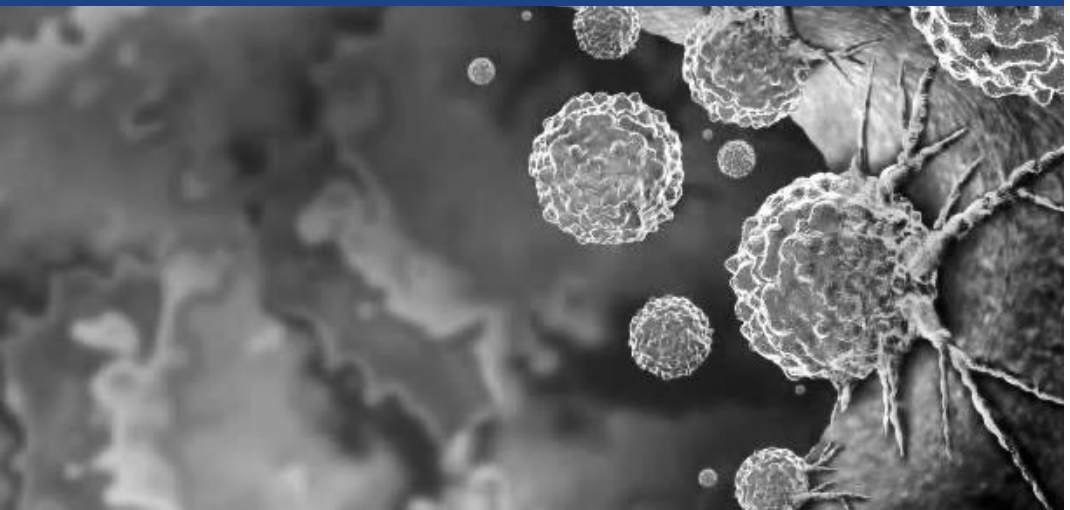


ImmunityBio®



ImmunityBio Investor Presentation

January 2025

Forward-Looking Statements and Intended Use

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, such as statements regarding data and results from clinical trials and potential implications therefrom, commercialization plans and timelines, including product availability and shipments, potential regulatory pathways and approval requests and submissions, FDA, UK MHRA, EU EMA and other regulatory agency meetings, timelines and potential results therefrom, global expansion efforts, the collaboration between ImmunityBio and the Serum Institute of India and expected results therefrom, the regulatory review process and timing thereof, market and prevalence data, potential benefits to patients, potential treatment outcomes for patients, the described mechanism of action and results and contributions therefrom, information regarding potential benefit to patients, information regarding ongoing pre-clinical studies and clinical trials, potential future uses and applications of ANKTIVA and use in cancer vaccines and across multiple tumor types, methods, ImmunityBio's financial condition, and ImmunityBio's approved product and investigational agents as compared to existing treatment options, among others. Statements in this presentation that are not statements of historical fact are considered forward-looking statements, which are usually identified by the use of words such as "anticipates," "believes," "continues," "goal," "could," "estimates," "scheduled," "expects," "intends," "may," "plans," "potential," "predicts," "indicate," "projects," "seeks," "should," "will," "strategy," and variations of such words or similar expressions. Statements of past performance, efforts, or results of our preclinical and clinical trials, about which inferences or assumptions may be made, can also be forward-looking statements and are not indicative of future performance or results. Forward-looking statements are neither forecasts, promises nor guarantees, and are based on the current beliefs of ImmunityBio's management as well as assumptions made by and information currently available to ImmunityBio. Such information may be limited or incomplete, and ImmunityBio's statements should not be read to indicate that it has conducted a thorough inquiry into, or review of, all potentially available relevant information. Such statements reflect the current views of ImmunityBio with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about ImmunityBio, including, without limitation, (i) the risks and uncertainties associated with commercial launch execution, success and timing, (ii) risks and uncertainties related to the regulatory submission and review process, (iii) the ability of ImmunityBio to continue its planned preclinical and clinical development of its development programs through itself and/or its investigators, and the timing and success of any such continued preclinical and clinical development, patient enrollment and planned regulatory submissions, (iv) potential delays in product availability and regulatory approvals, (v) risks and uncertainties associated with third party collaborations and agreements, (vi) whether the BCG manufactured by Serum will receive regulatory approval in the U.S. and/or other regions, (vii) ImmunityBio's ability to retain and hire key personnel, (viii) ImmunityBio's ability to obtain additional financing to fund its operations and complete the development and commercialization of its various product candidates, (ix) potential product shortages or manufacturing disruptions that may impact the availability and timing of product, (x) ImmunityBio's ability to successfully commercialize its approved product and product candidates and uncertainties around regulatory reviews and approvals, (xi) ImmunityBio's ability to scale its manufacturing and commercial supply operations for its approved product and future approved products, and (xii) ImmunityBio's ability to obtain, maintain, protect and enforce patent protection and other proprietary rights for its product candidates and technologies. More details about these and other risks that may impact ImmunityBio's business are described under the heading "Risk Factors" in the Company's Form 10-K filed with the U.S. Securities and Exchange Commission ("SEC") on March 19, 2024 and the Company's Form 10-Q filed with the SEC on November 12, 2024, and in subsequent filings made by ImmunityBio with the SEC, which are available on the SEC's website at www.sec.gov. ImmunityBio cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. ImmunityBio does not undertake any duty to update any forward-looking statement or other information in this press release, except to the extent required by law.

Our product candidates are investigational agents that are restricted by federal law to investigational use only. Except as set forth in specific product approvals, safety and efficacy have not been established by any agency, including the FDA.

This presentation contains references to our trademarks and trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this presentation, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us, by any other companies.

This presentation is intended to provide a company overview and is intended for investor use only. It is not promotional and should not be used with patients or health care professionals.

ImmunityBio Leadership Team

Patrick Soon-Shiong, M.D. FACS
Executive Chairman, Global Chief Medical & Scientific Officer

Rich Adcock
President & Chief Executive Officer

Leonard S. Sender, M.D.
Chief Medical Officer Liquid Tumors & Cell Therapy

Sandeep Reddy, M.D.
Chief Medical Officer Solid Tumors & Diagnostics

Enrique Diloné, Ph.D.
Chief Technology Officer

Charles G. Garlisi, Ph.D.
Senior Vice President, Regulatory Affairs

Sarah Singleton
Chief Communications Officer & Head of Patient Advocacy

Bruce Brown, M.D.
Senior Vice President Medical Affairs

Elizabeth Gabitzsch
Senior Vice President, Product Development & Vaccine Programs

David Sachs
Chief Financial Officer

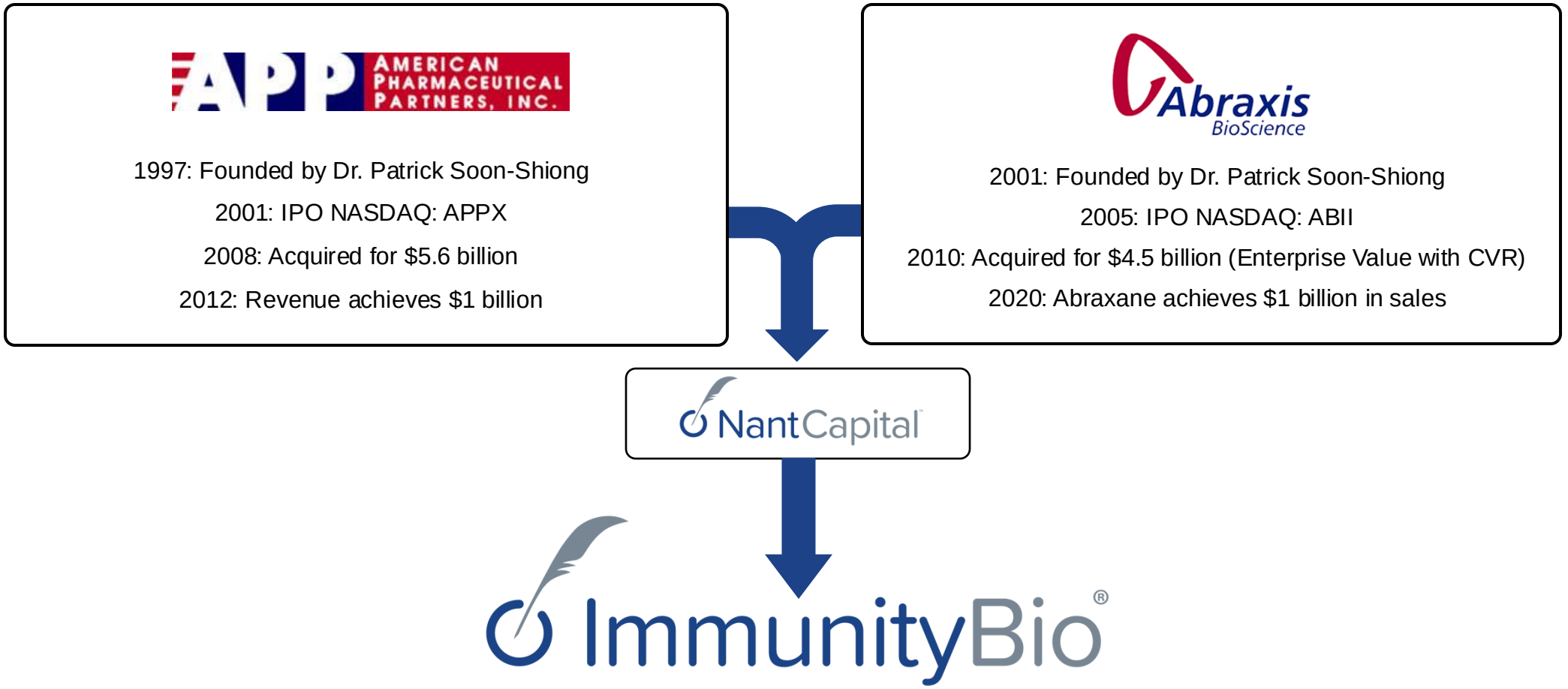
Regan Lauer
Chief Accounting Officer

Manju Saxena, Ph.D.
Senior Vice President of Product Development, Cell Therapy Program

Jason Liljestrom, Esq.
General Counsel

Barry Simon, M.D.
Chief Corporate Affairs Officer

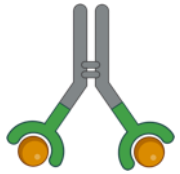
Track Record of Value Creation



Focused on Developing a Universal Cancer Immunotherapy Across All Tumor Types By Activating the Body's Own Immune System

ImmunityBio Cancer Immunotherapy Platforms

Fusion Proteins

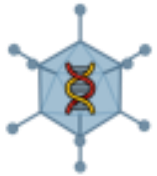


NK & T Cell Activator
Memory T Cell

ANKTIVA

FDA Approved April 2024

DNA Vaccine



Adenovirus (hAd5)
TriAd

hAd5 CEA, MUC1, Brachyury

hAd5 PSA

hAd5 HPV

Phase 2

Cell Therapy

CAR-NK

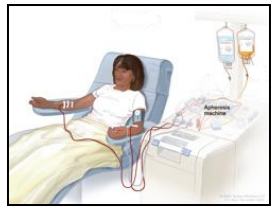
Off-The-Shelf
CAR-NK

PD-L1 t-haNK

CD19 t-haNK

Phase 2

M-ceNK



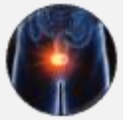
NK, iNKT &
Dendritic Cell Pathway

M-ceNK

Phase 2

ANKTIVA as a Potential Backbone Across All Tumor Types

Driving Innovation and Leadership in Disease Areas of Focus



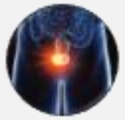
Bladder Cancer

BCG Unresponsive CIS NMIBC

>36K
WW Incidence[2]

FDA Approved April 2024

ANKTIVA + BCG



Bladder Cancer

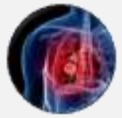
BCG NAÏVE NMIBC Interim Analysis[a]

~230K
WW Incidence[2]

Pivotal Phase 3

a. Data on File, BLA Submission at 9 Months FDA Interim Analysis Request

ANKTIVA + BCG



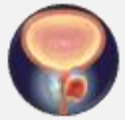
Lung Cancer

NSCLC Checkpoint Failures

~730K
WW Incidence[2]

Pivotal Phase 3

ANKTIVA + Checkpoint



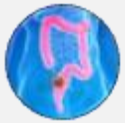
Prostate Cancer

High Risk Prostate Cancer

>1.4M
WW Incidence[2]

Phase 2

ANKTIVA + hAd5 PSA



Colon Cancer

First Line Neoadjuvant

Lynch Syndrome

>1.1M
WW Incidence[2]

Phase 2

ANKTIVA + TriAd

Hematologic Malignancies

Non-Hodgkin's Lymphoma

>1.3M
WW Incidence[2]

Phase 1

ANKTIVA + Rituximab

1. BMJ 2010;340:c3041; 2. Based on internal analysis using data from multiple sources, including the WHO International Agency for Research on Cancer, Cancer Tomorrow Data Visualization. Estimated annual incidence for 2020 (international) and 2024 (US).

Non-Muscle Invasive Bladder Cancer Market Opportunity

Incidence \ Prevalence

Outside US

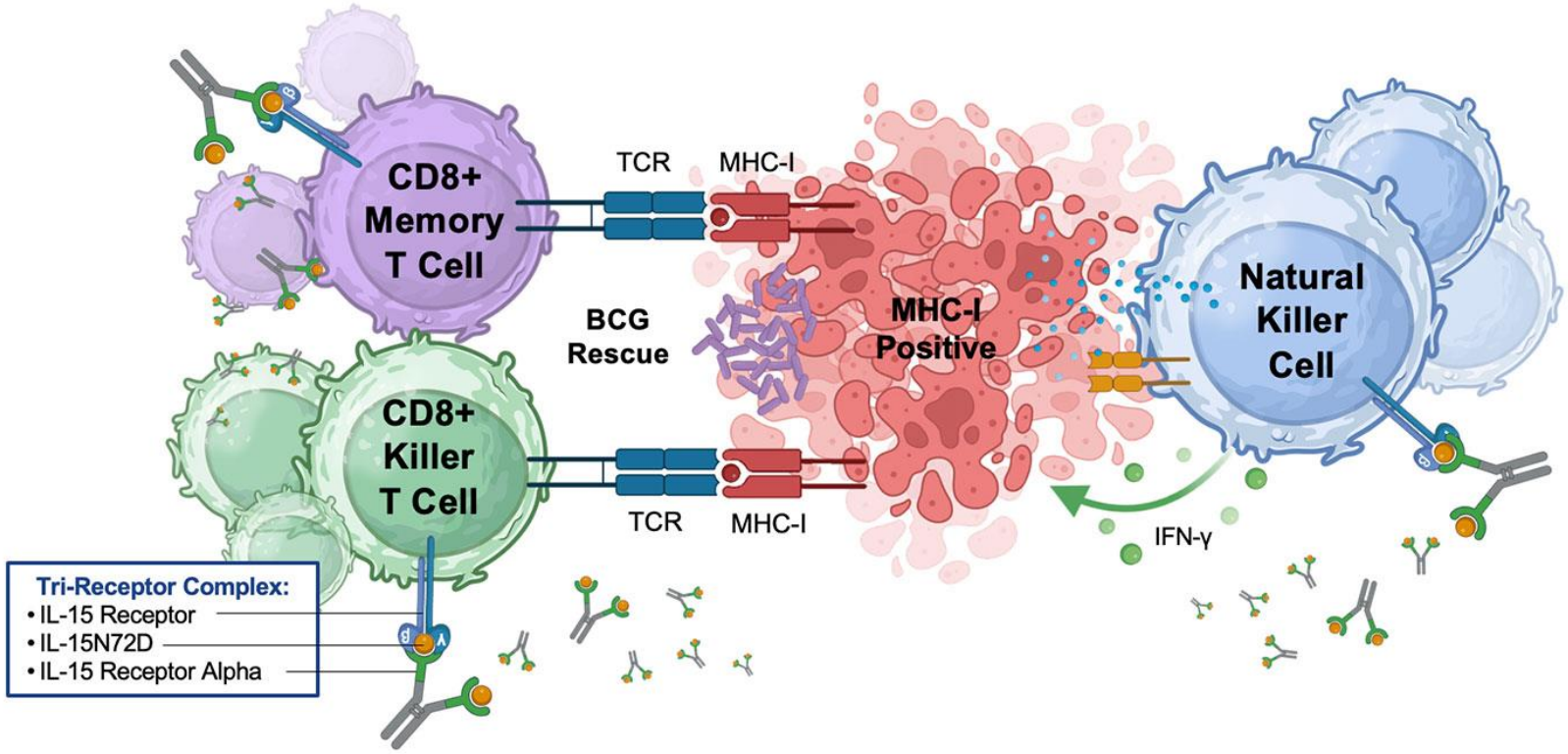
	Annual Incidence in Bladder Cancer Patients diagnosed with bladder cancer	**~80,000 – 100,000+**	**~485,000 (~5x US)** [(a)]
Patient Identification	**NMIBC Incidence %** **(Bladder Cancer x NMIBC Mix ~75%)**	**68,000 \ ~204,000**	**~340,000**
	High Risk Stage at Diagnosis **(Full population remains at 56%)**	**38,000 \ ~114,000** **(QUILT 2005: BCG Naïve)**	**~190,000**
Initial Patient Treatment	**BCG Treated** **(~90% of Population get BCG in US)**	**34,000 \ ~102,000**	**~170,000**
	BCG Unresponsive **(~70% are BCG Unresponsive)**	**24,000 \ ~72,000**	**~120,000**
Patient Opportunity (CIS Inclusive Only)	Bladder Sparing Treatment	**6,000 \ ~18,000** **(26% are BCG Unres. CIS** **FDA Approved Indication)**	**~30,000** **(26% are BCG Unres. CIS)**
	ANKTIVA Product Share		

~24,000 Subjects
Incidence + Prevalence
US Approved Indication

~30,000 Subjects
Incidence
Ex US (Pending EU/UK)

(a) Based on internal analysis using data from multiple sources, including ACS/SEER, AUA, NCCN and WHO International Agency for Research on Cancer, public research and Company estimates: Estimated annual incidence for 2020 (international) and 2024 (US).

ANKTIVA Mechanism of Action Rescue of BCG in NMIBC-CIS

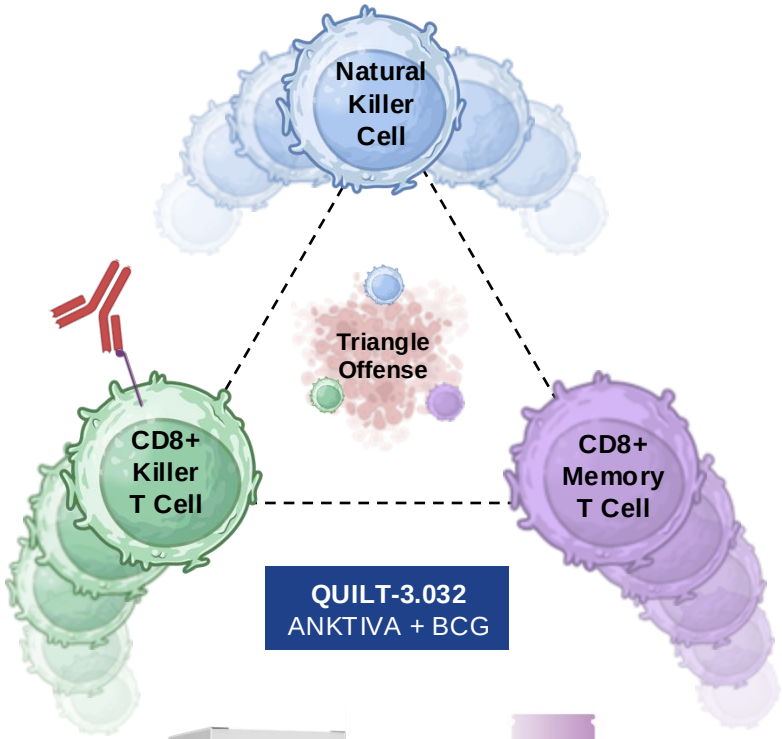


Immunogenic Cell Death by ANKTIVA in the Triangle Offense: The Three Steps to Transforming the MHCscore™

- **Step 1:** Conversion of MHC Negative (Cold) to MHC Positive Tumor (Hot)
- **Step 2:** Activation of IL-15 Receptor in Killer NK and T Cells
- **Step 3:** Proliferation of NK, CD8+ Killer, and CD8+ Memory Cells

1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024 **2.** Garrido F, Aptsiauri N. Cancer immune escape: MHC expression in primary tumors versus metastases. Immunology. 2019 Dec;158(4):255-266

Triangle Offense



QUILT-3.032
ANKTIVA + BCG

Long Term, Cancer Free Overall Survival
BCG Unresponsive in NMIBC: 47+ Months and Ongoing

FDA Label Validates our Approach

Activating NK Cells, CD4+, CD8+ T Cells and Inducing Memory T Cells

- FDA approval for BCG Unresponsive CIS Non-muscle invasive bladder cancer in April 2024 with a label stating:
  - *"…Binding of nogapendekin alfa inbakicept-pmln to its receptor results in proliferation and activation of NK, CD8+, and memory T cells without proliferation of immuno-suppressive Treg cells. In vivo, intravesicular nogapendekin alfa inbakicept-pmln alone or in combination with BCG showed anti-tumor activity when compared to BCG alone, in a carcinogen-induced model of bladder cancer in immunocompetent rats."*

FDA Approved
April 2024

ANKTIVA Best-in-Class Complete Response in BCG Unresponsive NMIBC-CIS

ANKTIVA FDA Label Q2 2024
UK MHRA Submission Q4 2024

N=77

62%

New England Journal of Medicine, 2022

N=82

71%

EU EMA Submission Q4 2024
30 Countries

N=100

71%

ANKTIVA Durable Complete Response

Chamie K, et al. IL-15 Superagonist NAI in BCG-Unresponsive Non-Muscle-Invasive Bladder Cancer. NEJM Evid. 2023 Jan;2(1): EVIDoa2200167. doi: 10.1056/EVIDoa2200167.

ANKTIVA Best-in-Class Duration of Response in BCG Unresponsive NMIBC-CIS

Adstiladrin	Pembrolizumab	ANKTIVA
DURATION	DURATION	DURATION
9.7	16.2	47*
Months	Months	Months & Ongoing
		Median Not Reached

DURATION is the key efficacy element to avoidance of cystectomy

* N=77, FDA Label

Data from Individual Registration Trials and Package Inserts with No Direct Comparisons of Trials
Data from each respective FDA Approved product label

ANKTIVA Safety Comparable to BCG Alone [1, 2, 3]

Safety and Tolerability Consistent with BCG Alone [2]

0% - 3.4%

Grade 3 & 4 Adverse Events [1]

0%

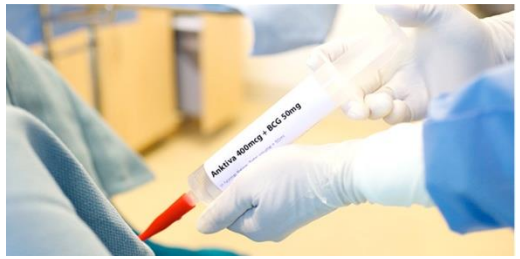
Grades 3 & 4* Dysuria, Urinary Frequency and Micturition Urgency [1]

0%

Treatment Related Grade 5 AEs [1, 3]

7%

Treatment Related Discontinuation [1]



The AE profile is consistent with PK results: No systemic absorption with local intravesical administration [1]

Adverse reactions (≥5%) resulting in interruption with ANKTIVA plus BCG were UTI (10%), dysuria (8%), hematuria (6%), and bladder irritation (6%) [1]

The most common (≥15%) adverse reactions, including laboratory test abnormalities, were increased creatinine, dysuria, hematuria, urinary frequency, micturition urgency, urinary tract infection, increased potassium, musculoskeletal pain, chills and pyrexia. [1]

*Serious adverse reactions occurred in 16% of patients receiving Anktiva with BCG

1. ANKTIVA Package Insert. ImmunityBio, Inc. 2024. 2. Chamie K, et al. IL-15 Superagonist NAI in BCG-Unresponsive Non-Muscle-Invasive Bladder Cancer. NEJM Evid. 2023 Jan;2(1): EVIDoa2200167. doi: 10.1056/EVIDoa2200167. 3. One death reported due to a cardiac arrest that was unrelated to ANKTIVA + BCG.

ANKTIVA Launch First 6 Months Since Approval

1. ANKTIVA Approval April 2024

$35,800 Per Vial

2. American Urological Association Annual Meeting Anktiva Launched May 2024

3. NCCN Guidelines Approval May 2024

4. J-Code Awarded Oct 2024, Effective Jan 2025

5. Global Submissions:
   - UK Nov 2024:
   - EU Dec 2024:

Market Access: 240 Million Medical Lives Covered November 2024

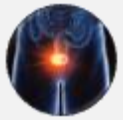
Florida Blue
VA | U.S. Department of Veterans Affairs
CVS caremark
cigna healthcare
EXPRESS SCRIPTS
KAISER PERMANENTE
United Healthcare
CENTENE Corporation
Horizon
HIGHMARK
Humana
HCSC Health Care Service Corporation
ucare
Anthem
of Tennessee
Independence
Optum
Blue Cross Blue Shield of Michigan
Elevance Health
EmblemHealth
BlueCross BlueShield of North Dakota
aetna COVENTRY
Blue Cross Blue Shield of Hawai'i
BlueCross BlueShield of North Carolina
BlueCross BlueShield of Alabama
BlueCross BlueShield Minnesota

ANKTIVA
No Change in Urology Order & BCG Administration Workflow

- ✔ One Day Delivery
- ✔ 36 Month Shelf Life
- ✔ No Special Freezers
- ✔ No Special Cleaning Agents
- ✔ No Change in BCG Workflow
- ✔ Same Order Flow as BCG

ANKTIVA as a Potential Backbone Across All Tumor Types

Driving Innovation and Leadership in Disease Areas of Focus



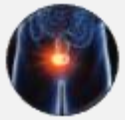
Bladder Cancer

BCG Unresponsive CIS NMIBC

>36K
WW Incidence[2]

FDA Approved April 2024

ANKTIVA + BCG



Bladder Cancer

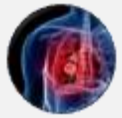
BCG NAÏVE NMIBC Interim Analysis[a]

~230K
WW Incidence[2]

Pivotal Phase 3

a. Data on File, BLA Submission at 9 Months FDA Interim Analysis Request

ANKTIVA + BCG



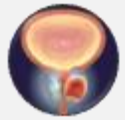
Lung Cancer

NSCLC Checkpoint Failures

~730K
WW Incidence[2]

Pivotal Phase 3

ANKTIVA + Checkpoint



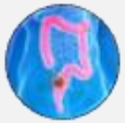
Prostate Cancer

High Risk Prostate Cancer

>1.4M
WW Incidence[2]

Phase 2

ANKTIVA + hAd5 PSA



Colon Cancer

First Line Neoadjuvant

Lynch Syndrome

>1.1M
WW Incidence[2]

Phase 2

ANKTIVA + Adeno TriAd

Hematologic Malignancies

Non-Hodgkin's Lymphoma

>1.3M
WW Incidence[2]

Phase 1

ANKTIVA + Rituximab

1. BMJ 2010;340:c3041; 2. Based on internal analysis using data from multiple sources, including the WHO International Agency for Research on Cancer, Cancer Tomorrow Data Visualization. Estimated annual incidence for 2020 (international) and 2024 (US).

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Patient Opportunity (CIS Inclusive Only)	ANKTIVA Product Share	**~24,000 Subjects** Incidence + Prevalence **US Approved Indication**	**~30,000 Subjects** **Incidence** **Ex US (Pending EU/UK)**

~230,000 Subjects
Global Incidence

(a) Based on internal analysis using data from multiple sources, including ACS/SEER, AUA, NCCN and WHO International Agency for Research on Cancer, public research and Company estimates: Estimated annual incidence for 2020 (international) and 2024 (US).

ANKTIVA in the NMIBC BCG Naïve Setting

QUILT-205 Trial[1, 2]

- **Complete Response and Disease Free in 9 out of 9 (100%) 2-year trial**
- 6 out of 9 were evaluable in 2023
- 2 subjects died of natural causes independent of bladder cancer
- 1 lost to follow up
- All 6 out of 6 (100%) remain in complete response (CIS) or disease free (Papillary) for >8.5 years
- **All 6 patients avoided cystectomy for >8.5 years**

As of 2023

6 out of 6 (100%) Remain Disease Free

≥ 8.5 Years

Conclusion: ANKTIVA + BCG in BCG Naïve Patients Results in Durable Complete Response with Quality of Life and Adverse Events Consistent with BCG Alone

1. Adapted From Rosser CJ, et al., Safety, Tolerability, and Long-Term Clinical Outcomes of an IL-15 analogue (N-803) Admixed with Bacillus Calmette-Guérin (BCG) for the Treatment of Bladder Cancer. Oncoimmunology. 2021 May 2. Data on File

Pivotal Phase 3 Trial of ANKTIVA in NMIBC BCG Naïve

Trial Design

BCG Alone N=188 **Vs.** **ANKTIVA + BCG N=188**

FDA Randomized Control Trial Cohort A

FDA Requested Interim Analysis (n=43)

BCG Alone 52% CR **Vs.** **ANKTIVA + BCG 84% CR**

Data on File, BLA Submission at 9 months, FDA Interim Analysis Requested

Status Update

- Expanding internationally beyond US
- Trial live in India and in process of going live in Europe

Potential Courses of Treatment in BCG Naïve Same as Current FDA Label for BCG Unresponsive (Up to 36 Doses Over 37 Months)

BCG Supply - ImmunityBio-Serum Institute of India

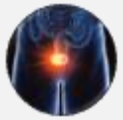
ImmunityBio, Serum Institute of India Agree on an Exclusive Arrangement for Global Supply of Bacillus Calmette-Guerin (BCG) Across All Cancer Types

Thursday, May 2, 2024

- Collaboration will result in BCG manufacture at large scale for use in combination with ANKTIVA®, ImmunityBio's recently approved treatment for non-muscle invasive bladder cancer (NMIBC)

ANKTIVA as a Potential Backbone Across All Tumor Types

Driving Innovation and Leadership in Disease Areas of Focus



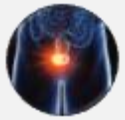
Bladder Cancer

BCG Unresponsive CIS NMIBC

>36K
WW Incidence[2]

FDA Approved April 2024

ANKTIVA + BCG



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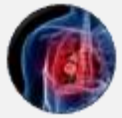
a. Data on File, BLA Submission at 9 Months FDA Interim Analysis Request

ANKTIVA + BCG



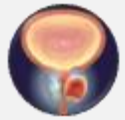
Lung Cancer

NSCLC Checkpoint Failures

~730K
WW Incidence[2]

Pivotal Phase 3

ANKTIVA + Checkpoint



Prostate Cancer

High Risk Prostate Cancer

>1.4M
WW Incidence[2]

Phase 2

ANKTIVA + hAd5 PSA

Colon Cancer

First Line Neoadjuvant

Lynch Syndrome

>1.1M
WW Incidence[2]

Phase 2

ANKTIVA + Adeno TriAd

Hematologic Malignancies

Non-Hodgkin's Lymphoma

>1.3M
WW Incidence[2]

Phase 1

ANKTIVA + Rituximab

1. BMJ 2010;340:c3041; 2. Based on internal analysis using data from multiple sources, including the WHO International Agency for Research on Cancer, Cancer Tomorrow Data Visualization. Estimated annual incidence for 2020 (international) and 2024 (US).

Non-Small Cell Lung Cancer Market Opportunity

Incidence

		US	Outside US
	Annual Incidence in Lung Cancer Patients diagnosed with Lung cancer	**~235,000**	**1,965,000 (~8.4x US)** [(a)]
Patient Identification	**NSCLC Incidence %** **(Lung Cancer x NSCLC Mix at 82.5%)**	**194,000**	**~1,620,000**
	Metastatic Cases **(70% Metastatic)**	**136,000**	**~1,135,000**
Initial Patient Treatment	**CPI Treated** **(~72.5% of Population get CPI in US)**	**98,000**	**~823,000**
	CPI Unresponsive Treatment Rate **(~79% are CPI Unresponsive)**	**78,000**	**~650,000**
Patient Opportunity (2nd Line Inclusive Only)	PD-L1 Expression (TPS) (100% - No TPS limitations)	**78,000**	**~650,000**
	ANKTIVA Potential Product Share	**~80,000 Subjects 2nd Line**	**~650,000 Subjects 2nd Line**

(a) Based on internal analysis using data from multiple sources, including ACS/SEER, AUA, NCCN and WHO International Agency for Research on Cancer, public research and Company estimates: Estimated annual incidence for 2020 (international) and 2024 (US).

ANKTIVA Activity in NSCLC Checkpoint Progressors
QUILT 3.055

NSCLC patients progressing after checkpoint therapy +/- chemotherapy have a dismal prognosis

- Overall survival ≤ 10 months
- Treatment options are limited; NCCN does not recommend retreatment with checkpoint therapy after checkpoint failure

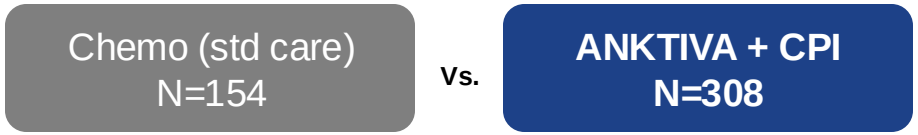
ANKTIVA + PD1 mAb in NSCLC patients who had progressed on checkpoint therapy, ANKTIVA showed rescue of CPI:

- 86 pts with 2nd and 3rd line+ NSCLC who had progressed on CPI alone or CPI + chemo were treated with Anktiva + PD1 Mab
- Median OS (n=86) was **14.1 months** (95% CI 11.7, 16.3) with 24 pts still on study; Rescue in both PD-L1+ve and PD-L1-ve patients
- Long-term survival: **33.7% at ≥18 months** and **31.4% ≥21 months**
- In **PD-L1-ve** patients, the median overall survival was **15.8 months** (95% CI: 11.5, 24.0)

Findings support the novel immune-mediated mechanism of action of ANKTIVA to rescue CPI in patients who had progressed on CPI

Pivotal Phase 3 Trial of ANKTIVA in 2L-NSCLC ResQ201a

Trial Design



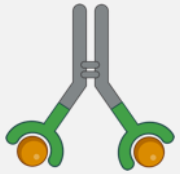
Status Update

- FDA Authorized IND
- CRO Contracted and Working on Roll-out
- Global Trial Locations in North America, Europe, Asia (~100)

ImmunityBio Patent Coverage

Driving Innovation and Leadership with Broad Patent Coverage

Antibody Cytokine Fusion Proteins



245
Granted/Allowed Worldwide

DNA Vaccines

104
Granted/Allowed Worldwide

Off-the-Shelf NK Cell Therapy

220
Granted/Allowed worldwide

ANKTIVA Biologics Exclusivity

ANKTIVA + BCG Patent

ANKTIVA + Checkpoint Patent

Until 2035[1]

Over 700+ issued patents worldwide covering ImmunityBio immunotherapy portfolio

[1] *Date does not include any patent term adjustment or extension. Biologics exclusivity extends to 2036.*

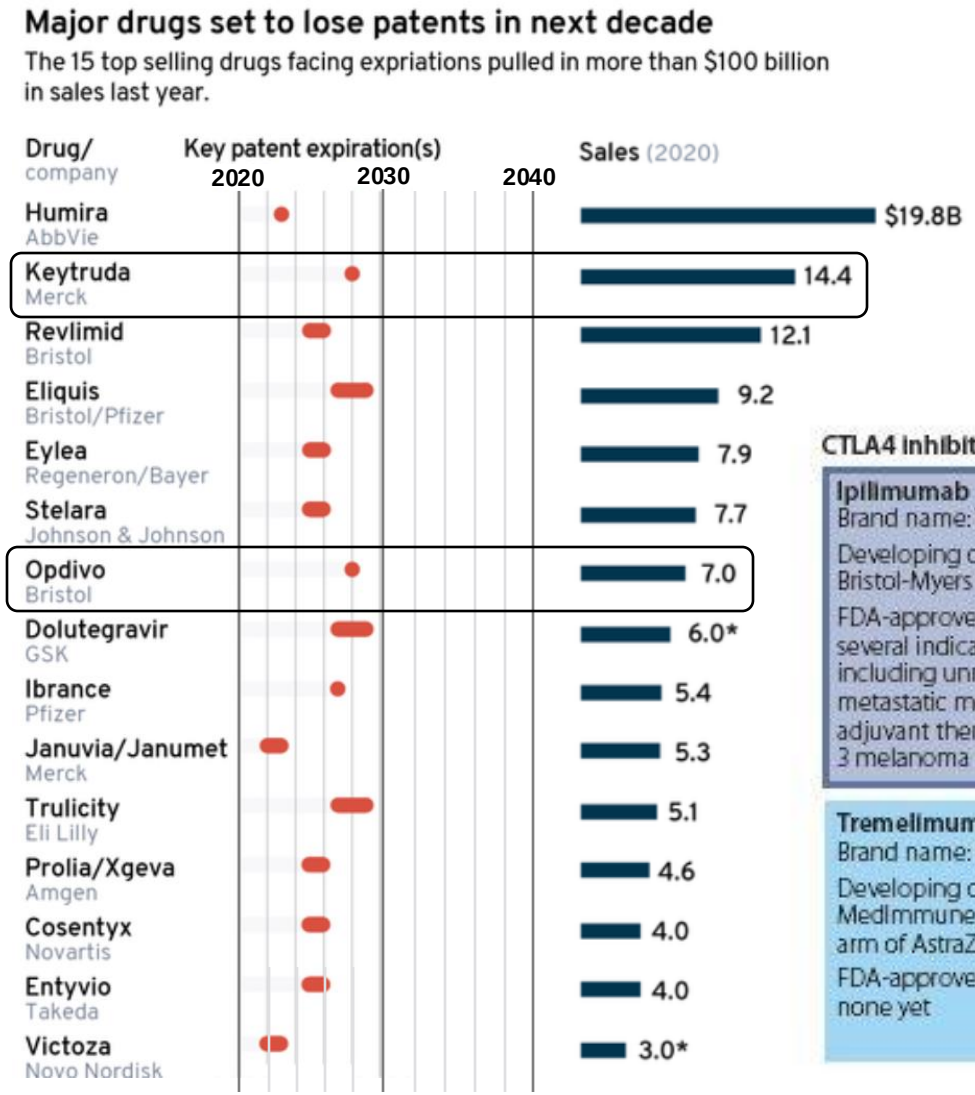
Key Upcoming Catalysts

		Anticipated Timeline	
Bladder Cancer 	NMIBC BCG-Unresponsive QUILT 3.032	Submit UK/EU	Nov/Dec 2024*
		UK/EU Approval/Launch	Late 2025 – Early 2026
	NMIBC Naïve QUILT 2.005	Anticipate Full Enrollment	Late 2025 – Early 2026
		Data Read Out	Second Half 2026
		BLA Submission to US FDA	Late 2026 – Early 2027
Lung Cancer 	NSCLC-2L CPI Failure ResQ201a	Anticipate Full Enrollment	Early 2026
		Data Read Out	Second Half 2027
		BLA Submission to US FDA	Early 2028

Any potential regulatory approvals and clinical trial activity and the related estimated timing are based on current assumptions and subject to numerous risks and uncertainties.
** Completed in 2024.*

Appendix:
Checkpoint Patent Cliff

Checkpoint Patent Cliff: 2027+



Modified from: https://www.fiercepharma.com/special-report/top-15-blockbuster-patent-expirations-coming-decade

The Addressable Market and IP Status of I/O

CTLA4 Inhibitors

Ipilimumab 2022
Brand name: Yervoy
Developing company: Bristol-Myers Squibb
FDA-approved indications: several indications including unresectable or metastatic melanoma; adjuvant therapy for stage 3 melanoma

Tremelimumab
Brand name: N/A
Developing company: MedImmune, the biologics arm of AstraZeneca
FDA-approved indications: none yet

PD1 Inhibitors

Nivolumab 2027
Brand name: Opdivo
Developing company: Bristol-Myers Squibb
FDA-approved indications: several indications including unresectable or metastatic melanoma, metastatic NSCLC, advanced RCC, Hodgkin lymphoma

Pembrolizumab 2028
Brand name: Keytruda
Developing company: Merck & Co.*
FDA-approved indications: several indications including unresectable or metastatic melanoma, metastatic NSCLC, recurrent or metastatic HNSCC

PDR001
Brand name: N/A
Developing company: Novartis
FDA-approved indications: none yet, in phase 3 trials

Tislelizumab 2033
Developing companies: Beigene/Celgene
FDA-approved indications: none yet

PDL1 Inhibitors

Atezolizumab 2028
Brand name: Tecentriq
Developing company: Genentech/Roche
FDA-approved indications: urothelial carcinoma and metastatic NSCLC

Avelumab 2033
Brand name: Bavencio
Developing companies: Merck KGaA and Pfizer
FDA-approved indications: metastatic urothelial carcinoma and Merkel cell carcinoma

Durvalumab
Brand name: Imfinzi
Developing company: MedImmune, the biologics arm of AstraZeneca
FDA-approved indications: metastatic urothelial carcinoma

Modified From: https://www.nature.com/articles/d43747-020-00376-x

2024 ASCO Presentations: The Challenge Facing Oncology in 2024 CPI Failure

2024 ASCO ANNUAL MEETING

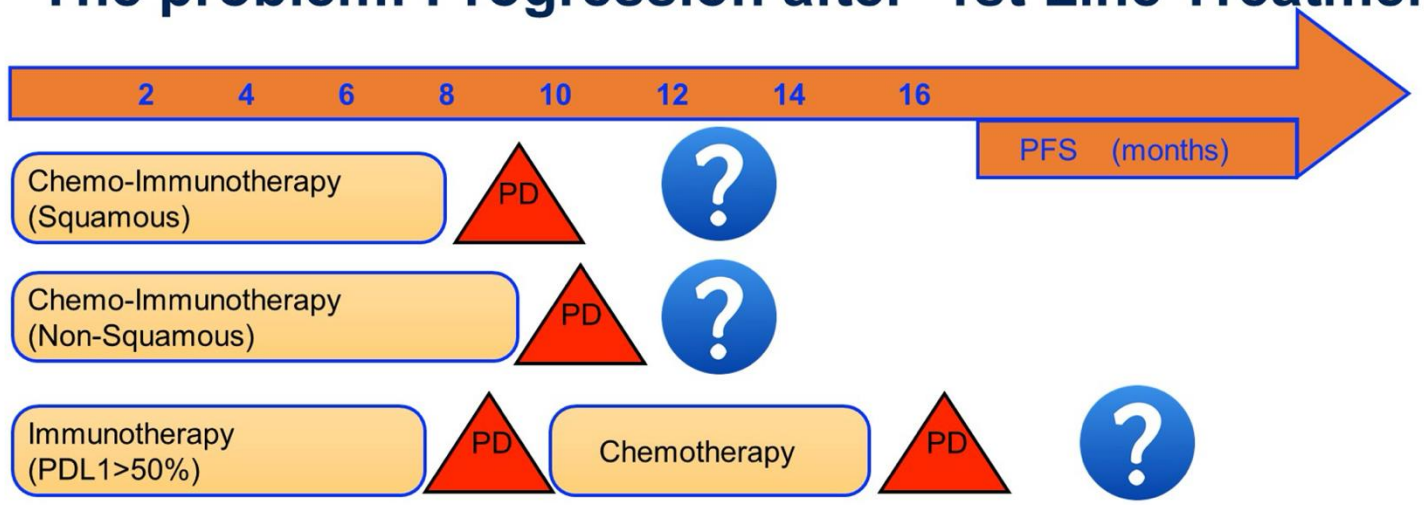
New Frontiers in Lung Cancer Treatment: Expanding Options Beyond chemo-immunotherapy

Is there a best option other than Docetaxel?

Giannis S. Mountzios MD, MSc, PhD
Medical Oncologist
Director, 4th Oncology Department and Clinical Trials Unit
Henry Dunant Hospital Center
Athens, Greece

2024 ASCO ANNUAL MEETING #ASCO24 PRESENTED BY: Giannis Mountzios MD, MSc, PhD

The problem: Progression after 1st Line Treatment



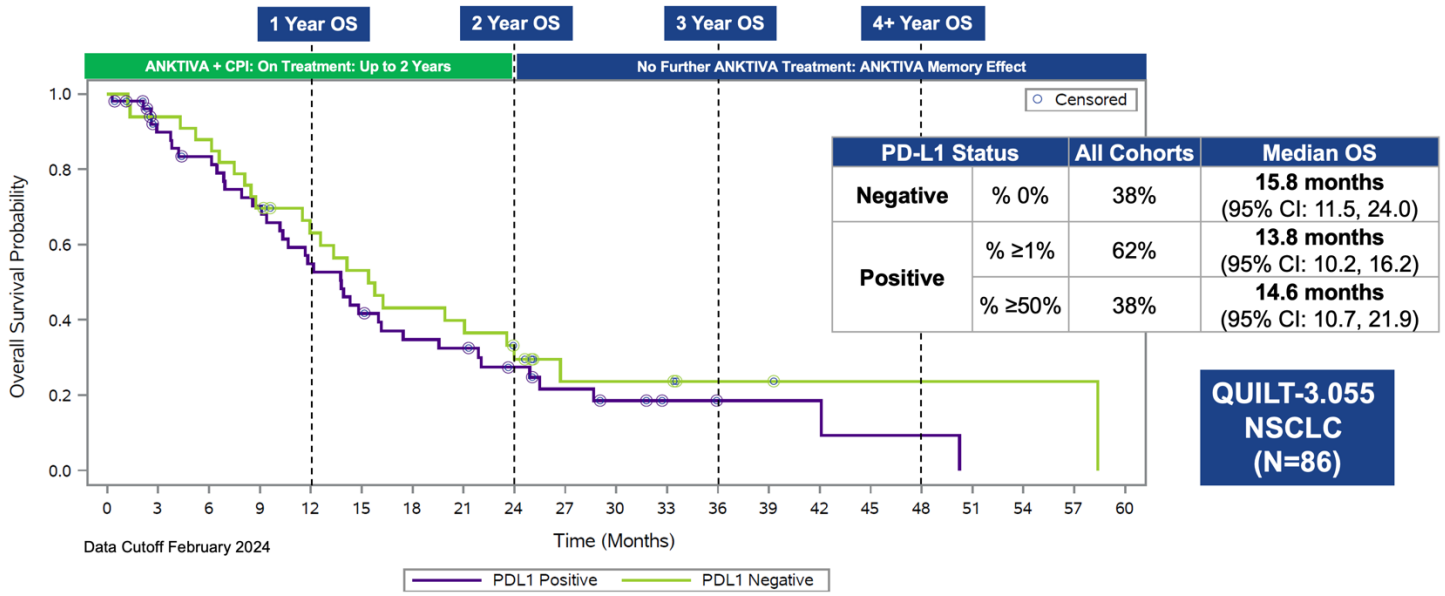
2024 ASCO ANNUAL MEETING #ASCO24 PRESENTED BY: Giannis Mountzios MD, MSc, PhD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

ANKTIVA in Combination Rescues Checkpoints Immunotherapy 2.0: Beyond T Cells (NSCLC)

ANKTIVA Rescues Checkpoint Failures Across All PD-L1 Status

Oral Presentation at World Lung 2024



PD-L1 Status		All Cohorts	Median OS
Negative	% 0%	38%	**15.8 months** (95% CI: 11.5, 24.0)
Positive	% ≥1%	62%	**13.8 months** (95% CI: 10.2, 16.2)
	% ≥50%	38%	**14.6 months** (95% CI: 10.7, 21.9)

QUILT-3.055 NSCLC (N=86)

Finding: ANKTIVA rescues CPI independent of PD-L1 status and consistent with NK cell activity

Registration Trial - ResQ201A-NSCLC Checkpoint Failure, 2nd Line

2024 World Congress on Lung Cancer - Novel Immunotherapy Strategies and Combinations
IL15 Superagonist (N-803, Anktiva) + Checkpoint Inhibitor (CPI) Prolongs OS in 2ndline or Greater NSCLC Patients Failing CPI J. Wrangle, S. Reddy, P. Soon-Shiong

ANKTIVA Plus Checkpoint Patent Term Extension Opportunity: 2035

vehicle before use. Apart from the active agent that reduces or ameliorates a neoplasia or infection, the composition may include suitable parenterally acceptable carriers and/or excipients. The active therapeutic agent(s) may be incorporated into micro spheres, microcapsules, nanoparticles, liposomes, or the like for controlled release. Furthermore, the composition may include suspending, solubilizing, stabilizing, pH-adjusting agents, tonicity adjusting agents, and/or dispersing, agents.

As indicated above, the pharmaceutical compositions comprising ALT-803 may be in a form suitable for sterile injection. To prepare such a composition, the suitable active antineoplastic/anti-infective therapeutic(s) are dissolved or suspended in a parenterally acceptable liquid vehicle. Among acceptable vehicles and solvents that may be employed are water, water adjusted to a suitable pH by addition of an appropriate amount of hydrochloric acid, sodium hydroxide or a suitable buffer, 1,3-butanediol, Ringer's solution, and isotonic sodium chloride solution and dextrose solution. The aqueous formulation may also contain one or more preservatives (e.g., methyl, ethyl or n-propyl p-hydroxybenzoate). In cases where one of the compounds is only sparingly or slightly soluble in water, a dissolution enhancing or solubilizing agent can be added, or the solvent may include 10-60% w/w of propylene glycol or the like.

The present invention provides methods of treating neoplastic or infectious disease and/or disorders or symptoms thereof which comprise administering a therapeutically effective amount of a pharmaceutical composition comprising a compound of the formulae herein to a subject (e.g., a mammal such as a human). Thus, one embodiment is a method of treating a subject suffering from or susceptible to a neoplastic or infectious disease or disorder or symptom thereof. The method includes the step of administering to the mammal a therapeutic amount of an amount of a compound herein sufficient to treat the disease or disorder or symptom thereof, under conditions such that the disease or disorder is treated.

The methods herein include administering to the subject (including a subject identified as in need of such treatment) an effective amount of a compound described herein, or a composition described herein to produce such effect. Identifying a subject in need of such treatment can be in the judgment of a subject or a health care professional and can be subjective (e.g. opinion) or objective (e.g. measurable by a test or diagnostic method).

The therapeutic methods of the invention (which include prophylactic treatment) in general comprise administration of a therapeutically effective amount of the compounds herein, such as a compound of the formulae herein to a subject (e.g., animal, human) in need thereof, including a mammal, particularly a human. Such treatment will be suitably administered to subjects, particularly humans, suffering from, having, susceptible to, or at risk for a neoplastic or infectious disease, disorder, or symptom thereof. Determination of those subjects "at risk" can be made by any objective or subjective determination by a diagnostic test or opinion of a subject or health care provider (e.g., genetic test, enzyme or protein marker, Marker (as defined herein), family history, and the like). ALT-803 may be used in the treatment of any other disorders in which an increase in an immune response is desired.

In one embodiment, the invention provides a method of monitoring treatment progress. The method includes the step of determining a level of diagnostic marker (Marker) (e.g., any target delineated herein modulated by a compound herein, a protein or indicator thereof, etc.) or diagnostic measurement (e.g., screen, assay) in a subject suffering from or susceptible to a disorder or symptoms thereof associated with neoplasia or infection in which the subject has been administered a therapeutic amount of a compound herein sufficient to treat the disease or symptoms thereof. The level of Marker determined in the method can be compared to known levels of Marker in either healthy normal controls or in other afflicted patients to establish the subject's disease status. In preferred embodiments, a second level of Marker in the subject is determined at a time point later than the determination of the first level, and the two levels are compared to monitor the course of disease or the efficacy of the therapy. In certain preferred embodiments, a pre-treatment level of Marker in the subject is determined prior to beginning treatment according to this invention; this pre-treatment level of Marker can then be compared to the level of Marker in the subject after the treatment commences, to determine the efficacy of the treatment.

Combination Therapies

Preferably, ALT-803 is administered in combination with an anti-neoplasia or anti-infectious therapeutic such as an antibody, e.g., a tumor-specific antibody or an immune-checkpoint inhibitor. The antibody and ALT-803 may be administered simultaneously or sequentially. In some embodiments, the antibody treatment is an established therapy for the disease indication and addition of ALT-803 treatment to the antibody regimen improves the therapeutic benefit to the patients. Such improvement could be measured as increased responses on a per patient basis or increased responses in the patient population. Combination therapy could also provide improved responses at lower or less frequent doses of antibody resulting in a better tolerated treatment regimen. As indicated, the combined therapy of ALT-803 and an antibody could provide enhances clinical activity through various mechanisms, including augmented ADCC, ADCP, and/or NK cell, T-cell, neutrophil or monocytic cell levels or immune responses.

If desired, ALT-803 is administered in combination with any conventional therapy, including but not limited to, surgery, radiation therapy, chemotherapy, protein-based therapy or biological therapy. Chemotherapeutic drugs include alkylating agents (e.g., platinum-based drugs, tetrazines, aziridines, nitrosoureas, nitrogen mustards), anti-metabolites (e.g., anti-folates, fluoropyrimidines, deoxynucleoside analogues, thiopurines), anti-microtubule agents (e.g., *vinca* alkaloids, taxanes), topoisomerase inhibitors (e.g., topoisomerase I and II inhibitors), cytotoxic antibiotics (e.g., anthracyclines) and immunomodulatory drugs (e.g., thalidomide and analogs).

Kits or Pharmaceutical Systems

Pharmaceutical compositions comprising ALT-803 may be assembled into kits or pharmaceutical systems for use in treating a neoplasia or infection. Kits or pharmaceutical systems according to this aspect of the invention comprise a carrier means, such as a box, carton, tube, having in close confinement therein one or more container means, such as vials, tubes, ampoules, bottles, syringes, or bags. The kits or pharmaceutical systems of the invention may also comprise associated instructions for using ALT-803.

Recombinant Protein Expression

In general, preparation of the fusion protein complexes of the invention (e.g., components of ALT-803) can be accomplished by procedures disclosed herein and by recognized recombinant DNA techniques.

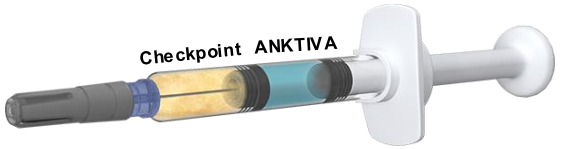
In general, recombinant polypeptides are produced by transformation of a suitable host cell with all or part of a

(12) **United States Patent**
Liu et al.

(10) **Patent No.: US 10,537,615 B2**
(45) **Date of Patent: Jan. 21, 2020**

(54) **IL-15-BASED MOLECULES AND METHODS OF USE THEREOF**

(52) **U.S. Cl.**
CPC ***A61K 38/2086*** (2013.01); ***A61K 39/39558*** (2013.01); ***C07K 14/5443*** (2013.01); ***C07K***



What is claimed is:

1. A method for killing diseased cells expressing a target antigen, the method comprising:

treating immune cells with an effective amount of an IL-15N72D:IL-15RaSu/Fc complex (ALT-803),

mixing the ALT-803-treated immune cells with an antibody specific to a target antigen and diseased cells expressing said target antigen,

killing the diseased cells via ADCC or ADCP mediated by the ALT-803-treated immune cells and target antigen-specific antibody.

2. The method of claim **1**, wherein the level of diseased cell killing is increased by at least 5% compared to that mediated by immune cells that were not treated with ALT-803.

3. The method of claim **1**, wherein the IL-15N72D molecule comprises SEQ ID NO: 3.

4. The method of claim **1**, wherein the IL-15RaSu/Fc comprises SEQ ID NO: 6.

5. The method of claim **1**, wherein said antibody is a tumor-specific antibody or an antiviral antibody.

6. The method of claim **1**, wherein said antibody is an immune-checkpoint inhibitor.

7. The method of claim **1**, wherein said antibody comprises an anti-gp75 antibody, an anti-CD20 antibody, an anti-HER2 antibody, an anti-EGFR antibody, an anti-cytotoxic T-lymphocyte antigen 4 (CTLA-4) antibody, an anti-programmed cell death-1 (PD-1) antibody, an anti-programmed cell death-ligand 1 (PD-L1) antibody, or an anti-programmed cell death-ligand 2(PD-L2) antibody.

* * * * *

Potential Patent Life Extension of Checkpoints to 2035

Kits or Pharmaceutical Systems

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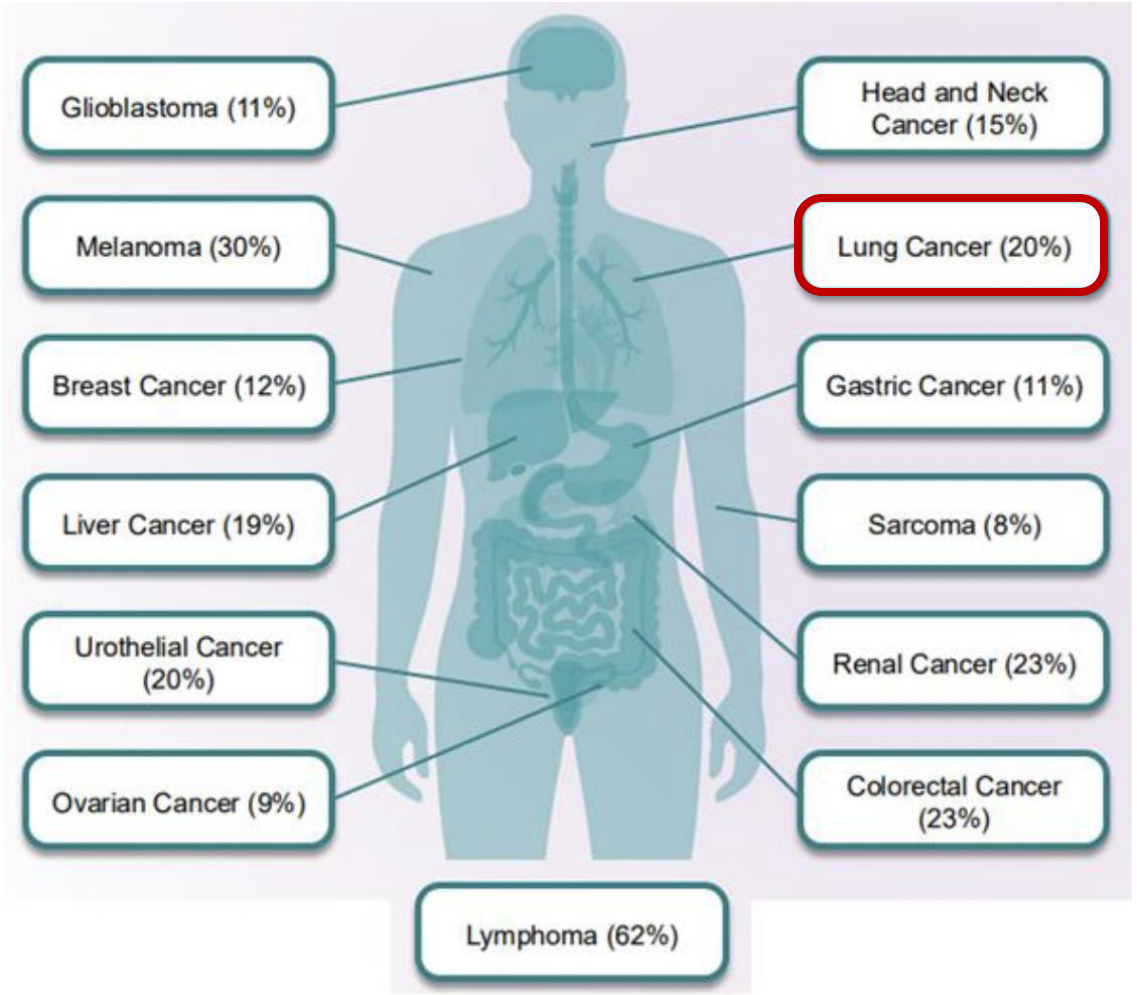
Recombinant Protein Expression

Immunotherapy 2.0
ANKTIVA Combination as the Potential Backbone to Checkpoint Inhibitors: 2025 to 2035

ANKTIVA

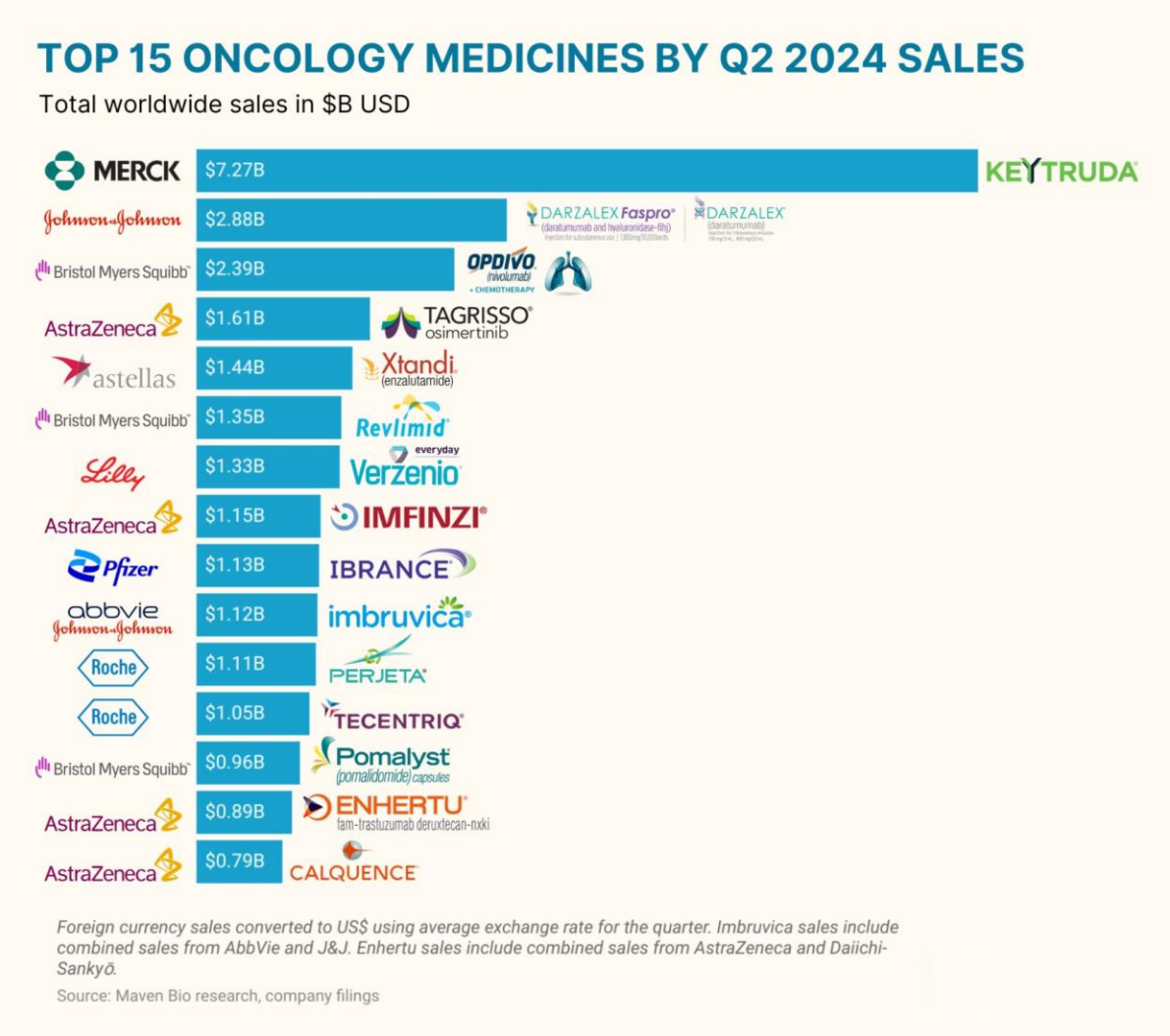
Checkpoint Inhibitor

Immunotherapy 2.0 – Beyond Checkpoints
IBRX Issued Patent Term 2035



Response Rates for Approved Checkpoint Inhibitor Indications
Source: TuHURA Biosciences

Checkpoint Inhibitor Market Expected to Reach Worldwide Sales of $148 Billion by 2030



+

Checkpoint Inhibitor

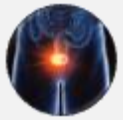
:

Immunotherapy 2.0 – Beyond Checkpoints
IBRX Issued Patent Term 2035

Appendix:
Additional Programs

ANKTIVA as a Potential Backbone Across All Tumor Types

Driving Innovation and Leadership in Disease Areas of Focus



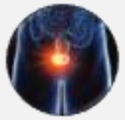
Bladder Cancer

BC Unresponsive CIS NMIBC

>36K
WW Incidence[2]

FDA Approved April 2024

ANKTIVA + BCG



Bladder Cancer

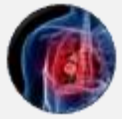
BCG NAÏVE NMIBC Interim Analysis[a]

~230K
WW Incidence[2]

Pivotal Phase 3

a. Data on File, BLA Submission at 9 Months FDA Interim Analysis Request

ANKTIVA + BCG



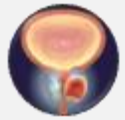
Lung Cancer

NSCLC Checkpoint Failures

~730K
WW Incidence[2]

Pivotal Phase 3

ANKTIVA + Checkpoint



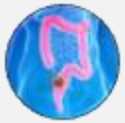
Prostate Cancer

High Risk Prostate Cancer

>1.4M
WW Incidence[2]

Phase 2

ANKTIVA + hAd5 PSA



Colon Cancer

First Line Neoadjuvant

Lynch Syndrome

>1.1M
WW Incidence[2]

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ANKTIVA + Adeno TriAd

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ANKTIVA + Rituximab

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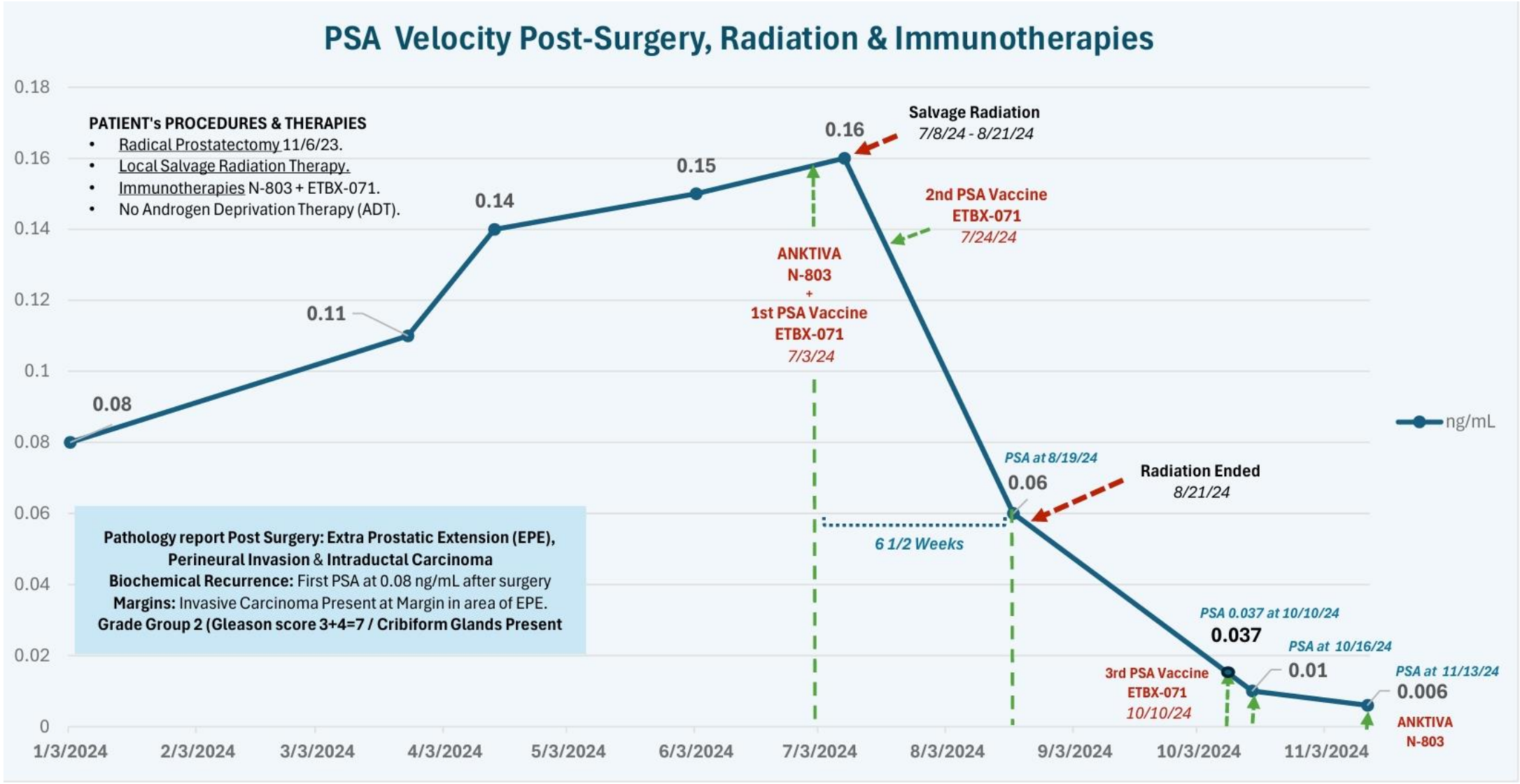
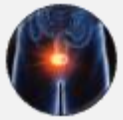
High Risk Prostate Cancer Recurrence



Single patient report

ANKTIVA as a Potential Backbone Across All Tumor Types

Driving Innovation and Leadership in Disease Areas of Focus



Bladder Cancer

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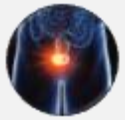
WW Incidence[2]

FDA Approved April 2024

ANKTIVA + BCG



Bladder Cancer

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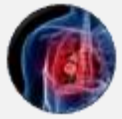

Lung Cancer

NSCLC Checkpoint Failures

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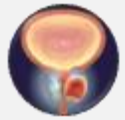
ANKTIVA + Checkpoint



Prostate Cancer

High Risk Prostate Cancer

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Phase 2

ANKTIVA + hAd5 PSA

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First Line Neoadjuvant

Lynch Syndrome

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WW Incidence[2]

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ANKTIVA + Adeno TriAd

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Phase 1

ANKTIVA + Rituximab

1. BMJ 2010;340:c3041; 2. Based on internal analysis using data from multiple sources, including the WHO International Agency for Research on Cancer, Cancer Tomorrow Data Visualization. Estimated annual incidence for 2020 (international) and 2024 (US).

NCI Sponsored, Phase 2 Preventative Lynch Syndrome

ImmunityBio Platforms: Anktiva + Adenovirus 5 CEA/MUC1/Brachyury Vaccine (Tri-Ad5)

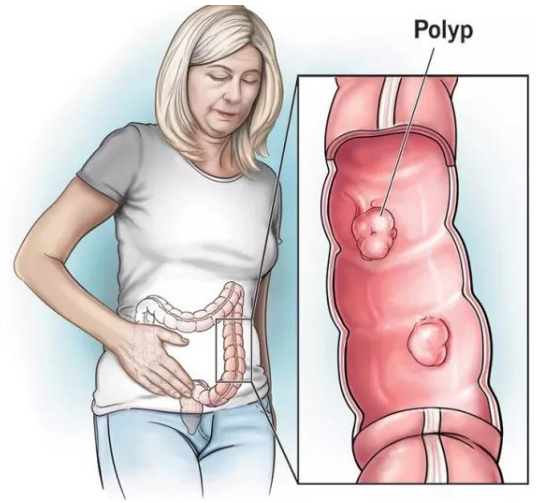


Image Credit: Colorectal Cancer Alliance

Lynch syndrome, often called hereditary nonpolyposis colorectal cancer (HNPCC), is an inherited disorder that increases the risk of many types of cancer, particularly cancers of the colon. It is estimated that 1 in 279 of the population carry mutations in DNA mismatch repair genes

Win AK, et al. Prevalence and Penetrance of Major Genes and Polygenes for Colorectal Cancer. Cancer Epidemiol Biomarkers Prev. 2017 Mar;26(3):404-412. doi: 10.1158/1055-9965.EPI-16-0693. Epub 2016 Oct 31. PMID: 27799157; PMCID: PMC5336409.

NCT05419011 – Phase 2 Preventative Lynch Syndrome

Anktiva (N-803) + Tri-Ad5 Vaccine

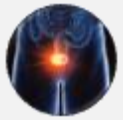
Antigens: MUC1, CEA, Brachyury

NIH NATIONAL CANCER INSTITUTE

This phase IIb trial tests whether Tri-Ad5 in combination with ANKTIVA works to prevent colon and other cancers in participants with Lynch syndrome. Each of the three injections in Tri-Ad5 vaccine contain a different substance that is in precancer and cancer cells. Injecting these substances may cause the immune system to develop a defense against cancer that recognizes and destroys any precancer and cancer cells that produce these proteins in the future. ANKTIVA may increase immune responses to other vaccines. Giving Tri-Ad5 in combination with immune enhancing ANKTIVA may lower the chance of developing colon and other cancers in participants with Lynch syndrome.

ANKTIVA as a Potential Backbone Across All Tumor Types

Driving Innovation and Leadership in Disease Areas of Focus



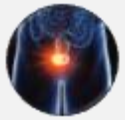
Bladder Cancer

BC Unresponsive CIS NMIBC

>36K
WW Incidence[2]

FDA Approved April 2024

ANKTIVA + BCG



Bladder Cancer

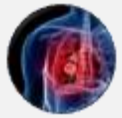
BCG NAÏVE NMIBC Interim Analysis[a]

~230K
WW Incidence[2]

Pivotal Phase 3

a. Data on File, BLA Submission at 9 Months FDA Interim Analysis Request

ANKTIVA + BCG



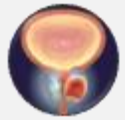
Lung Cancer

NSCLC Checkpoint Failures

~730K
WW Incidence[2]

Pivotal Phase 3

ANKTIVA + Checkpoint



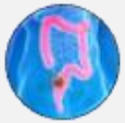
Prostate Cancer

High Risk Prostate Cancer

>1.4M
WW Incidence[2]

Phase 2

ANKTIVA + hAd5 PSA



Colon Cancer

First Line Neoadjuvant

Lynch Syndrome

>1.1M
WW Incidence[2]

Phase 2

ANKTIVA + Adeno TriAd

Hematologic Malignancies

Non-Hodgkin's Lymphoma

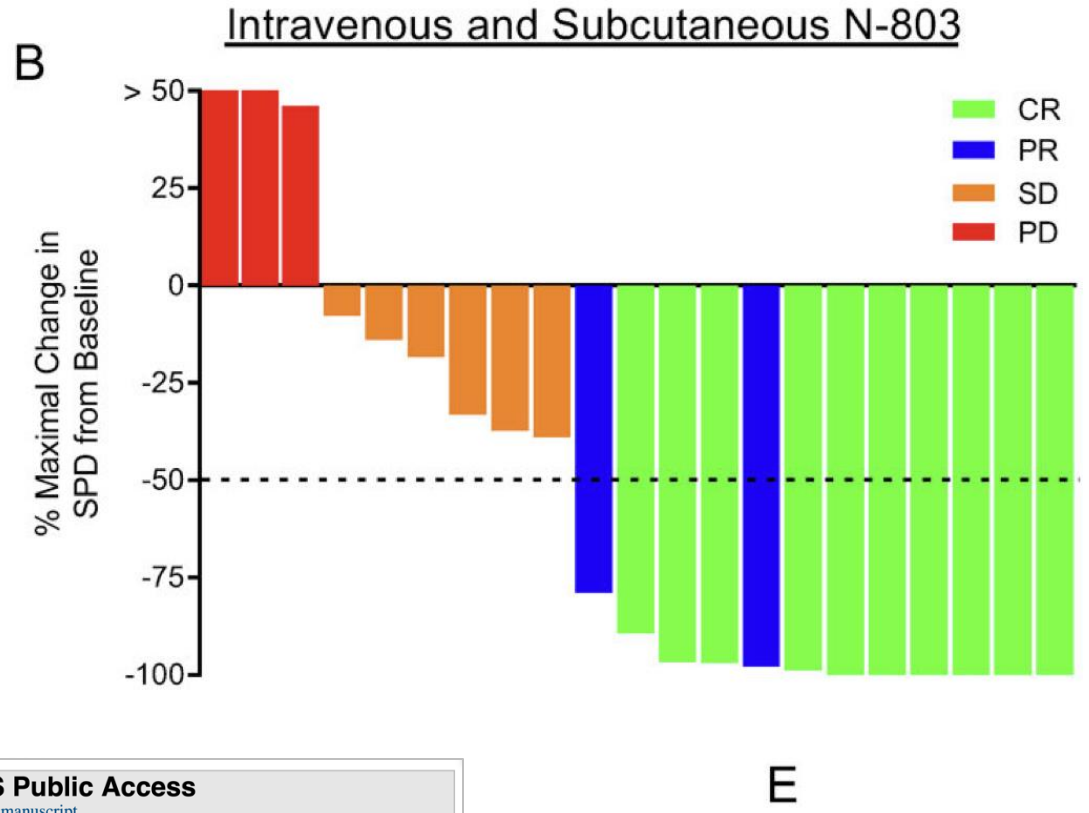
>1.3M
WW Incidence[2]

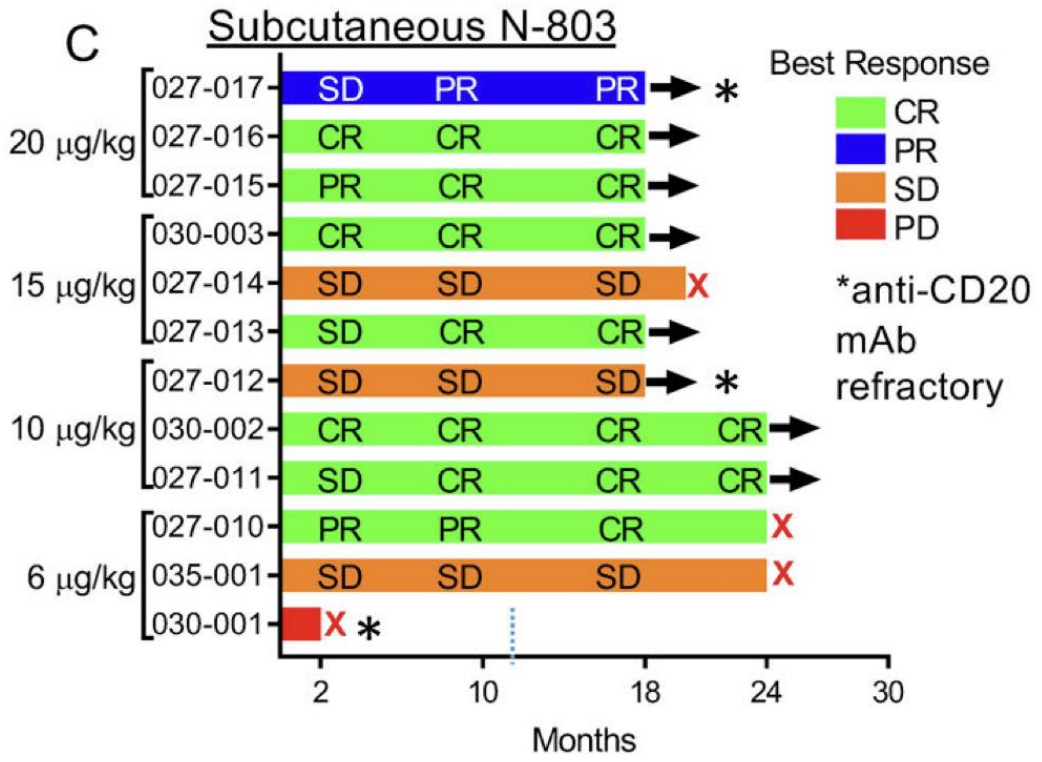
Phase 1

ANKTIVA + Rituximab

1. BMJ 2010;340:c3041; 2. Based on internal analysis using data from multiple sources, including the WHO International Agency for Research on Cancer, Cancer Tomorrow Data Visualization. Estimated annual incidence for 2020 (international) and 2024 (US).

7 out of 7 (100%) Complete Remission with ANKTIVA + Rituximab in CD20 Sensitive Subjects





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Phase 1 trial of N-803, an IL-15 receptor agonist, with rituximab in patients with indolent non-Hodgkin lymphoma

Jennifer A. Foltz[1], Brian T. Hess[2], Veronika Bachanova[3], Nancy L. Bartlett[1], Melissa M. Berrien-Elliott[1], Ethan McClain[1], Michelle Becker-Hapak[1], Mark Foster[1], Timothy Schappe[1], Brad Kahl[1], Neha Mehta-Shah[1], Amanda F. Cashen[1], Nancy D. Marin[1], Kristen McDaniels[1], Chaz Moreno[1], Matthew Mosior[1], Feng Gao[1], Obi L. Griffith[1], Malachi Griffith[1], Julia A. Wagner[1], Narendranath Epperla[4], Amy D. Rock[5], John Lee[5], Allegra A. Petti[1], Patrick Soon-Shiong[5], Todd A. Fehniger[1]

In the anti-CD20 mAb sensitive, 7 out of 7 (100%) subjects had a complete remission (CR)

Foltz JA, Fehniger TA. Phase I Trial of N-803, an IL15 Receptor Agonist, with Rituximab in Patients with Indolent Non-Hodgkin Lymphoma. Clin Cancer Res. 2021 Jun 15;27(12):3339-3350. doi: 10.1158/1078-0432.CCR-20-4575. Epub 2021 Apr 8. PMID: 33832946; PMCID: PMC8197753.