NASDAQ: LNTH

LANTHEUS

Lantheus Investor Presentation

Building on our Foundation to Power the Future of Radiopharmaceuticals

TD Cowen 45th Annual Health Care Conference

March 4, 2025

FIND. FIGHT. FOLLOW.

Safe Harbor Statements

Cautionary Statement Regarding Forward-Looking Statements

This document contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, that are subject to risks and uncertainties and are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements may be identified by their use of terms such as "advance," "anticipated," "assumes," "believes," "building," "commitment," "continue," "could," "deliver," "drive," "expand/expansion," "expected," "growth," "guidance," "increasing," "intend", "launching," "long-term," "may," "milestone," "opportunity," "pipeline," "plan," "position," "potential," "predict," "should," "subject to," "sustained/sustainable," "target," "will," and other similar terms. Such forward-looking statements include our guidance for the fiscal year 2025, our plans to expand our portfolio of late-stage assets and high potential early-stage candidates, our potential acquisitions of Life Molecular Imaging Ltd., ("Life Molecular") and Evergreen Theragnostics Inc. ("Evergreen"), and our expectations relating to adding a commercial team in the Alzheimer's space and a CDMO business from the Life Molecular acquisition, and are based upon current plans, estimates and expectations that are subject to risks and uncertainties that could cause actual results to materially differ from those described in the forward-looking statements. The inclusion of forward-looking statements should not be regarded as a representation that such plans, estimates and expectations will be achieved. Readers are cautioned not to place undue reliance on the forward-looking statements contained herein, which speak only as of the date hereof. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by law. Risks and uncertainties that could cause our actual results to materially differ from those described in the forward-looking statements include: (i) continued market expansion and penetration for our established commercial products, particularly PYLARIFY and DEFINITY, in a competitive environment, and our ability to clinically and commercially differentiate our products; (ii) our ability to have third parties manufacture our products and our ability to manufacture DEFINITY in our in-house manufacturing facility, in the amounts and at the times needed; (iii) availability of raw materials, key components, and equipment, either used in the production of our products and product candidates, or in the use by HCPs of our products and product candidates, including, but not limited to PET scanners used for PYLARIFY, MK-6240 and NAV-4694; (iv) our ability to satisfy our obligations under our existing clinical development partnerships using MK-6240 or NAV-4694 as a research tool and under the license agreements through which we have rights to MK-6240 and NAV-4694, and to further develop and commercialize MK-6240 and NAV-4694 as approved products, including the timing for any potential regulatory submissions for these investigational assets; (v) our ability to successfully secure necessary shareholder and regulatory approvals relating to potential acquisitions, including of Life Molecular and Evergreen, the time and expense involved in seeking to secure those approvals, potential disruption to our business operations or those of the companies we plan to acquire while the acquisitions are pending or as a result of regulatory requirements related to the acquisitions; potential disruption to operations and productivity during the integration process after necessary approvals are secured and the potential that we are unable to integrate and realize the anticipated benefits that each acquisition is predicted to bring; (vi) our strategies, future prospects, and our projected growth, including revenue related to our collaboration agreements with POINT Biopharma Global Inc., including our ability to obtain U.S. Food and Drug Administration ("FDA") approval for PNT2002 and PNT2003 and to be successful in the patent litigation associated with PNT2003; (vii) the cost, efforts and timing for clinical development, regulatory approval, adequate coding, coverage and payment and successful commercialization of our product candidates and new clinical applications and territories for our products, in each case, that we or our strategic partners may undertake; (viii) our ability to identify opportunities to collaborate with strategic partners and to acquire or in-license additional diagnostic and therapeutic product opportunities in oncology, neurology and other strategic areas and continue to grow and advance our pipeline of products.; and (ix) the risk and uncertainties discussed in our filings with the Securities and Exchange Commission (including those described in the Risk Factors section in our Annual Reports on Form 10-K and our Quarterly Reports on Form 10-Q).

All trademarks, logos and service marks used in this presentation are the property of their respective owners.

Non-GAAP Financial Measures

The Company uses non-GAAP financial measures, such as adjusted net income and its line components; adjusted net income per share - fully diluted; adjusted operating income and free cash flow. The Company's management believes that the presentation of these measures provides useful information to investors. These measures may assist investors in evaluating the Company's operations, period over period. However, these measures may exclude items that may be highly variable, difficult to predict and of a size that could have a substantial impact on the Company's reported results of operations for a particular period. Management uses these and other non-GAAP measures internally for evaluation of the performance of the business, including the allocation of resources and the evaluation of results relative to employee performance compensation targets. Investors should consider these non-GAAP measures only as a supplement to, not as a substitute for or as superior to, measures of financial performance prepared in accordance with GAAP.

LANTHEUS™

Lantheus is the **leading radiopharmaceutical-focused company** and is committed to enabling clinicians to **Find, Fight and Follow** disease to deliver better patient outcomes.

FIND. FIGHT. FOLLOW.®

Lantheus: Setting the Stage for Sustained, Double-Digit Growth

Key Drivers

PYLARIFY® Piflufolastat F 18 Injection

DEFINITY VIAL FOR (Perflutren Lipid Microsphere) INJECTABLE SUSPENSION

NeuraCeq® * florbetaben F18 injection

1

2 **2026-2027 Anticipated Product Launches**

MK-6240	F18 tau-targeted PET radiodiagnostic
NAV-4694	F18 β amyloid-targeted PET radiodiagnostic
OCTEVY*	Ga68 GEP-NET PET radiodiagnostic
PNT2003	SSTR+ GEP-NET radioequivalent

3 **Pipeline**

LNTH-1363S	Cu64 FAP-targeted radiodiagnostic
LNTH-2401	RM2, GRPR-targeted radiodiagnostic
LNTH-2402	RM2, GRPR-targeted radiotherapeutic
LNTH-2403	LRRC15-targeted radiotherapeutic
LNTH-2404	TROP2-targeted radiotherapeutic

*Acquisitions subject to customary closing conditions and anticipated to close 2H 2025
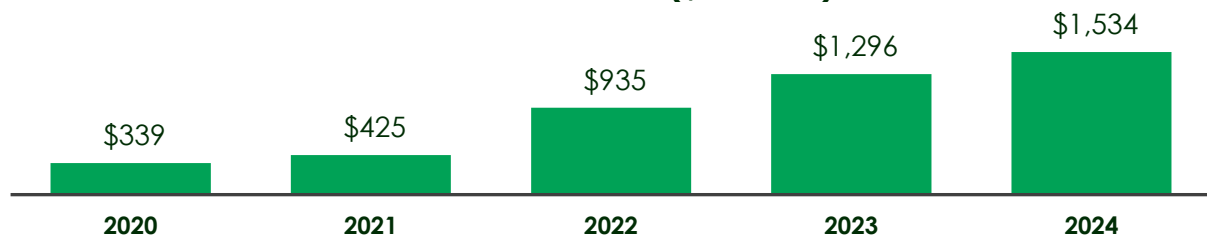
Key Recent Strategic Announcements*

Life Molecular Imaging HEALTH CARE

- Adds Neuraceq, an approved PET radiodiagnostic, and commercial franchise
- Enhances R&D and clinical development capabilities
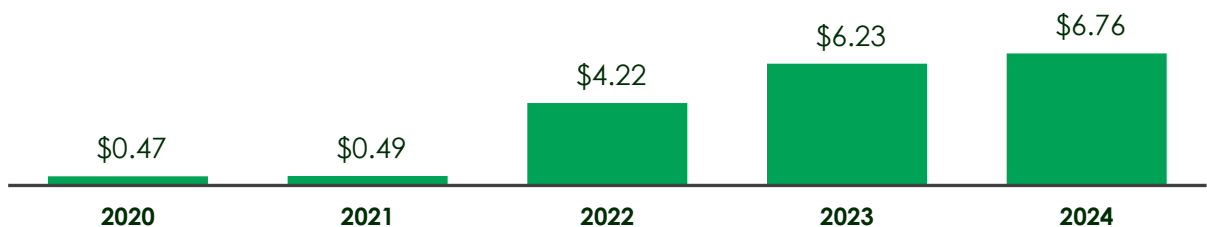
EVERGREEN® THERAGNOSTICS

- Adds OCTEVY, a registrational-stage PET radiodiagnostic, complementary to PNT2003
- Establishes clinical and commercial radiopharmaceutical manufacturing
- Enhances early R&D capabilities

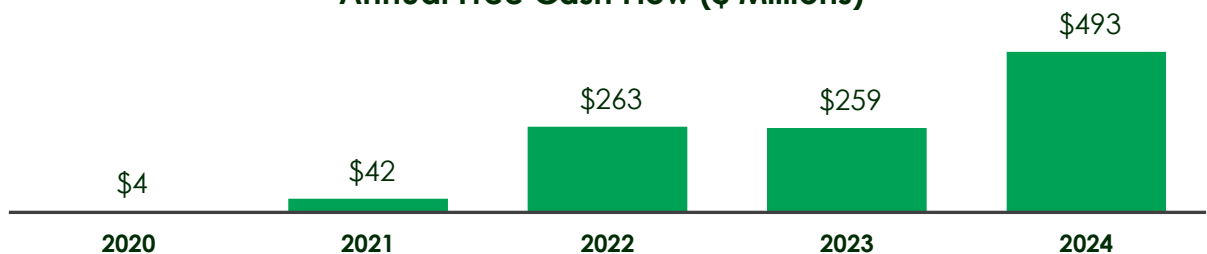**LANTHEUS™**

Continued Strong Financial Performance[1]

Annual Revenue ($ Millions)

2020	2021	2022	2023	2024
$339	$425	$935	$1,296	$1,534

Annual Adj. EPS

2020	2021	2022	2023	2024
$0.47	$0.49	$4.22	$6.23	$6.76

Annual Free Cash Flow ($ Millions)

2020	2021	2022	2023	2024
$4	$42	$263	$259	$493

The Company guidance for the full year 2025 is as follows[2]:

FY 2025	Revenue	$1.545B – $1.610B
	Adjusted Fully Diluted EPS[3]	$7.00 – $7.20

Free Cash Flow to continue to expand throughout 2025 with an anticipated amount of $550M - $600M
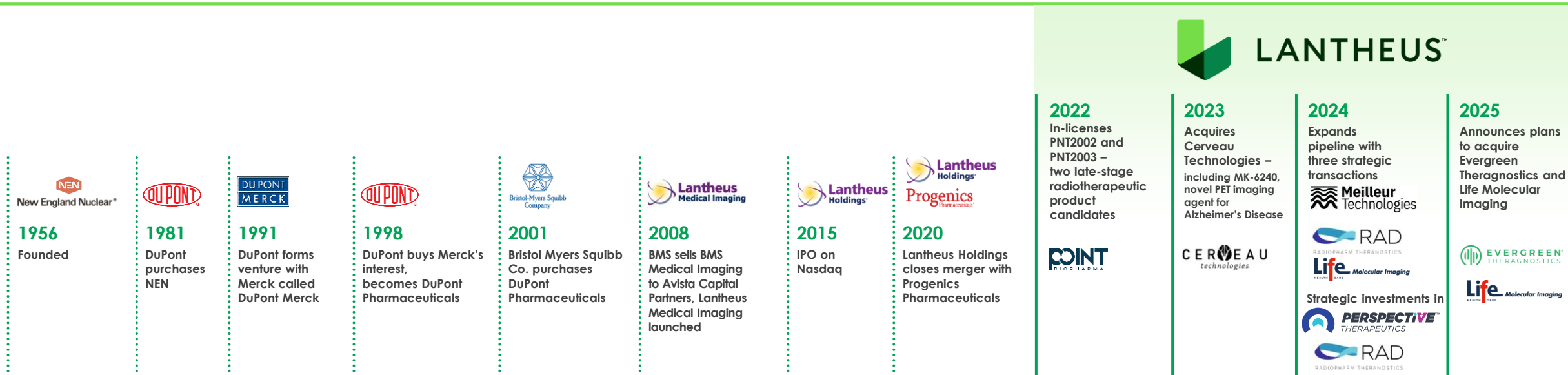
As of December 31, 2024

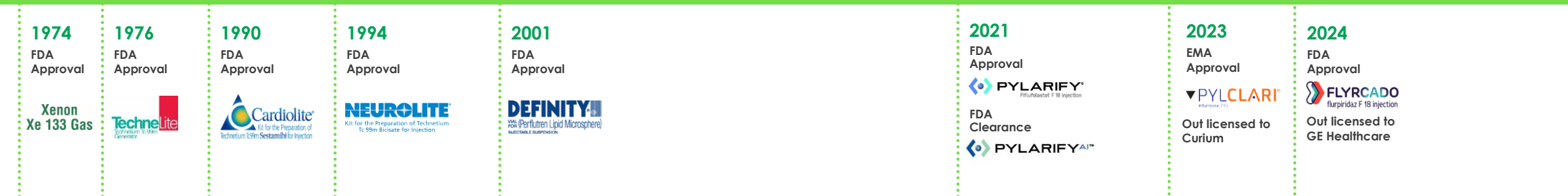**$912.8M** Cash on Hand[4]

$750M Available Revolving Credit

LANTHEUS

Lantheus' Journey has Driven Growth and Success **Over 65 Years**

CORPORATE GROWTH

1956 — New England Nuclear — Founded

1981 — DuPont — DuPont purchases NEN

1991 — DuPont Merck — DuPont forms venture with Merck called DuPont Merck

1998 — DuPont — DuPont buys Merck's interest, becomes DuPont Pharmaceuticals

2001 — Bristol-Myers Squibb Company — Bristol Myers Squibb Co. purchases DuPont Pharmaceuticals

2008 — Lantheus Medical Imaging — BMS sells BMS Medical Imaging to Avista Capital Partners, Lantheus Medical Imaging launched

2015 — Lantheus Holdings — IPO on Nasdaq

2020 — Lantheus Holdings / Progenics Pharmaceuticals — Lantheus Holdings closes merger with Progenics Pharmaceuticals

2022 — In-licenses PNT2002 and PNT2003 – two late-stage radiotherapeutic product candidates — POINT Biopharma

2023 — Acquires Cerveau Technologies – including MK-6240, novel PET imaging agent for Alzheimer's Disease — CERVEAU technologies

2024 — Expands pipeline with three strategic transactions — Meilleur Technologies, RAD Radiopharm Theranostics, Life Molecular Imaging — Strategic investments in PERSPECTIVE THERAPEUTICS, RAD Radiopharm Theranostics

2025 — Announces plans to acquire Evergreen Theragnostics and Life Molecular Imaging — EVERGREEN THERAGNOSTICS, Life Molecular Imaging

FDA APPROVAL & CLEARANCE

1974 — FDA Approval — Xenon Xe 133 Gas

1976 — FDA Approval — TechneLite Technetium Tc 99m Generator

1990 — FDA Approval — Cardiolite Kit for the Preparation of Technetium Tc99m Sestamibi for Injection

1994 — FDA Approval — NEUROLITE Kit for the Preparation of Technetium Tc 99m Bicisate for Injection

2001 — FDA Approval — DEFINITY VIAL FOR (Perflutren Lipid Microsphere) INJECTABLE SUSPENSION

2021 — FDA Approval — PYLARIFY Piflufolastat F 18 Injection — FDA Clearance — PYLARIFY AI

2023 — EMA Approval — PYLCLARI Piflufolastat (18F) — Out licensed to Curium

2024 — FDA Approval — FLYRCADO flurpiridaz F 18 injection — Out licensed to GE Healthcare

Lantheus' Journey has Driven Growth and Success **Over 65 Years**

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2020
Lantheus Holdings closes merger with Progenics Pharmaceuticals

Lantheus Holdings

Progenics Pharmaceuticals

2022
In-licenses PNT2002 and PNT2003 – two late-stage radiotherapeutic product candidates

POINT BIOPHARMA

2023
Acquires Cerveau Technologies – including MK-6240, novel PET imaging agent for Alzheimer's Disease

CERVEAU technologies

2024
Acquires Meilleur Technologies – including NAV-4694

Meilleur Technologies

Acquires LRRC15 and TROP2 from

RAD RADIOPHARM THERANOSTICS

Strategic investments in

PERSPECTIVE THERAPEUTICS

RAD RADIOPHARM THERANOSTICS

2025
Announces plans to acquire Evergreen Theragnostics and Life Molecular Imaging

EVERGREEN THERAGNOSTICS

Life Molecular Imaging

CORPORATE GROWTH

FDA APPROVAL & CLEARANCE

2021
FDA Approval

PYLARIFY Piflufolastat F 18 Injection

FDA Clearance

PYLARIFY AI

2023
EMA Approval

PYLCLARI

Out licensed to Curium

2024
FDA Approval

FLYRCADO flurpiridaz F 18 injection

Out licensed to GE Healthcare

LANTHEUS

Leading Commercial Portfolio

PYLARIFY®
Piflufolastat F 18 Injection

4Q 2024

$266.0M
4Q 2024 Net Sales

+15.7% Growth
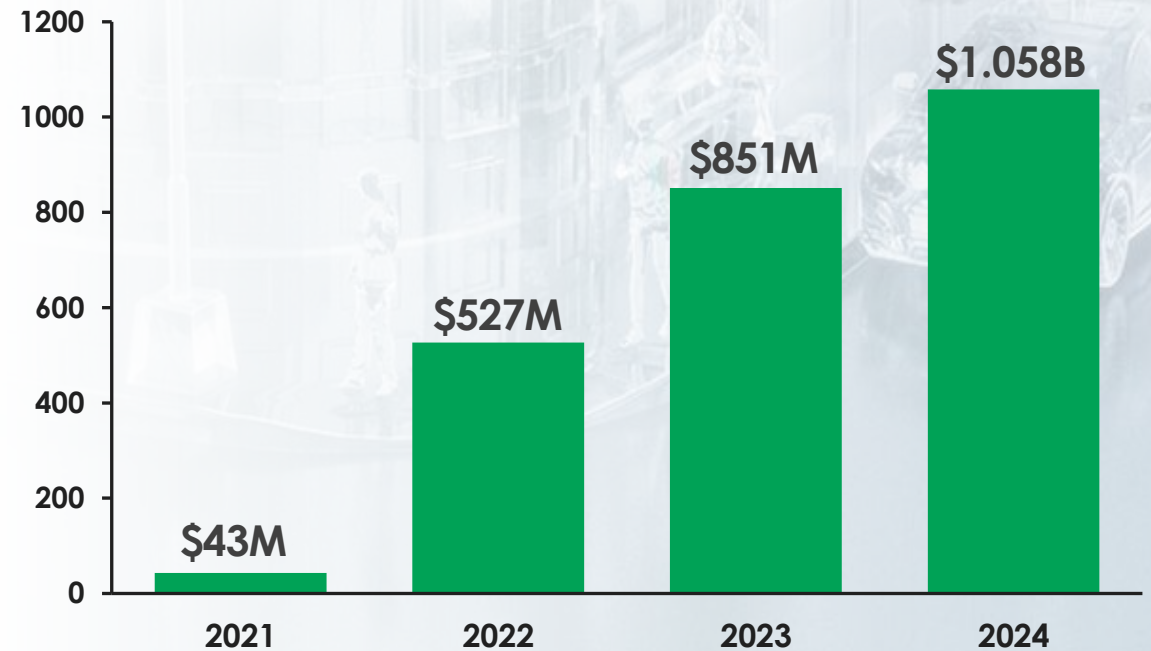4Q 2024 Year-over-Year

FY 2024

$1.058B
FY 2024 Net Sales

+24.3% Growth
FY 2024 Year-over-Year

2025 Revenue Expectation
Year-over-Year Low to Mid-Single Digit Growth

PYLARIFY Sales Year-over-Year

Year	Sales
2021	$43M
2022	$527M
2023	$851M
2024	$1.058B

First Radiodiagnostic to Achieve BLOCKBUSTER STATUS

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PYLARIFY Offers Clear Clinical Value to Patients and Healthcare Providers

Change in Intended Patient Management[1-3]

In PYLARIFY's Phase 3 pivotal study, nearly two out of three patients in the study with BCR who received PYLARIFY® after negative or uninformative conventional imaging had a change in intended prostate cancer treatment

Note: It is not known if changes in intended patient management lead to improved outcomes for patients

99%

PYLARIFY's change in intended patient management is based on 99% of enrolled patients in our CONDOR study
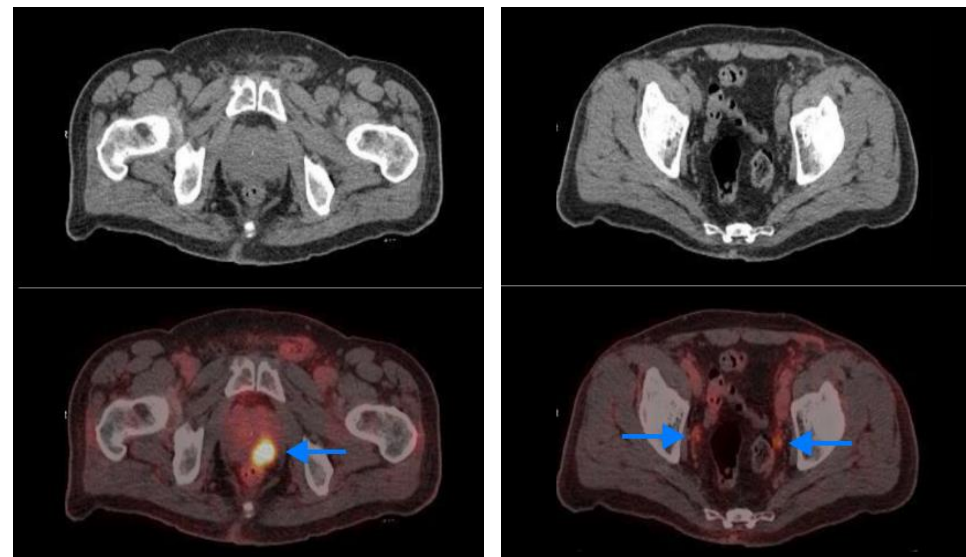
Courtesy (with permission) from Gary Ulaner, MD, PhD, FACNM, Hoag Family Cancer Institute

Study Design
CONDOR was a multicenter, phase 3 trial of 208 patients with suspected recurrent or metastatic prostate cancer with negative or equivocal results using standard imaging. The primary endpoint was CLR; the key secondary endpoint was the percentage of patients with a change in intended PC treatment plan. CLR is a measure of positive predictive value enhanced with precise anatomic location of the site of disease. CLR is based on anatomic lesion matching, or co-localization, of lesions identified by PYLARIFY® (piflufolastat F 18) injection and lesions identified by the standard of truth.[3]*

*Change in intended prostate cancer treatment plan was a secondary endpoint in CONDOR. Future studies ll be necessary to demonstrate whether PYLARIFY® PET/CT-directed changed in intended patient management lead to improved outcomes for patients with prostate cancer.[1]
1. Data on file, Lantheus.
2. PYLARIFY® [package insert]. North Billerica, MA: Progenics Pharmaceuticals, Inc., a Lantheus company.
3. Morris MJ, Rowe SP, Gorin MA, et al. Diagnostic performance of 18F-DCFPyL-PET/CT in men with biochemically recurrent prostate cancer: results from the CONDOR phase III, multicenter study. *Clin Cancer Res*. 2021 July 01;27(13):3674-3682. doi:10.1158/1078-0432.CCR-20-4573

Patient Treatment Logistics Require Real-Time Delivery of Doses

PYLARIFY Synthesis, Distribution and Utilization
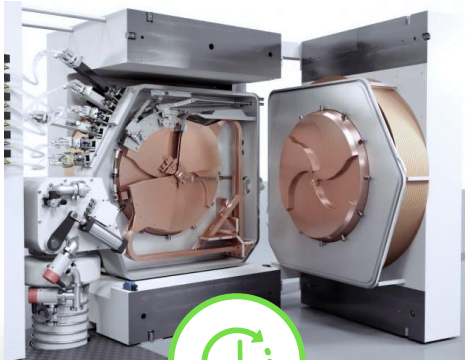
F18 is produced on a cyclotron

PYLARIFY is manufactured and formulated in a synthesis box

Finished as a bulk vial

Robust quality control and testing

Drawn into patient-ready doses

PYLARIFY patient-ready doses "out the door"

110-minute half-life advantage

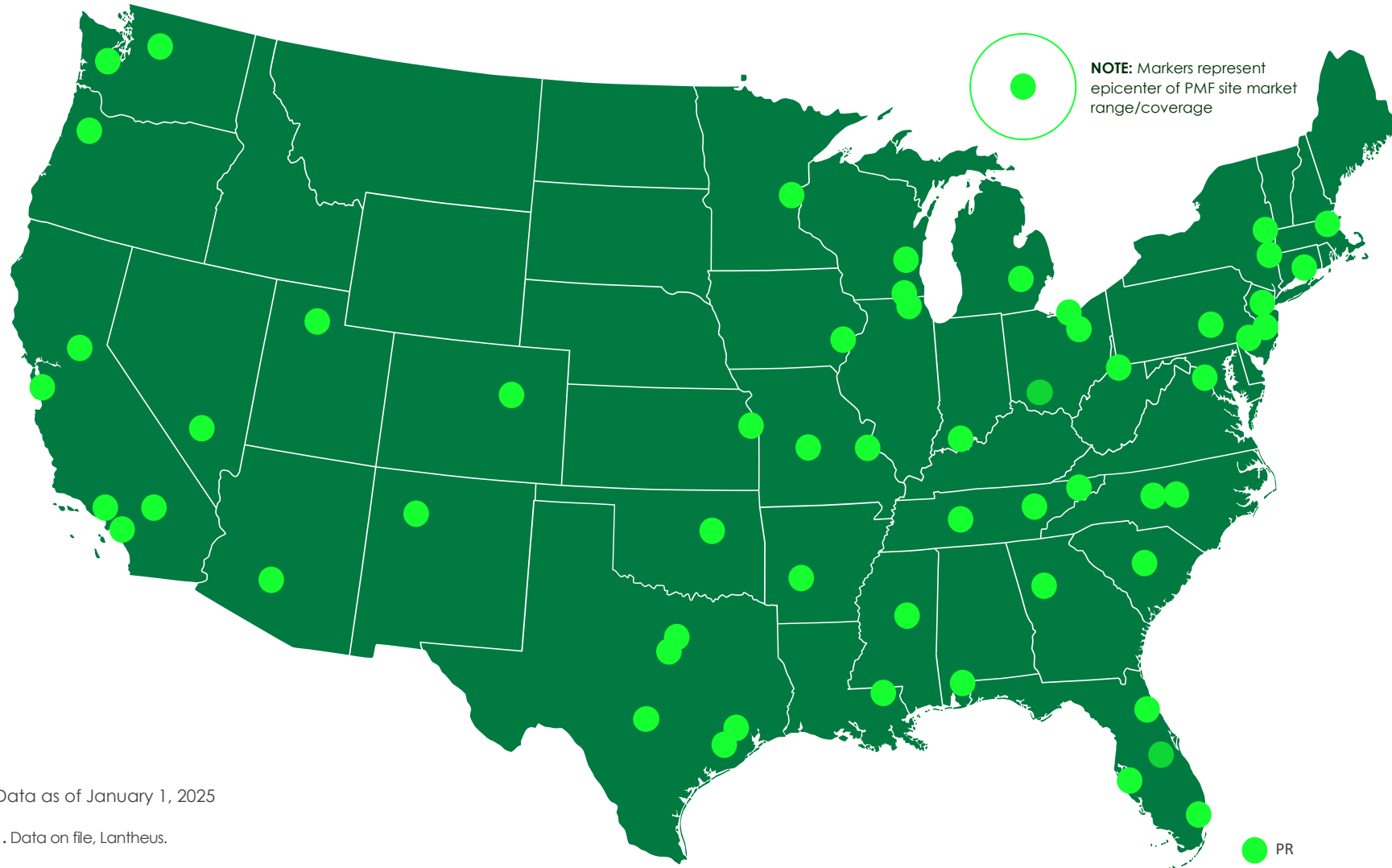Easily transported any time of day within a ~3-hour radius

Patient is injected and scanned

PYLARIFY Batch Manufacturing Process Can Produce Ample Supply to Meet the Needs of this Sizeable Patient Population

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PYLARIFY is widely available through a diverse, multi-partner F18 distributor supply network, ensuring convenient and reliable supply

PMF Capacity, Coverage and Dose Availability Varies from Site to Site

NOTE: Markers represent epicenter of PMF site market range/coverage

PYLARIFY®
Piflufolastat F 18 Injection

Extensive manufacturing network* with multiple radiopharmacies serving imaging centers in 48 states, District of Columbia, and Puerto Rico[1]

Coverage and reliability within and between radiopharmacies, with an increasing number of cyclotrons to expand capacity and extend calibration windows
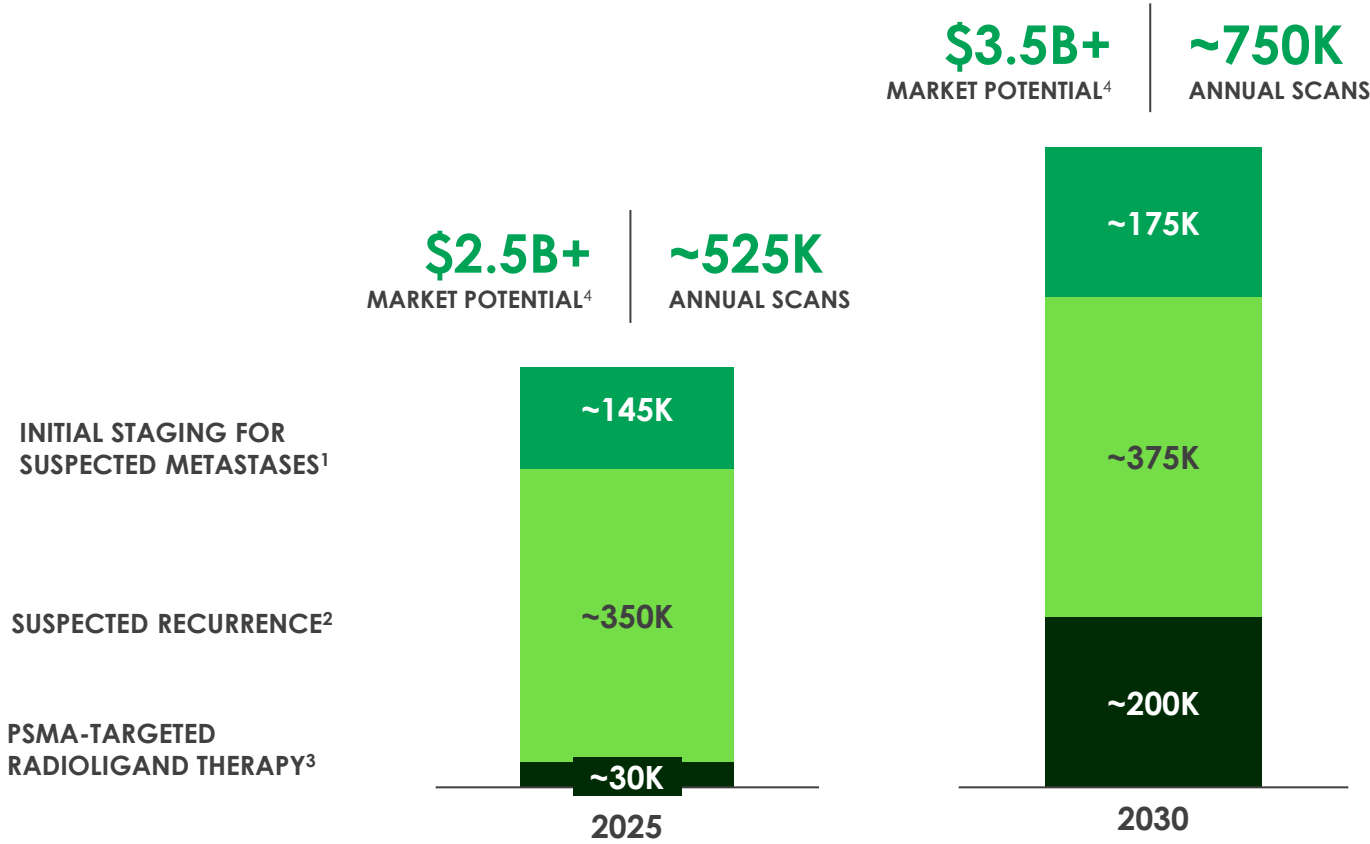
Commitment to continued expansion and excellent customer service with enhancements to the online ordering platform offering added flexibility

PR

*Data as of January 1, 2025

1. Data on file, Lantheus.

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U.S. PSMA PET Imaging Market Potential of $3.5B+ by 2030

Annual Market and Scan Potential

2030
$3.5B+
MARKET POTENTIAL[4]

~750K
ANNUAL SCANS

- ~175K
- ~375K
- ~200K

2025
$2.5B+
MARKET POTENTIAL[4]

~525K
ANNUAL SCANS

- ~145K
- ~350K
- ~30K

INITIAL STAGING FOR SUSPECTED METASTASES[1]

SUSPECTED RECURRENCE[2]

PSMA-TARGETED RADIOLIGAND THERAPY[3]

Factors Influencing Market Expansion:

Expansion of Radiotherapeutics into earlier lines of treatment (i.e., from 3L mCRPC to include 2L, 1L and mHSPC populations)

Increasing clinical utility of PSMA PET imaging in BCR population (increased number of scans per patient)

Expansion of Initial Staging population to include patients with an Intermediate Favorable risk profile

Overall **increase in epidemiological population,** 2-3% per year

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PYLARIFY MIRROR Study: Phase 4 Study in Favorable Intermediate Risk (FIR) Prostate Cancer
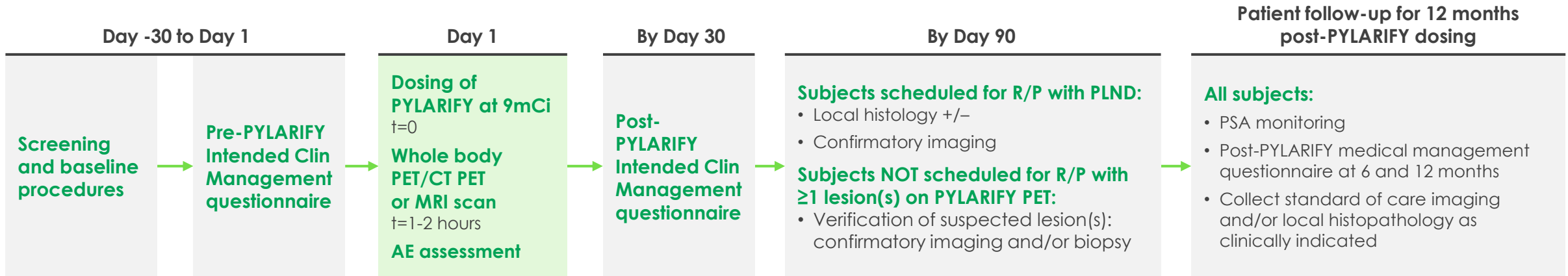
Study Objective: Determine whether PYLARIFY PSMA PET imaging can detect the presence or absence of additional prostate cancer lesions in patients with FIR prostate cancer, as well as how it may change the patient's intended management (NCT06074510)

Primary Endpoint

Detection rate of intraprostatic ISUP grade ≥3 lesion(s) as confirmed by pathology; or the presence of extra-prostatic extension, seminal vesicle invasion, regional lymph node involvement, distant metastases as assessed by central readers

Secondary Endpoints

- Change in intended clinical management
- True detection rate
- Correct localization rate
- Sensitivity
- Specificity
- Positive Predictive Value
- Negative Predictive Value
- Safety

Day -30 to Day 1		Day 1	By Day 30	By Day 90	Patient follow-up for 12 months post-PYLARIFY dosing
Screening and baseline procedures	**Pre-PYLARIFY Intended Clin Management questionnaire**	**Dosing of PYLARIFY at 9mCi** t=0 **Whole body PET/CT PET or MRI scan** t=1-2 hours **AE assessment**	**Post-PYLARIFY Intended Clin Management questionnaire**	**Subjects scheduled for R/P with PLND:** • Local histology +/– • Confirmatory imaging **Subjects NOT scheduled for R/P with ≥1 lesion(s) on PYLARIFY PET:** • Verification of suspected lesion(s): confirmatory imaging and/or biopsy	**All subjects:** • PSA monitoring • Post-PYLARIFY medical management questionnaire at 6 and 12 months • Collect standard of care imaging and/or local histopathology as clinically indicated

Phase 4
n = 274

Population: Newly diagnosed Favorable Intermediate Risk Prostate Cancer confirmed by standard of care

See appendix for definition of abbreviated terms.

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Early detection of recurrent prostate cancer using ^{18}F-DCFPyL PET/CT in patients with minimal PSA levels

Ida Sonni[1,2], Nicholas G. Nickols[3,4], Derace Schaffer[5], Karl Sjöstrand[5], Louis Montagut[5], Aseem Anand[5], Gholam R. Berenji[1,2], Matthew B. Rettig[6,7,8]

1. Department of Radiological Sciences, University of California, Los Angeles, CA, USA; 2. Department of Nuclear Medicine, VA Greater Los Angeles Healthcare System, Los Angeles, CA, USA; 3. Department of Radiation Oncology, University of California-Los Angeles, Los Angeles, CA, USA; 4. Department of Radiation Oncology, VA Greater Los Angeles Healthcare System, Los Angeles, CA, USA; 5. Lantheus, Bedford, MA, USA; 6. Department of Hematology-Oncology, VA Greater Los Angeles Healthcare System, Los Angeles, CA, USA; 7. Department of Medicine, University of California-Los Angeles, Los Angeles, CA, USA; 7. Department of Urology, University of California-Los Angeles, Los Angeles, CA, USA
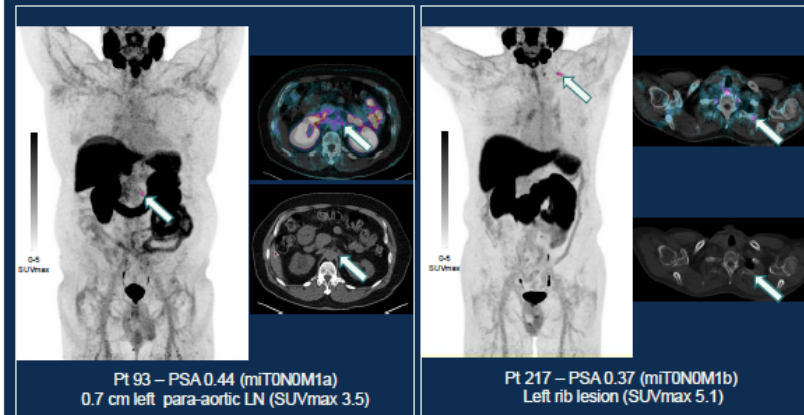
Background / Aim

- PSMA PET imaging has shown to be highly sensitive and specific for detecting prostate cancer (PCa) in the setting of **biochemical recurrence (BCR)**.
- Following definitive treatment, **conventional imaging** (e.g. CT and bone scans) have limited ability to localize recurrent disease in patients with minimally detectable serum PSA levels, potentially delaying diagnosis and initiation of curative treatments.
- There is growing interest in using **PSMA PET/CT** for **detecting and localizing BCR** in patients with **low PSA levels** (<0.5 ng/ml).
- There is limited literature on the detection rates of different PSMA PET radiotracers in this setting.

➤ **THE AIM** of this study was to investigate the *detection rates of 18F-DCFPyL in patients with BCR from PCa showing minimally detectable serum PSA levels.*
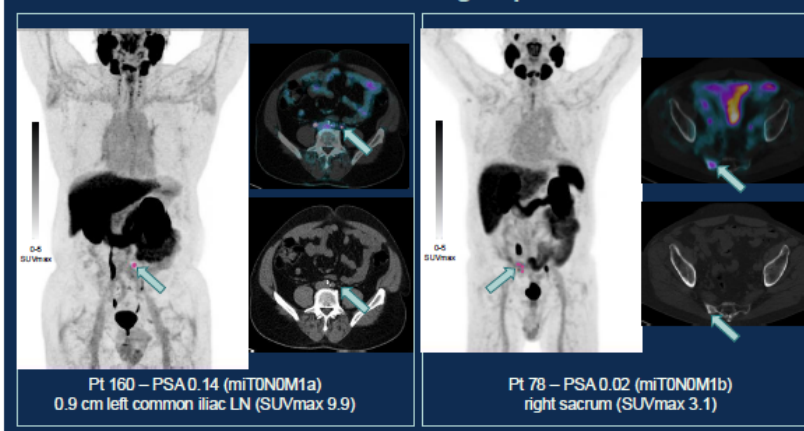
Methods

- This is a pooled retrospective analysis including patients from investigator-initiated trials at West Los Angeles Veterans Affairs and the phase III CONDOR clinical trial with serum PSA levels ≤ 0.5 ng/ml.
- Patients who underwent *18F-DCFPyL PET/CT* for rising PSA levels after definitive treatment (BCR) were included in this analysis and categorized in two groups, based on the serum PSA levels: *low PSA* (0.2≤0.5 ng/ml) and *ultra-low PSA* (0<0.2 ng/ml).
- 18F-DCFPyL PET/CT reads were assisted by automated deep learning enabled *Prostate Cancer Molecular Imaging Standardized Evaluation* (**aPROMISE**) platform, and results were verified by an experienced and independent nuclear medicine physician.
- **Detection rate** was calculated and defined as the number of patients with positive PSMA lesions relative to total number of patients.

Low PSA group

Pt 93 – PSA 0.44 (miT0N0M1a)
0.7 cm left para-aortic LN (SUVmax 3.5)

Pt 217 – PSA 0.37 (miT0N0M1b)
Left rib lesion (SUVmax 5.1)

Ultra-low PSA group

Pt 160 – PSA 0.14 (miT0N0M1a)
0.9 cm left common iliac LN (SUVmax 9.9)

Pt 78 – PSA 0.02 (miT0N0M1b)
right sacrum (SUVmax 3.1)

Results

A total of 129 patients were identified and included in the analysis.
- The **low PSA group** (0.2 ≤ 0.5 ng/ml) included 93 patients.
- The **ultra-low PSA group** (0 < 0.2 ng/ml) included 36 patients.

Detection rate for the low-PSA group was 51% and for the ultra-low PSA group and was 36%.

	Ultra-low PSA: 0 < 0.2 ng/ml (n=36)	Low PSA: 0.2≤0.5 ng/ml (n=93)
Total Detection Rate	**36% (n=13/36)**	**51% (n=47/93)**
Prostate Bed	8% (3)	4% (4)
Lymph Node Only	14% (5)	31% (29)
Lymph Node and Bone	33% (12)	42% (39)
Bone Only	22% (8)	15% (14)
Visceral (Lung or Liver)	3% (1)	11% (10)
Total SUVmean	3.8	4.2
Total SUVmax	10.9	12.4
Total disease volume (mean)	4.9 ml	1.9 ml

Conclusions

- **18F-DCFPyL PET/CT** demonstrates a **significant detection rate** for **recurrent prostate cancer** in patients with **minimally detectable PSA levels.**
- Our findings highlight the potential of 18F-DCFPyL PET/CT in the **early identification of metastatic disease**.
- Current thresholds for initiating PSMA PET/CT imaging in patients with BCR may need reconsideration.
- Further studies are necessary to refine guidelines and assess the cost-effectiveness of incorporating PSMA imaging at very low PSA levels.

Presented at ASCO GU 2025 in San Francisco, February 2025.

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DEFINITY®
VIAL FOR (Perflutren Lipid Microsphere)
INJECTABLE SUSPENSION

#1 Utilized Ultrasound Enhancing Agent[1]

4Q 2024

$86.2M
4Q 2024 Net Sales

+17.9% Growth
4Q 2024 Year-over-Year

FY 2024

$317.8M
FY 2024 Net Sales

+13.6% Growth
FY 2024 Year-over-Year

**Used in echocardiography exams for >3.5M patients in 2024[2]**

1. DRG Real World Data (RWD) report; 2. Internal analyses and data on file.

As the #1 utilized UEA, DEFINITY is the clear standard for patients who present with a suboptimal echocardiogram

#1 UTILIZED UEA
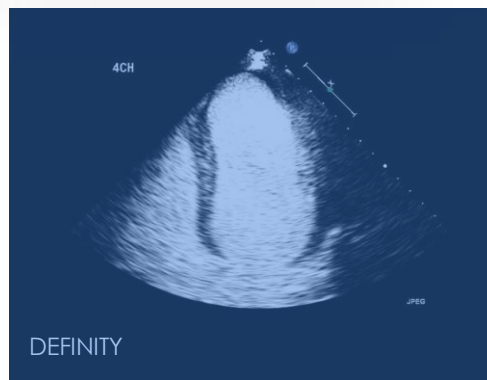**20 MILLION+ ECHOS**
20+ YEARS EXPERIENCE

DEFINITY improved cardiac diagnosis and streamlined patient management[1-3]

CONVERTED 90%

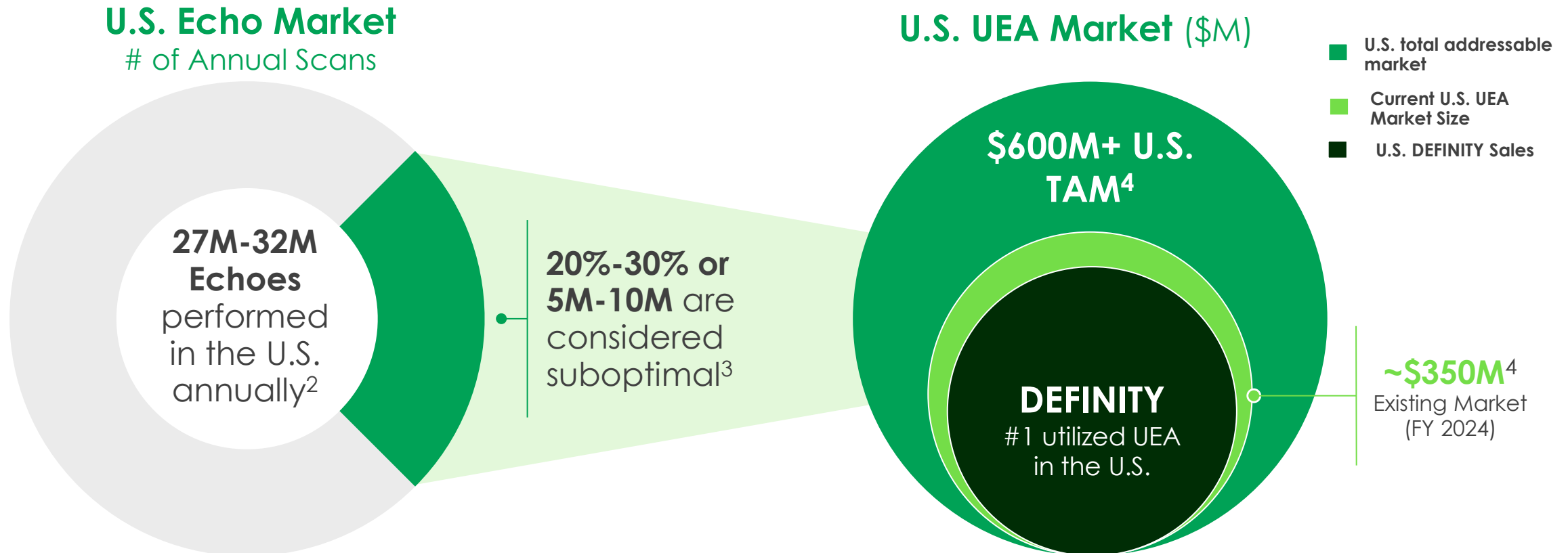of suboptimal echos → to adequate echos[3]
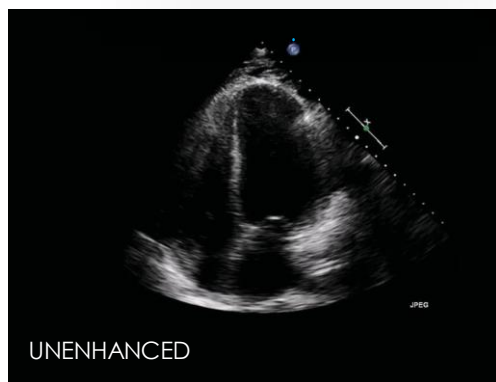
UNENHANCED

DEFINITY

33% of patients avoided additional diagnostic procedures[3,4]

36% of patients experienced a significant change in medical management, procedures, or both[3,4]

>50% of SICU patients avoided additional diagnostic procedures[3,4]

SICU, surgical intensive care unit; UEA, ultrasound enhancing agents.

References: 1. Data on file, Lantheus. **2.** DEFINITY. Prescribing Information. Lantheus. **3.** Kurt M, Shaikh KA, Peterson L, et al. Impact of contrast echocardiography on evaluation of ventricular function and clinical management in a large prospective cohort. *J Am Coll Cardiol.* 2009;53(9):802-810. doi:10.1016/j.jacc.2009.01.005. **4.** Results from a prospective study of the impact of UEAs on cardiac diagnoses in 632 patients with technically difficult echocardiograms.

DEFINITY®
VIAL FOR (Perflutren Lipid Microsphere) INJECTABLE SUSPENSION

LANTHEUS™

U.S. Ultrasound Enhancing Agent TAM is $600M+[1]

Significant Opportunity Remains in the Suboptimal Echo Market

U.S. Echo Market
# of Annual Scans

27M-32M Echoes performed in the U.S. annually[2]

20%-30% or 5M-10M are considered suboptimal[3]

U.S. UEA Market ($M)

- U.S. total addressable market
- Current U.S. UEA Market Size
- U.S. DEFINITY Sales

$600M+ U.S. TAM[4]

DEFINITY #1 utilized UEA in the U.S.

~$350M[4] Existing Market (FY 2024)

1. U.S. market; Internal Lantheus estimate.
2. Source: AMR, Echocardiography Monthly Monitor and Real World Data; Kurt M et al. Journal of the American College of Cardiology, March 2009; Senior R et al., The European Society of Cardiology, 2006. ©2020 Millennium Research Group, Inc. All rights reserved. Reproduction, distribution, transmission or publication is prohibited. Reprinted with permission.
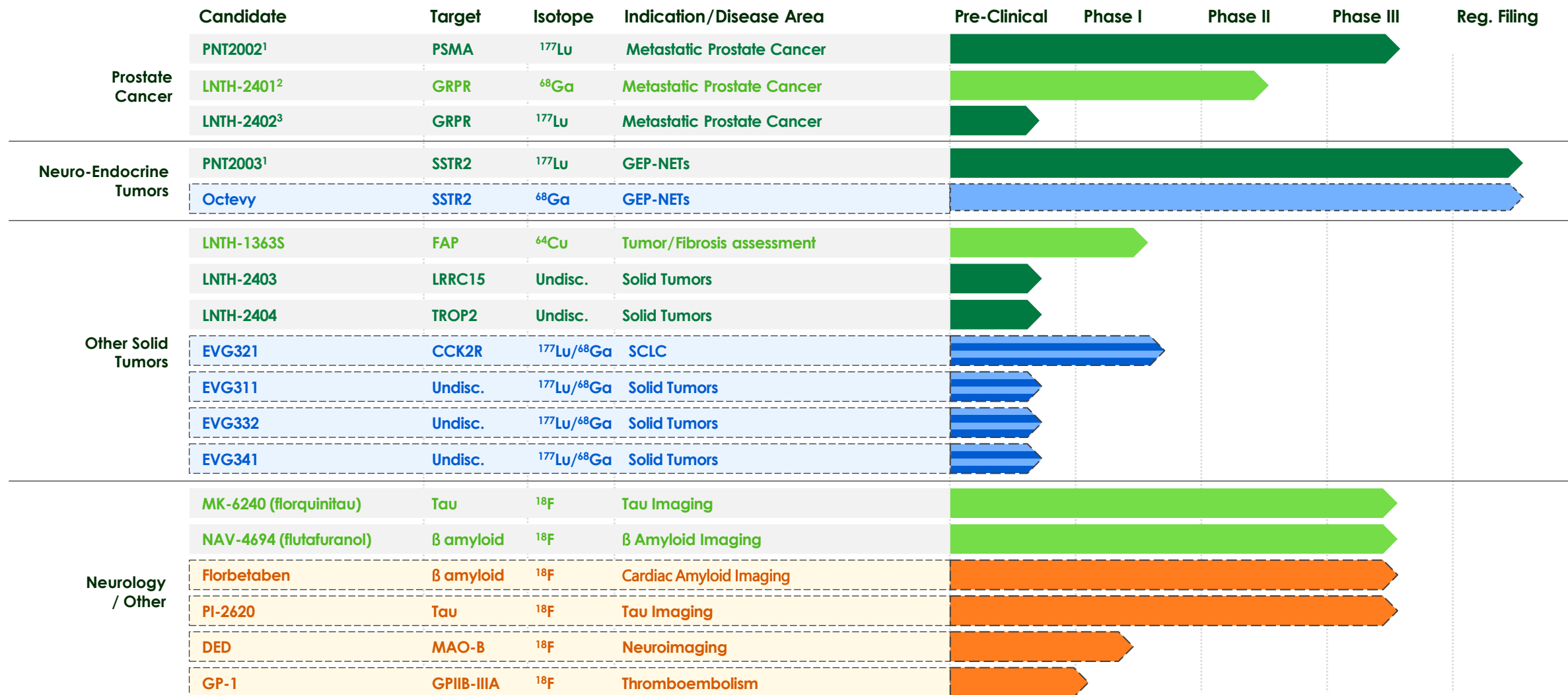3. 20%-30% of echocardiograms result in sub-optimal images. Sources: i. Kurt M et al. Impact of contrast echocardiography on evaluation of ventricular function and clinical management in a large prospective cohort. Journal of the American College of Cardiology, Vol 53, No 9, March 2009, 802-810; ii. Platts DG and Fraser JF. Contrast echocardiography in critical care: echoes of the future? A review of the role of microsphere contrast echocardiography. Critical Care and Resuscitation, Vol 12, No 1, March 2011, 44-55; iii. Senior R et al. Clinical benefits of contrast-enhanced echocardiography during rest and stress examinations. The European Society of Cardiology 6, Suppl. 2, 2005, S6-S13.
4. Internal Lantheus estimate.

LANTHEUS

Advancing Innovative Radiotherapeutic & Radiodiagnostic Pipeline

Innovation that Makes an Impact
*Includes Pipeline Assets of Life Molecular Imaging and Evergreen Theragnostics**

	Candidate	Target	Isotope	Indication/Disease Area	Pre-Clinical	Phase I	Phase II	Phase III	Reg. Filing
Prostate Cancer	PNT2002[1]	PSMA	^{177}Lu	Metastatic Prostate Cancer	████████████████████████				
	LNTH-2401[2]	GRPR	^{68}Ga	Metastatic Prostate Cancer	████████████████				
	LNTH-2402[3]	GRPR	^{177}Lu	Metastatic Prostate Cancer	████				
Neuro-Endocrine Tumors	PNT2003[1]	SSTR2	^{177}Lu	GEP-NETs	████████████████████████				
	Octevy	SSTR2	^{68}Ga	GEP-NETs	████████████████████████				
Other Solid Tumors	LNTH-1363S	FAP	^{64}Cu	Tumor/Fibrosis assessment	████████				
	LNTH-2403	LRRC15	Undisc.	Solid Tumors	███				
	LNTH-2404	TROP2	Undisc.	Solid Tumors	███				
	EVG321	CCK2R	^{177}Lu/^{68}Ga	SCLC	███████				
	EVG311	Undisc.	^{177}Lu/^{68}Ga	Solid Tumors	███				
	EVG332	Undisc.	^{177}Lu/^{68}Ga	Solid Tumors	███				
	EVG341	Undisc.	^{177}Lu/^{68}Ga	Solid Tumors	███				
Neurology / Other	MK-6240 (florquinitau)	Tau	^{18}F	Tau Imaging	████████████████████████				
	NAV-4694 (flutafuranol)	ß amyloid	^{18}F	ß Amyloid Imaging	████████████████████████				
	Florbetaben	ß amyloid	^{18}F	Cardiac Amyloid Imaging	████████████████████████				
	PI-2620	Tau	^{18}F	Tau Imaging	████████████████████████				
	DED	MAO-B	^{18}F	Neuroimaging	████████				
	GP-1	GPIIB-IIIA	^{18}F	Thromboembolism	███████				

See Appendix for definition of abbreviated terms
*Pipeline includes assets from Life Molecular Imaging and Evergreen Theragnostics. These assets are not currently owned or controlled by Lantheus. The acquisitions are subject to the closing of the transactions, both of which are anticipated to close this year.
1. Collaboration with POINT Biopharma Global Inc. 2. Also known as ^{68}Ga-RM2 3. Also known as ^{177}Lu-RM2

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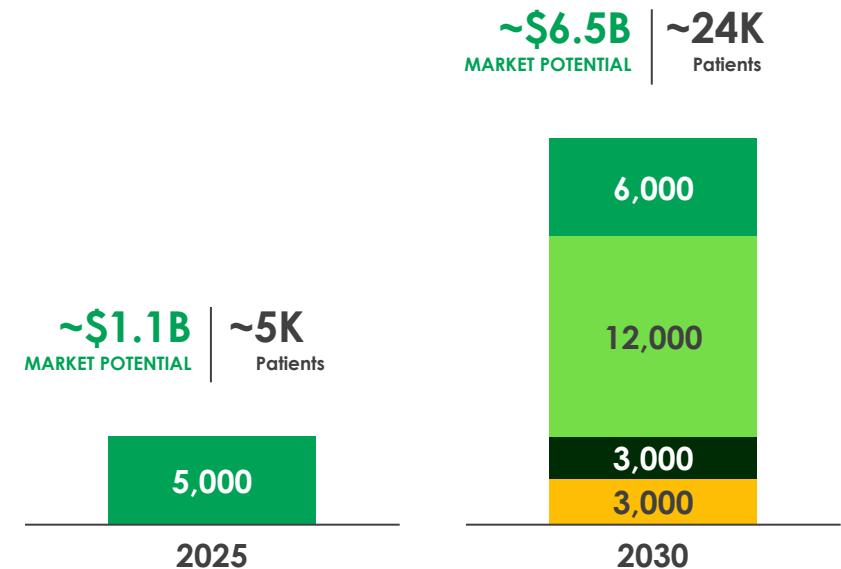# PNT2003: Somatostatin Receptor (SSTR)–Targeted Radiotherapeutic

Potential therapeutic agent for the treatment of **SSTR-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut and hindgut neuroendocrine tumors in adults**

✓ FDA accepted Abbreviated New Drug Application (ANDA) – **first to file[1]**

✓ Anticipated to be a radioequivalent to **LUTATHERA®** (Lutetium Lu 177 Dotatate)
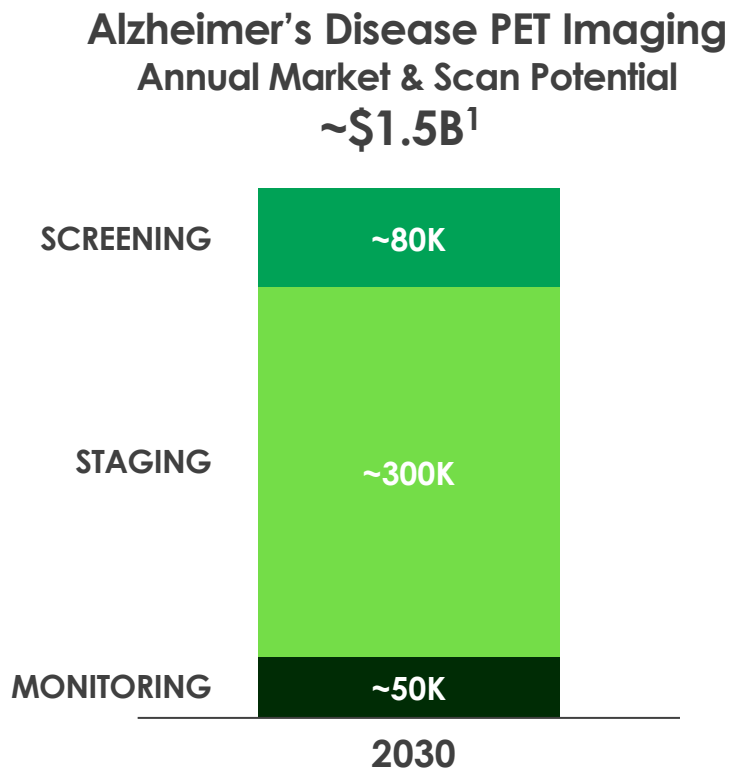
Potential launch in 2026[2]

U.S. GEP-NET Radiotherapeutic Market Annual Market Potential[3]

■ Metastatic 2L+ GEP-NETs   ■ Metastatic 1L GEP-NETs   ■ Lung-NETs   ■ Pheo/Para[4]

~$6.5B MARKET POTENTIAL | **~24K** Patients

~$1.1B MARKET POTENTIAL | **~5K** Patients

2025	2030
5,000	6,000
	12,000
	3,000
	3,000

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The Expanding Role of Radiodiagnostics in Alzheimer's Disease

Alzheimer's Disease PET Imaging
Annual Market & Scan Potential ~$1.5B[1]

- SCREENING: ~80K
- STAGING: ~300K
- MONITORING: ~50K

2030

ALZHEIMER'S® ASSOCIATION

SNMMI — SOCIETY OF NUCLEAR MEDICINE & MOLECULAR IMAGING

recently updated their guidelines[2,3] to expand the appropriate use for both β Amyloid and Tau PET imaging

90%
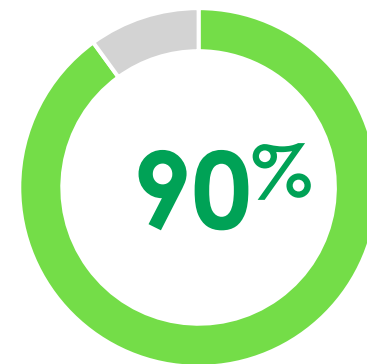
of ~300 dementia experts surveyed project **Tau PET to add value to clinical practice**[4]

Advancing the Diagnosis of Alzheimer's Disease: Detection, Staging, and Monitoring

---

1. Addressable market based on current management estimates, internal data, and current WAC / 340B pricing.; 2.. Jack CR, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimer's Dement. 2024; 20: 5143–5169; 3. Rabinovici GD, et.al. Updated appropriate use criteria for amyloid and tau PET: A report from the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging Workgroup. Alzheimers Dement. 2025 Jan;21(1):e14338. Epub 2025 Jan 8.; 4. Vermeiren MR, et.al. Survey among experts on the future role of tau-PET in clinical practice and trials. Alzheimers Dement (Amst). 2024 Nov 22;16(4):e70033.

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MK-6240: Tau

PRODUCT DESCRIPTION & MECHANISM OF ACTION
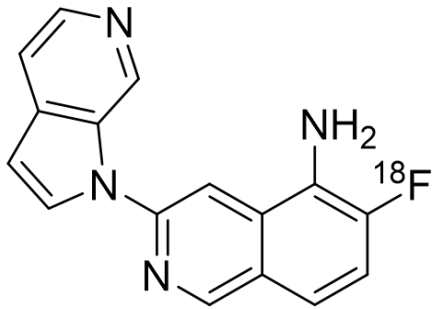
^{18}F-MK-6240

^{18}F-MK-6240 is a-potential second-generation tau radioligand investigational PET imaging agent without appreciable off-target binding in multiple brain structures
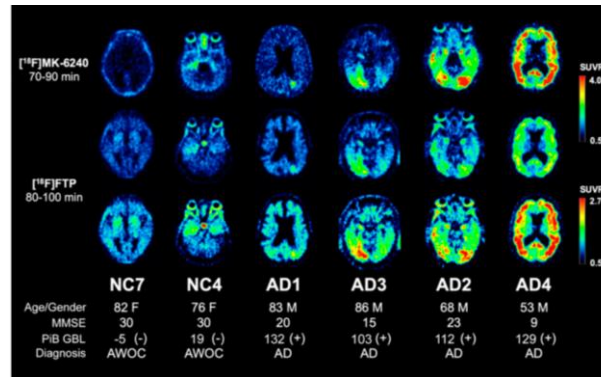
DIFFERENTIATING FEATURES ANTICIPATED[1]

MK-6240 was more specific and elicited less off-target binding compared to a first-generation tracer

Compared to Tauvid ^{18}F-MK-6240 had an approximately 2-fold greater dynamic range in PET signal due to its higher affinity to tau

the image shown is only a portion of the full image included as the visual abstract in the publication

EVIDENCE FOR TARGET VALIDATION[2,3]

Tau is a protein that helps stabilize the internal skeleton of neurons; in Alzheimer's disease (AD) specifically, a build up of an irregular form of tau causes this internal skeleton to disassemble

Neurofibrillary tau is a pathological hallmark of AD and the extent of deposition in brain correlates with clinical severity

In human AD brains, tau is three to four-fold more hyperphosphorylated than the normal adult brain tau

MK-6240 binding is elevated in AD patients, and simplified measures such as standardized uptake value ratio (SUVR) correlate with results from kinetic modeling

DIFFERENTIATED VALUE PROPOSITION ANTICIPATED[2,3]

- ✓ Aid in diagnosing and staging as well as monitoring treatment progress and making informed decisions regarding the continuation or discontinuation of therapy
- ✓ High affinity and selectivity for AD/MCI vs non-AD

HIGH-LEVEL TIMELINES

INDICATION	ISOTOPE	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	NOTES
Alzheimer's Disease	[18]F					*NDA filing expected in 2025*

1. Gogola et al., 2022; 2. Kreisl et al., 2018; 3. Tabeshmehr, P., & Eftekharpour, E., 2023

MK-6240: Widespread Use as a Diagnostic Research Tool

15 Pharmaceutical companies in partnership

Bristol Myers Squibb™

NOVARTIS · gsk · Eisai

MERCK · Janssen · Biogen

37 Research institutions in collaboration

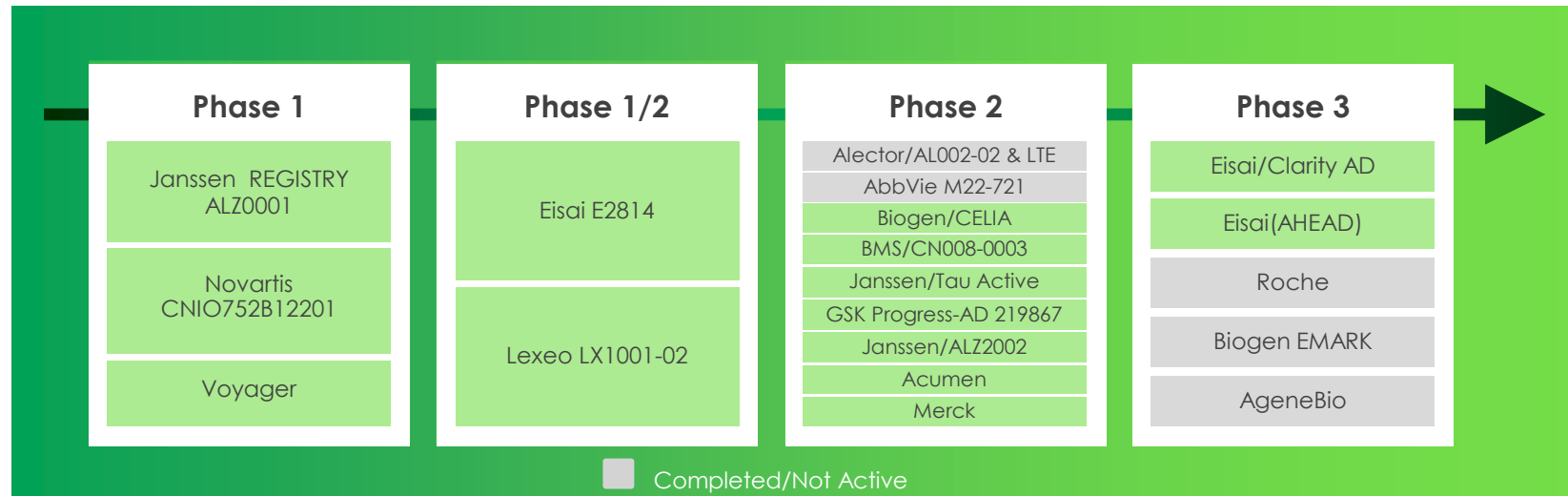**103** Studies

WISCONSIN UNIVERSITY OF WISCONSIN–MADISON

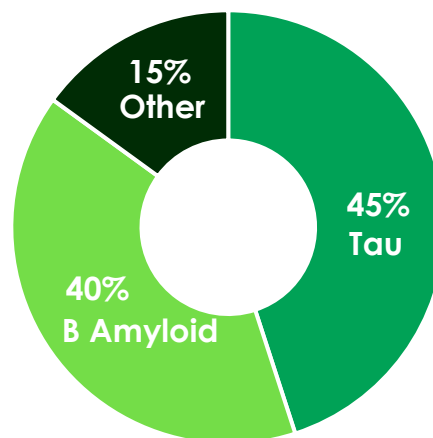Academia/Research Institution that has more than one clinical trials

U.S. POINTER · DIAN · DIAN TU · ACTC

Phase 1
- Janssen REGISTRY ALZ0001
- Novartis CNIO752B12201
- Voyager

Phase 1/2
- Eisai E2814
- Lexeo LX1001-02

Phase 2
- Alector/AL002-02 & LTE
- AbbVie M22-721
- Biogen/CELIA
- BMS/CN008-0003
- Janssen/Tau Active
- GSK Progress-AD 219867
- Janssen/ALZ2002
- Acumen
- Merck

Phase 3
- Eisai/Clarity AD
- Eisai(AHEAD)
- Roche
- Biogen EMARK
- AgeneBio

▢ Completed/Not Active

MK-6240 STUDY BREAKDOWN

- 15% Other
- 45% Tau
- 40% B Amyloid

Protein Specificity	Treatment Modality	# of Studies	Totals
Tau	Small Molecule	1	
	Antibody	6	9
	ASO	2	
β Amyloid	Small Molecule	1	
	Antibody	5	8
	AAV or siRNA	2	
Other	Biomarker/Obs	1	
	Antibody	2	3

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Longitudinal multicenter head-to-head harmonization of tau-PET tracers: an overview of the HEAD study

Firoza Z. Lussier[1], Guilherme Povala[1], Guilherme Bauer-Negrini[1], Livia Silva do Amaral[1], Pamela Lukasewicz Ferreira[1], Bruna Bellaver[1], Juli Cehula[1], Joseph Masdeu[2], Dana L. Tudorascu[1], David Soleimani-Meigooni[3], Juan Fortea[4], Val Lowe[5], Hwamee Oh[6], Belen Pascual[2], Brian A. Gordon[7], Pedro Rosa-Neto[8], Suzanne Baker[9], Tharick A. Pascoal[1]

[1]University of Pittsburgh, Pittsburgh, PA, USA; [2]Houston Methodist Research Institute, Houston, TX, USA; [3]University of California San Francisco, Memory and Aging Center, San Francisco, CA, USA; [4]Hospital de la Santa Creu i Sant Pau, Sant Pau Memory Unit, Barcelona, Spain; [5]Mayo Clinic, Rochester, MN, USA; [6]Brown University, Providence, RI, USA; [7]Washington University in St. Louis, St. Louis, MO, USA; [8]Translational Neuroimaging Laboratory, McGill University Research Centre for Studies in Aging, Douglas Research Institute, Montréal, QC, Canada; [9]Lawrence Berkeley National Laboratory, Berkeley, CA, USA.

Background & Aims

Standardizing tau pathology quantification in vivo is challenged by differences in binding characteristics between tau-PET tracers. The HEAD study aims to generate a **leading, longitudinal head-to-head dataset** of MK-6240, Flortaucipir, RO948, and PI-2620 tau-PET. This dataset will be used to compare tau-PET tracers' cross-sectional and longitudinal performance in tracking tau accumulation and conduct head-to-head comparison of associations of plasma biomarker assays with multiple tau-PET tracer estimates. The principal aim of the HEAD study is to develop a **standardized tau-PET harmonization scale** to improve the interpretation and integration of findings from research studies and drug trials utilizing these tracers, and develop tools to increase accessibility of our harmonization scale. Here, we provide an **overview of the HEAD study design** and an **update on the progress of the HEAD study**, including a description of the clinical characteristics of the cohort and currently available data.

Study Design & Methods

The HEAD study is a **multicentric study – 9 performance sites** in the US, Canada, and Spain are actively involved, with the **University of Pittsburgh** being the coordinating site. Across all sites, the HEAD study set out to recruit **620 individuals** between 18-28 or 50-90 years of age (study groups: **Young, CU, MCI, AD**). The HEAD study protocol involves clinical & neuropsychological testing harmonized to ADRCs (**NACC Uniform Data Set**), blood collection for the banking of plasma, serum, buffy coat, and whole blood following **NCRAD** protocols, and **MRI** acquisition based on **ADNI4** acquisition protocols. All participants undergo **Amyloid-PET** with PiB, NAV4694, Florbetaben, or Flutemetamol and **head-to-head tau-PET** with at least two tau-PET, including **MK-6240** (90-110 mins), **Flortaucipir** (80-100 mins), **PI-2620** (45-75 mins), and **RO948** (70-90 mins). A subset of participants will undergo tau-PET with all 4 tracers head-to-head. PET data is reconstructed to maximize cross-scanner harmonization and is processed uniformly similarly to ADNI4 PET. The Laboratory of Neuroimaging (**LONI**) provides a centralized database for imaging and neuropsychological data. The National Centralized Repository for ADRD (**NCRAD**) provides a biorepository for all blood samples. All study procedures are **repeated at 18-month follow-up** to generate longitudinal data. Study progress and data collection is monitored by the University of Pittsburgh study team.

The HEAD Study Cohort

Over the past **26 months** (November 2022 – January 2025), **N=660** study participants are actively enrolled into the HEAD across all 9 sites, exceeding our aim at **106% of our proposed enrollment target**. Mean age of older adults is **72.1 years**, female distribution is **54%**, and **24%** of individuals come from underrepresented groups (race/ethnicity/rurality). Group distribution of enrolled participants is shown in *Fig.1* – **40%** of participants are **cognitively impaired** (MCI, AD). Measure collection is summarized below, with **over 88%** of enrolled participants having completed all imaging procedures at baseline, and **N=535 (86%)** of participants having completed the initial timepoint (TP). Thus far, **1,441 total head-to-head tau-PET scans have been acquired** in the HEAD study, using MK-6240, Flortaucipir, PI-2620, and RO948 (mean acquisition window=31.6 days). A growing subset currently composed of **101** individuals have undergone **four head-to-head tau-PET**. Two representative cases (CU, AD) of head-to-head tau-PET with 4 tracers are shown in *Fig.2*. Clinical characteristics of the HEAD cohort including APOEε4 carriership, plasma biomarkers distribution (Aβ42/40 ratio/NfL/GFAP/PTau217), consensus visual rating of amyloid-PET, and Braak stage classification are summarized in *Fig.3*.

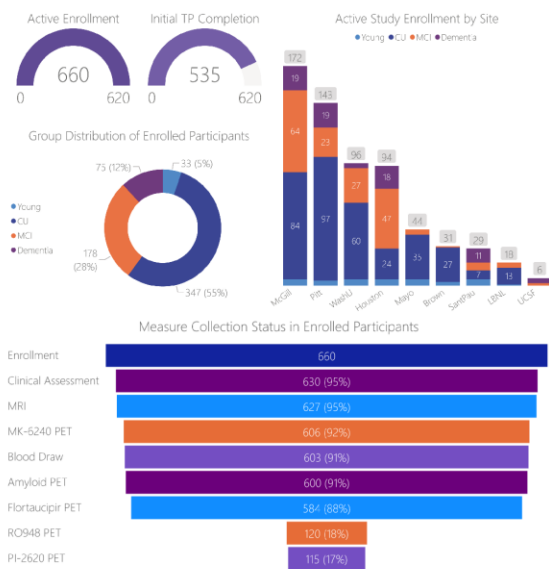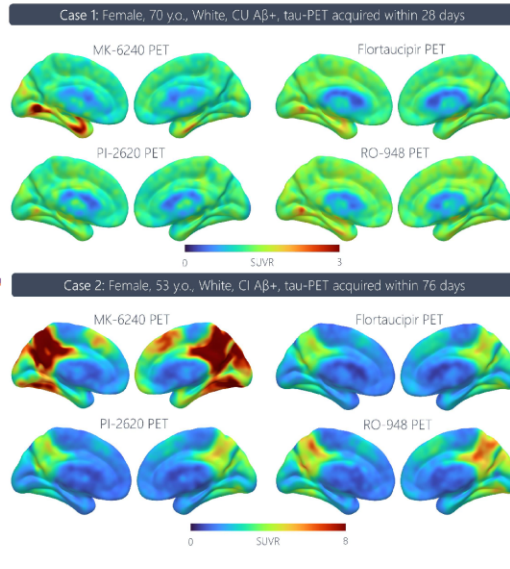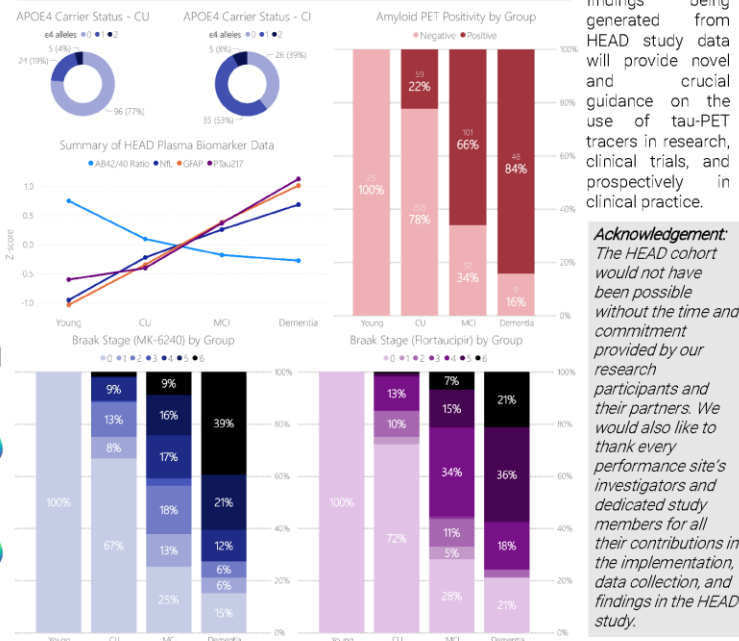### Figure 1: Enrollment and Measure Collection in HEAD

Figure 2: Representative Cases with 4 Head-to-Head Tau-PET

Case 1: Female, 70 y.o., White, CU Aβ+, tau-PET acquired within 28 days

Case 2: Female, 53 y.o., White, CI Aβ+, tau-PET acquired within 76 days

Study Outcomes

The HEAD study is **actively ongoing** at all performance sites. Principal outcomes of the HEAD study is the **Unit tau-PET harmonization scale and Unit Ecosystem Tool**, which are actively being disseminated to the scientific community. Plasma **biomarker analysis** in the HEAD study is ongoing, and **longitudinal** (18-month follow-up) data collection has been initiated and is expected to be completed by mid-2026. The HEAD study cohort represents the largest head-to-head tau-PET dataset to date and represents a continued effort in the optimization of AD imaging markers.

Figure 3: Clinical Characteristics of the HEAD Study Cohort

Results and findings are being generated from HEAD study data will provide novel and crucial guidance on the use of tau-PET tracers in research, clinical trials, and prospectively in clinical practice.

Participating Sites: UCSF Memory and Aging Center; BERKELEY LAB; Institut de Recerca Sant Pau; MAYO CLINIC; McGill UNIVERSITY; Washington University in St. Louis; HOUSTON Methodist; BROWN

Biorepository & Databasing: NCRAD; LONI

Partners: Avid Radiopharmaceuticals; Roche; LANTHEUS; Life Molecular Imaging

Pascoal Lab
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pascoallab.org
@LabPascoal

Head-to-head trajectories of tau PET and plasma p-tau217 as a function of Aβ

Bruna Bellaver[1]*, Guilherme Povala[1]*, Pamela C.L. Ferreira[1], Guilherme Bauer-Negrini[1], Firoza Z. Lussier[1], Livia Amaral[1], Carolina Soares[1], Andreia Rocha[1], Joseph Masdeu[2], Dana Tudorascu[1], David Soleimani-Meigooni[3], Juan Fortea[4], Val Lowe[5], Hwamee Oh[6], Belen Pascual[2], Brian Gordon[7], Pedro Rosa-Neto[8], Suzanne Baker[9], Tharick A. Pascoal[1,10].

[1]Department of Psychiatry, University of Pittsburgh School of Medicine. [2]Houston Methodist Research Institute, Department of Neurology. [3]Mayo Clinic, Department of Radiology. [4]Hospital de la Santa Creu i Sant Pau, Sant Pau Memory Unit, Department of Neurology, Barcelona, Spain. [5]University of California San Francisco, Memory and Aging Center. [6]Brown University, Department of Psychiatry and Human Behavior. [7]Washington University in St. Louis, Department of Radiology. [8]Translational Neuroimaging Laboratory, McGill University Research Centre for Studies in Aging, Douglas Research Institute. [9]Lawrence Berkeley National Laboratory, Berkeley. [10]Department of Neurology, University of Pittsburgh School of Medicine. *Authors contributed equally to this work.

Introduction

→ Tau PET tracers present distinct binding characteristics that might influence their trajectories and relationship with other biomarkers along the AD continuum.

In a head-to-head study, we investigated the relationship between the emergence of PET tracers MK6240 and Flortaucipir, and plasma p-tau217 abnormalities as a function of Aβ PET deposition. We further assessed the concordance between tau PET and plasma p-tau217 positivity.

Methods

353 individuals from the HEAD cohort:

19 cognitively unimpaired young (<25 years old)

186 cognitively unimpaired elderly

148 cognitively impaired

- Aβ PET — [18F]MK6240
- Tau PET — [18F]Flortaucipir

- P-tau217 (AlzPath)

- Tau PET and plasma p-tau217 trajectories were modeled as functions of Aβ burden (Centiloid scale) using the Lowess method.

- Biomarkers were z-scored using young individuals as anchors.

- Tau PET (Braak I region) and plasma p-tau217 were considered positive/abnormal when surpassing 2.5 z-score.

Results

Trajectories of tau PET tracers and plasma p-tau217 as a function of Aβ
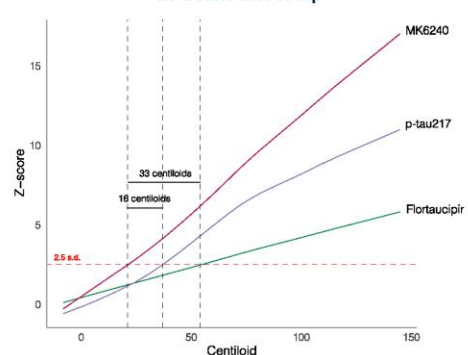

Figure 1. Robust linear regressions show MK6240 (Braak I region), Flortaucipir (Braak 1 region) and plasma p-tau217 increase as a function of Aβ burden (n = 353). Young individuals (n = 19, < 25 years old) were used as anchors to z-scores.

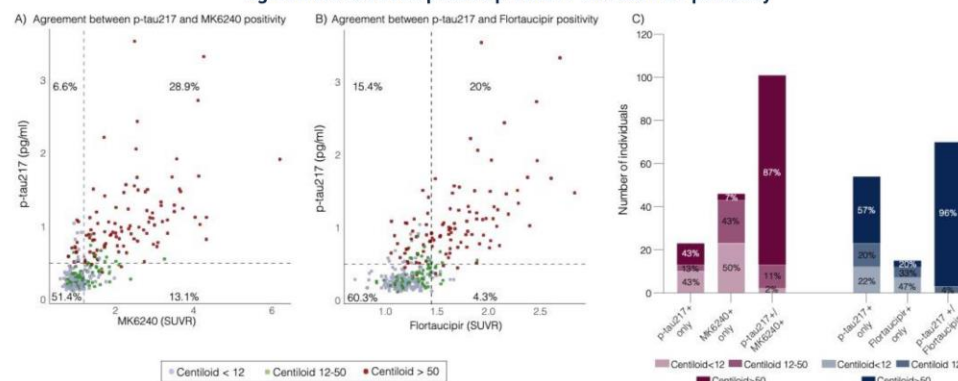### Agreement between plasma p-tau217 and tau PET positivity

Figure 2. Agreement between plasma p-tau217 and (A) MK6240 or (B) Flortaucipir positivity. The dotted lines represent the cutoff for plasma p-tau217 and tau PET (in Braak 1 region) defined as 2.5 s.d. higher than the mean of young individuals. (C) Number of individuals according to their plasma p-tau217, MK6240 and Flortaucipir status and Centiloid distribution.

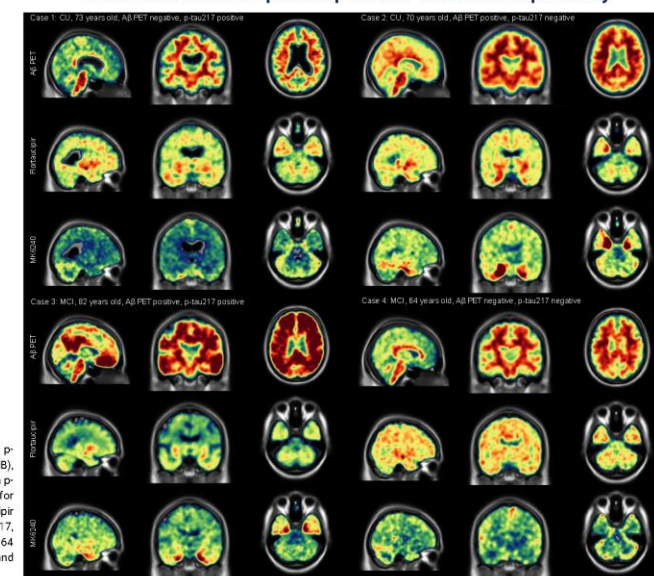### Discordant cases of plasma p-tau217 and tau PET positivity

Figure 3. Case 1: cognitively unimpaired (CU), 73 years old plasma p-tau217 positive individual with negative scan for Aβ PET (PIB), Flortaucipir and MK6240. Case 2: CU 70 years old individual plasma p-tau217 negative (0.28 pg/ml measured in duplicate; threshold for positivity = 0.504 pg/ml) with positive Aβ PET (AZD4694), Flortaucipir and MK6240. Case 3: MCI, 82 years old positive for plasma p-tau217, Aβ PET (PIB) and MK6240 but negative for Flortaucipir. Case 4: MCI, 64 years old negative for plasma p-tau217, Aβ PET (AZD4694) and MK6240 but positive for Flortaucipir.

Conclusion

MK6240 becomes abnormal at lower levels of Aβ burden compared to plasma p-tau217 and Flortaucipir. The relatively high prevalence of discordant tau PET positive or plasma p-tau217 positive suggests that some individuals may show tau PET positivity first, while others may exhibit plasma p-tau217 positivity first.
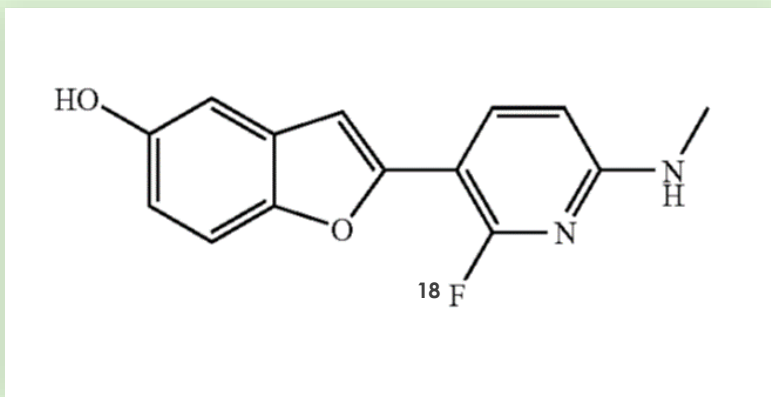
LANTHEUS

# NAV-4694 (flutafuranol): ß amyloid

PRODUCT DESCRIPTION

^{18}F-NAV-4694 - flutaforanol

NAV-4694 is a potential best-in-class ^{18}F-radiolabeled ß amyloid investigational PET imaging agent for AD diagnosis and patient selection for therapy

DIFFERENTIATING FEATURES ANTICIPATED[1,2,4]

Highest conformance to the gold standard, Pittsburgh Compound B, among [18]F β-amyloid imaging agents

Detected lower levels of cortical β-amyloid in earlier stages of AD, via lower non-specific white matter binding, improved dynamic range, and improved signal-to-noise ratio vs. first generation tracers
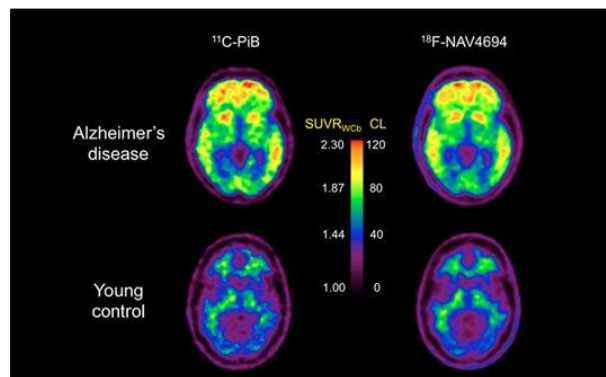
EVIDENCE FOR TARGET VALIDATION[1,3]

ß amyloid is an extensively researched protein and is commonly assumed to be a central biological feature of AD, making it a promising target for treatment

It is strongly believed that the accumulation of toxic ß amyloid in the central nervous system is the main cause of AD

DIFFERENTIATED VALUE PROPOSITION ANTICIPATED

- ✓ Synergetic offering with MK-6240 as the AD-modifying therapeutic market expands
- ✓ Recent approvals of disease-modifying therapies requiring β-amyloid for patient selection and the removal of CMS' restriction on reimbursement are expected to significantly increase demand
- ✓ Offers the potential for earlier diagnosis of AD, increasing the ability to identify patients earlier for therapy

HIGH-LEVEL TIMELINES

INDICATION	ISOTOPE	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	NOTES
Alzheimer's Disease	[18]F					*NDA filing expected in 2026*

1. Data on file; 2. Rowe et all., 2016; 3. Ma et al., 2022; 4. Krishnadas et al., 2021

NAV-4694 (flutafuranol): β Amyloid
## *Performance Characteristics*

HIGHEST CONFORMANCE TO THE GOLD STANDARD[1,3]

NAV4694 SUVR$_{WCb}$ = 1.09 × PiB SUVR$_{WCb}$ - 0.08 SUVR$_{WCb}$
R^2 = 0.99
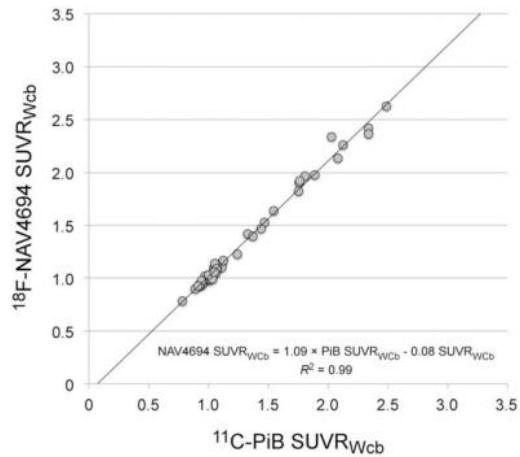
NAV-4694 demonstrated the greatest conformance to C11 PIB among F18 ß amyloid imaging agents with the least variance across the spectrum of patients from young controls to extensive disease

NAV-4694 showed notably lower variance compared to Amyvid, Vizamyl and Neuraceq

NAV-4694 closely aligns to C11 PIB across the scale
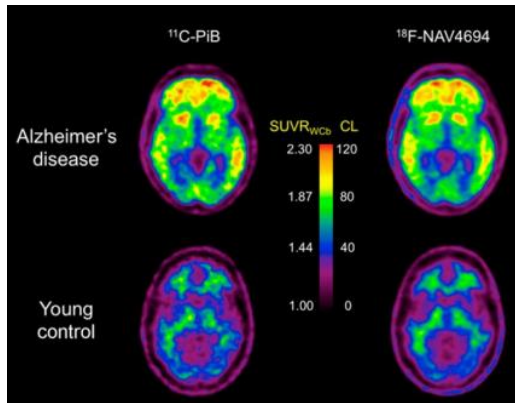
Pittsburgh Compound B (C11 PIB) is the index compound for centiloid scaling, the tool used to enable comparison of β amyloid imaging across tracers

The centiloid scale anchors at 0 to normal expression of β amyloid at the low end and extends to characterize high amyloid burden at 100

TABLE 1
CENTILOID CONVERSION EQUATIONS FOR COMMONLY-USED F18 ß AMYLOID TRACERS[2]

Tracer	Variance (CL SD) Young Controls	Variance Ratio (Tracer SD/PiB SD)	Slope (Tracer SUVR to PiB SUVR)	Intercept	R^2	CL equation CL =...
[18]F-Florbetapir	12	4.6	0.54	0.5	0.89	$175.4 \times SUVR_{fbp} - 182.3$
[18]F-Flutemetamol	5.4	1.54	0.78	0.2	0.95	$121.4 \times SUVR_{flute} - 121.2$
[18]F-Florbetabenl	6.8	1.96	0.61	0.4	0.96	$153.4 \times SUVR_{fbb} - 154.9$
^{18}F-NAV4694l	3.7	1.00	1.09	0.1	0.99	$85.3 \times SUVR_{nav} - 88$
[11]C-PiB	3.5	n/a	n/a	n/a	n/a	$93.7 \times SUVR_{pib} - 94.6$

SUPERIOR GREY MATTER/ WHITE MATTER SIGNAL RATIO AND DYNAMIC RANGE[5]
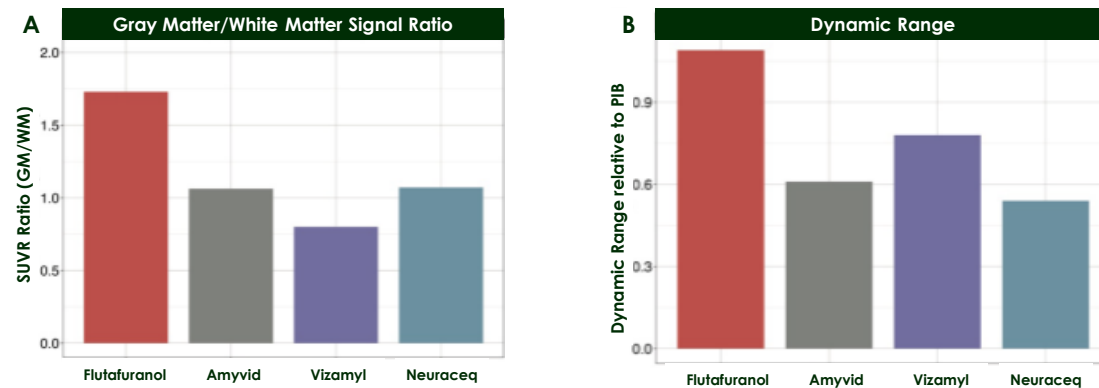

Due to these properties, **NAV-4694 generates high contrast images** that are easy to interpret by visual read and the ability to **detect low levels** of β-amyloid pathology **with high accuracy**

Source: 1. Rowe CC, et al. *J Nucl Med*. 2016;57(8):1233-1237; 2. Krishnadas et al. Seminars in Nuclear Medicine, Volume 51, Issue 3, 2021,Pages 241-252; 3. Klunk WE, Koeppe RA, Price JC, et al. The Centiloid Project: standardizing quantitative amyloid plaque estimation by PET. Alzheimers Dement. Jan 2015;11(1):1-15 e1-4. doi:10.1016/j.jalz.2014.07.00; 4. Rowe CC, Dore V, Jones G, et al. (18)F-Florbetaben PET beta-amyloid binding expressed in Centiloids. Eur J Nucl Med Mol Imaging. Nov 2017;44(12):2053-2059. doi:10.1007/s00259-017-3749-6; 5. Navitsky M, Joshi AD, Kennedy I, et al. Standardization of amyloid quantitation with florbetapir standardized uptake value ratios to the Centiloid scale. Alzheimers Dement. Dec 2018;14(12):1565-1571. doi:10.1016/j.jalz.2018.06.1353; 6. Battle MR, Pillay LC, Lowe VJ, et al. Centiloid scaling for quantification of brain amyloid with [(18)F]flutemetamol using multiple processing methods. EJNMMI Res. Dec 5 2018;8(1):107. doi:10.1186/s13550-018-0456-

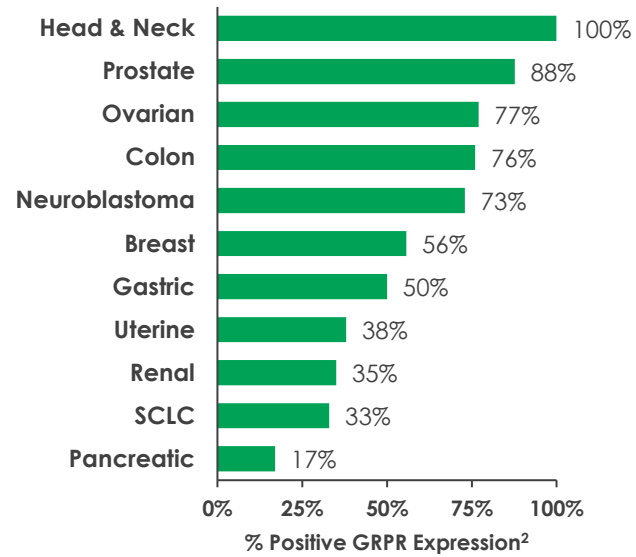LANTHEUS

LNTH-2401/2402: GRPR
Potential best-in-class opportunity

PRODUCT DESCRIPTION & MECHANISM OF ACTION
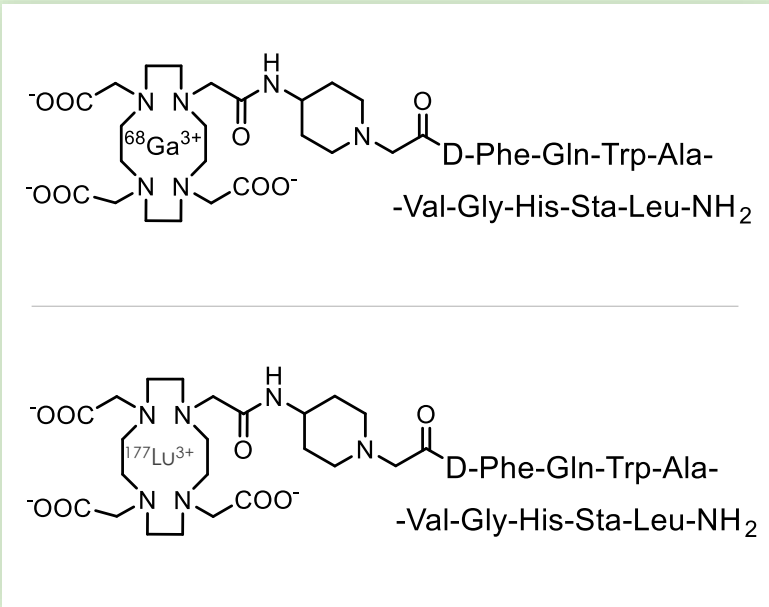
^{68}Ga / ^{177}Lu-LNTH-2401

LNTH-2401 / LNTH-2402 RM2 is an investigational gastrin-releasing peptide receptor (GRPR) targeted-peptide

SUMMARY OF GRPR EXPRESSION IN CANCER

Cancer	% Positive GRPR Expression[2]
Head & Neck	100%
Prostate	88%
Ovarian	77%
Colon	76%
Neuroblastoma	73%
Breast	56%
Gastric	50%
Uterine	38%
Renal	35%
SCLC	33%
Pancreatic	17%

EVIDENCE FOR TARGET VALIDATION[2,3,4,6]

GRPR / BBN expression characterized as ranging from 63% - 100% in primary prostate cancer, but minimally expressed in normal tissue; patients may express PSMA and GRPR heterogeneously

Potential to target Prostate Cancer patients whose tumor(s) do not express PSMA or are ineligible for PSMA-targeted RLT

~15% - 25% of mCRPC patients have low to no PSMA expression

### DIFFERENTIATED VALUE PROPOSITION ANTICIPATED

- ✓ Complementary to portfolio and offers potential commercial synergies
- ✓ Unlike PSMA-targeted RLT, where the kidneys are the limiting organ, the pancreas takes more absorption but can tolerate higher radiation doses
- ✓ High density expression in a broad range of other cancers[2]

HIGH-LEVEL TIMELINE

INDICATION	ISOTOPE	IND-ENABLING	PHASE 1	PHASE 2	NOTES
mCRPC	^{68}Ga	LNTH-2401			*IND filing expected 4Q 2025*
	^{177}Lu	LNTH-2402			*Phase 1 initiation planned 2026*

1. Data on file; 2. Cornelio et al., 2007; Percentages include % positive binding and immunohistochemistry (IHC) scores; 3. Rinne, S.S., Abouzayed, A., Gagnon, K. et al. 66Ga-PET-imaging of GRPR-expression in prostate cancer: production and characterization of [66Ga]Ga-NOTA-PEG2-RM26. Sci Rep 11, 3631 (2021); 4. Ananias, Hildo JK, et al. "Expression of the gastrin-releasing peptide receptor, the prostate stem cell antigen and the prostate-specific membrane antigen in lymph node and bone metastases of prostate cancer." The Prostate 69.10 (2009): 1101-1108; 5. Baun et al. 2024, Seminars in Nuclear Medicine Volume 54, Issue 2, March 2024, Pages 256-269; 6. Verhoeven et al., PMC10502172.

LANTHEUS

LNTH-2401/2402: GRPR
Potential best-in-class opportunity

^{68}Ga-RM26 PET/CT detected primary tumors, multiple lymph node involvement, and bone metastasis lesion, whereas those lesions did not significantly show up on ^{99m}Tc-MDP bone scintigraphy and showed extremely mild uptake on ^{68}Ga-BBN PET/CT.[1]
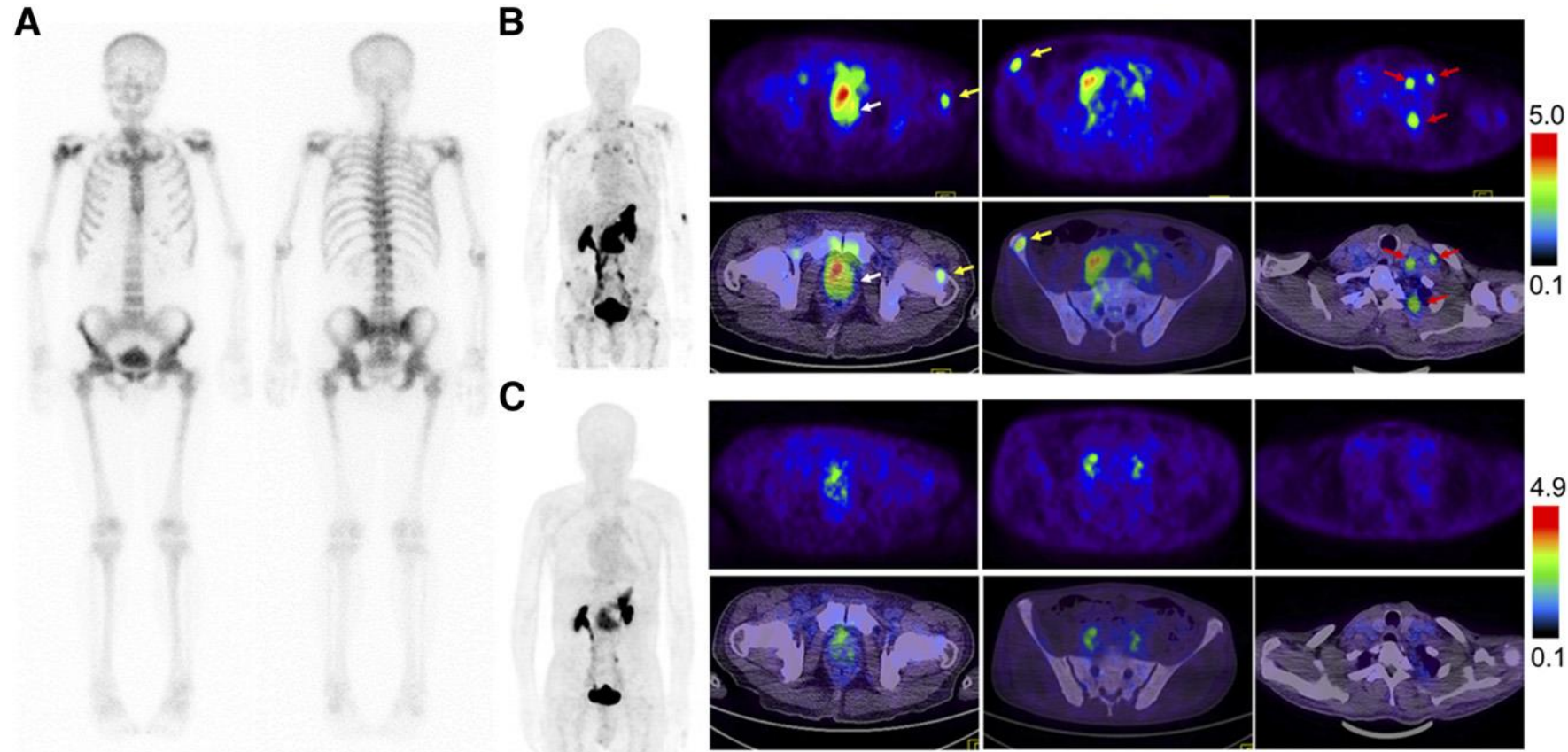
A: ^{99m}Tc-MDP bone scintigraphy, B: ^{68}Ga-RM26 PET/CT, C: ^{68}Ga-BBN PET/CT

73-y-old man diagnosed as having prostate cancer (white arrow) with lymph node involvement (red arrow) and bone metastasis (yellow arrow) before prostatectomy.

1. Zhang J, Niu G, Fan X, Lang L, Hou G, Chen L, Wu H, Zhu Z, Li F, Chen X. PET Using a GRPR Antagonist 68Ga-RM26 in Healthy Volunteers and Prostate Cancer Patients. J Nucl Med. 2018 Jun;59(6):922-928. doi: 10.2967/jnumed.117.198929. Epub 2017 Nov 9. PMID: 29123014; PMCID: PMC6004560.

LANTHEUS

LNTH-2403: LRRC15
Potential First-in-Class Therapy in a Range of Solid Tumor Types

PRODUCT DESCRIPTION & MECHANISM OF ACTION
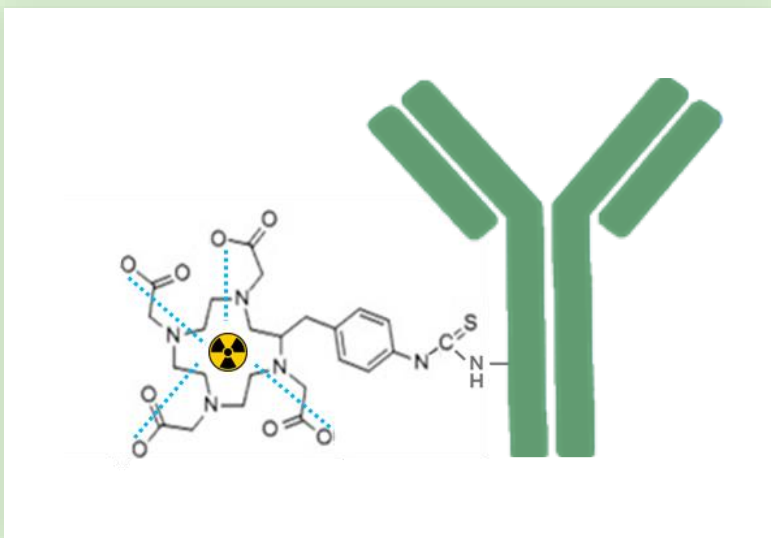
177Lu-LNTH-2403

DUNP19 is an investigational Leucin Rich Repeat Containing 15 (LRRC15)-targeted, fully humanized, mAb

LNTH-2403 is DUNP19 conjugated to radioisotope 177-Lutetium via a DOTA chelator

SUMMARY OF LRRC15 EXPRESSION IN CANCER[1]
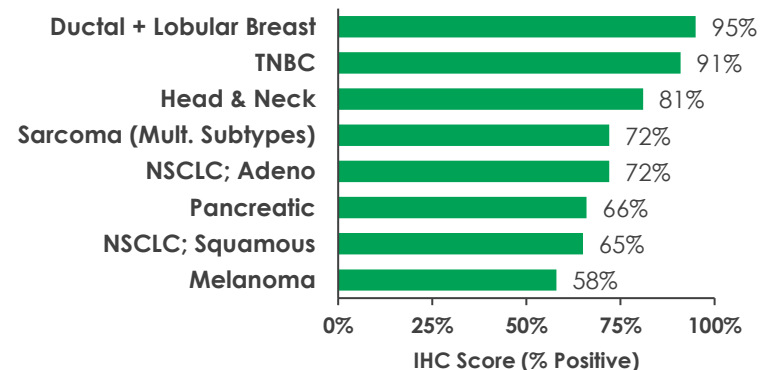

Cancer Type	IHC Score (% Positive)
Ductal + Lobular Breast	95%
TNBC	91%
Head & Neck	81%
Sarcoma (Mult. Subtypes)	72%
NSCLC; Adeno	72%
Pancreatic	66%
NSCLC; Squamous	65%
Melanoma	58%

HIGH-LEVEL TIMELINE

INDICATION	IND-ENABLING	NOTE
Osteosarcoma	LNTH-2403	*IND filing expected 4Q 2025*

A basket study is currently being planned in additional indications, including 3 different types of cancer.

DIFFERENTIATED VALUE PROPOSITION ANTICIPATED

✓ DUNP19 has unique "dual action," targeting ability, targeting both tumor cells and the surrounding environment (stroma)

✓ LRRC15 is widely expressed across a range of tumors, opening a pan-tumor opportunity for treatment of various cancers

EVIDENCE FOR TARGET VALIDATION[2]

LRRC15 is highly expressed on cancer-associated fibroblasts (CAFs) within the tumor stroma of a wide range of malignancies, and on cancer cells from a subset of mesenchymal tumors with low expression in normal tissues

Expression of LRRC15 is associated with TGF beta driven aggressive malignant disease

Studies carried out in various tumor models with LRRC15+ cancer cells and LRRC15+ CAFs have demonstrated that DUNP19 selectively accumulated in LRRC15+ cells after systemic injection and co-localizes with LRRC15

EXPRESSION IN HEALTHY & MALIGNANT TISSUES
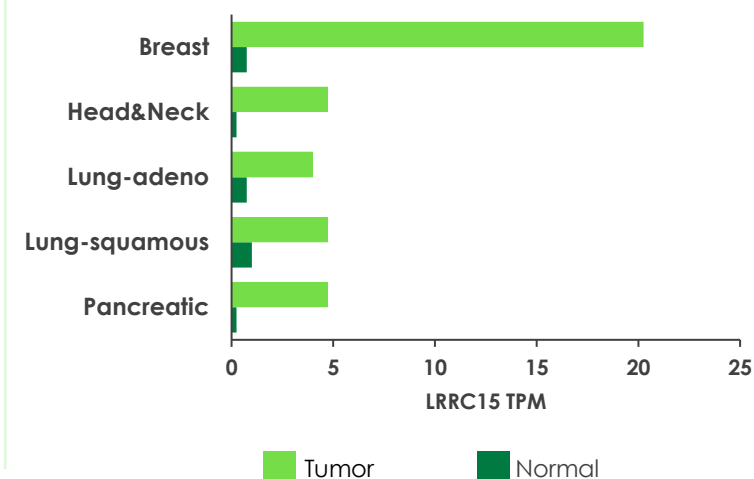
LRRC15 TPM

■ Tumor ■ Normal

LANTHEUS™

LNTH-1363S: FAP
Potential to Replace 18F-FDG Particularly in Brain, Liver, Gastro-Intestinal Cancers

PRODUCT DESCRIPTION
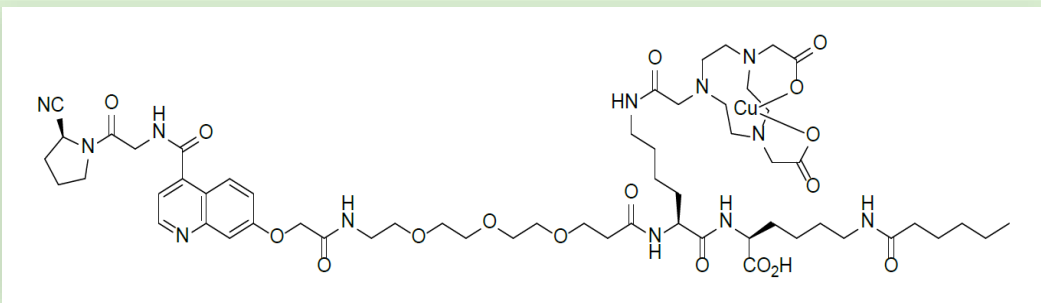
64Cu-LNTH-1363S

LNTH-1363S is a novel, investigational FAP-targeted, small molecule compound comprising a FAP binding domain, an albumin-binding domain for PK modulation and a chelator to contain a radionuclide

LNTH-1363S can be labeled with Cu-64 or Ga-68 radioisotopes for PET imaging use

DEVELOPMENT PLAN

INDICATION	ISOTOPE	IND-ENABLING	PHASE 1	NOTES
Met. Sarcoma	64Cu			*FPI expected in 2025*
Cardiac	64Cu			
COPD/CLAD	64Cu			*Exploratory collaborative studies in discussion*
MASH	68Ga / 64Cu			
Fibrosis	Undisclosed			

68Ga-FAPI UPTAKE IN VARIOUS TUMORS[1]

Tumor	Average SUV_{max}
Sarcoma	18
Salivary Gland	15
Esophageal	14
Breast	13
Lung	12
Prostate	11
Pancreatic	10
Head & Neck	9
Ovarian	8
MTC	7
NETs	7
Colorectal	7
Cervical	6
Hepatocellular	5
Gastric	4

Average SUV_{max}

EVIDENCE FOR TARGET VALIDATION[1,2,3]

FAP is expressed in many solid tumors, either in the cancer cells themselves or in the supporting stroma

FAP is nearly absent in healthy tissues, but highly upregulated during tissue remodeling in embryogenesis, cancer, and fibrosis

In chronic diseases, persistent activation of FAP+ fibroblasts (promoted by TGF-β) leads to excessive extracellular matrix deposition contributing to organ fibrosis in conditions like pulmonary fibrosis, cardiac fibrosis, and liver cirrhosis

DIFFERENTIATED VALUE PROPOSITION ANTICIPATED

- ✓ FAP is expressed widely across a range of tumor types, opening a very large opportunity for imaging of various cancers
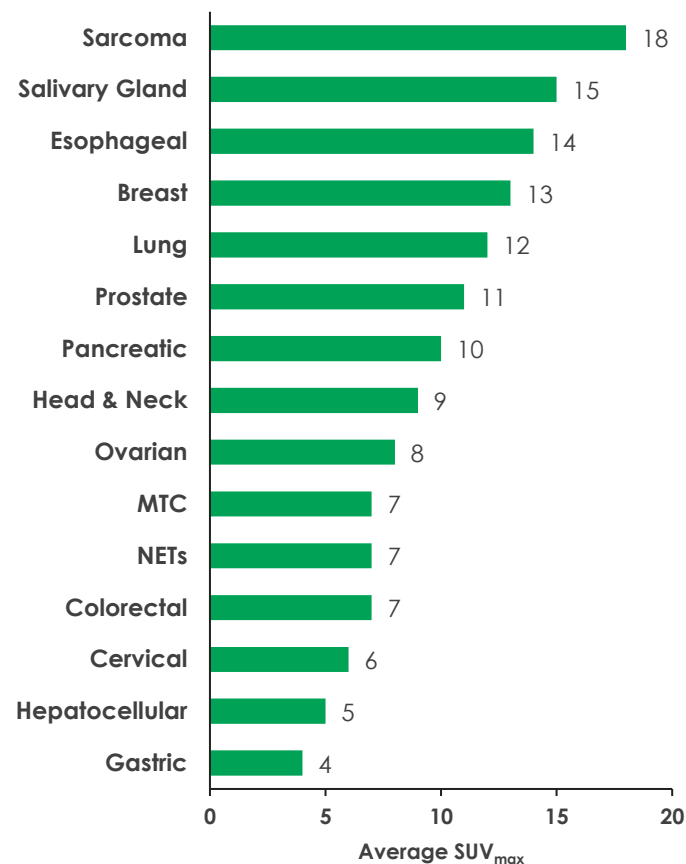
- ✓ FAP-targeted agents may advance detecting and monitoring fibrotic diseases, including liver cirrhosis, pulmonary fibrosis, and cardiac fibrosis, thereby extending their utility beyond oncology

- ✓ Based on imaging studies, low background and high uptake may differentiate LNTH-1363S from FDG in some tumor types and locations

- Imaging studies with 68Ga-FAPI-04 have demonstrated positive uptake in a wide range of tumors

Source: Human Protein Atlas; 1. Kratochwil et all., 2019. 2. Liu et all., 2015. Fibroblast Activation Protein Overexpression and Clinical Implications in Solid Tumors: A Meta-Analysis; 3. Mori et al., 2024
MASH: Metabolic Dysfunction-Associated Steatohepatitis; COPD: Chronic Obstructive Pulmonary Disease; CLAD: Chronic lung allograft dysfunction; SUV = Standardized Uptake Value; FPI = First Patient Initiated

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Key 2025 Milestones
Advancing our Diversified Portfolio in High Value Markets

Prostate Cancer	PNT2002[1] — PSMA	Phase 3
	LNTH-2401[2] — GRPR	Phase 2
	LNTH-2402[3] — GRPR	(Therapeutic)
Neuro-Endocrine Tumors	PNT2003[1] — SSTR2	Registrational-stage
Other Solid Tumors	LNTH-1363S — FAP	Phase 1
	LNTH-2403 — LRRC15	(Therapeutic)
	LNTH-2404 — TROP2	(Therapeutic)
Neurology	MK-6240 (florquinitau) — Tau	Phase 3
	NAV-4694 (flutafuranol) — ß amyloid	Phase 3

KEY 2025 MILESTONES

PROSTATE CANCER
- Non-Prostate PYLARIFY Study Initiated (2Q)
- MIRROR Study Enrollment Completion (4Q)
- RM2 IND Submission (4Q)

GEP-NETs
- PNT2003 Tentative ANDA Approval (2025)

OTHER SOLID TUMORS
- LNTH-1363S First Patient Dosed (2025)
- LRRC15 IND Submission (4Q)

ALZHEIMER'S DISEASE
- MK-6240 NDA Submission (2025)

EVERGREEN THERAGNOSTIC CLOSE*
2H 2025

LMI CLOSE*
2H 2025

Legend: ▇ Diagnostic ▇ Therapeutic

LANTHEUS™

Deliver on Long-Term Growth and Sustainable Value Creation

Powering the Future of Radiopharmaceuticals
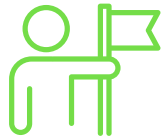
Industry Leadership

Strengthen position as a fully integrated radiopharmaceutical leader with enhanced end-to-end expertise and capabilities

- Ability to scale production of radiopharmaceuticals
- Positioned to accelerate development and lifecycle management through end-to-end supply chain

Portfolio Diversification

Further diversify our diagnostic and therapeutic portfolio with high-potential, complementary assets

- Efficient advancement of catalyst-rich pipeline driven by R&D expertise

Sharpened Strategic Focus

Augment our resources in innovative radiopharmaceuticals

- Long-term and diversified revenue generation enables capital flexibility to invest in pipeline assets

Driven by a Purpose to Improve Patient Outcomes

Lantheus continues to advance innovative radiopharmaceuticals and drive scientific and commercial excellence across oncology, neurology and cardiology

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Appendix

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Reconciliation of GAAP to Non-GAAP Financial Measures
(in thousands, except per share data – unaudited)

	Three Months Ended December 31,		Twelve Months Ended December 31,			Three Months Ended December 31,		Twelve Months Ended December 31,	
	2024	2023	2024	2023		2024	2023	2024	2023
Net (loss) income	$ (11,790)	$ 103,380	$ 312,442	$ 326,661	Net (loss) income per share - diluted	$ (0.17)	$ 1.47	$ 4.36	$ 4.65
Stock and incentive plan compensation	22,164	14,172	76,393	50,507	Stock and incentive plan compensation	0.31	0.20	1.07	0.72
Amortization of acquired intangible assets	11,846	11,308	43,807	46,440	Amortization of acquired intangible assets	0.16	0.16	0.61	0.66
Campus consolidation costs	35	679	72	3,864	Campus consolidation costs	-	0.01	-	0.06
Contingent consideration fair value adjustments	(1,294)	200	(2,699)	(9,275)	Contingent consideration fair value adjustments	(0.02)	-	(0.04)	(0.13)
Non-recurring refinancing related fees	-	5	-	221	Non-recurring refinancing related fees	-	-	-	-
Non-recurring fees	6,723	-	6,723	(54,523)	Non-recurring fees	0.09	-	0.09	(0.78)
Gain on sale of assets	(2,161)	-	(8,415)	-	Gain on sale of assets	(0.03)	-	(0.12)	-
Strategic collaboration and license costs	(8)	-	66,213	-	Strategic collaboration and license costs	-	-	0.92	-
Investment in equity securities - unrealized loss	119,056	-	43,564	-	Investment in equity securities - unrealized loss	1.65	-	0.61	-
Acquisition-related costs	207	169	1,553	676	Acquisition-related costs	-	-	0.02	0.01
Impairment of long-lived assets	-	-	-	138,050	Impairment of long-lived assets	-	-	-	1.97
ARO Acceleration and other related costs	-	1,187	-	2,232	ARO Acceleration and other related costs	-	0.02	-	0.03
Other	447	531	2,720	2,725	Other	0.01	0.01	0.04	0.04
Income tax effect of non-GAAP adjustments[a]	(29,794)	(8,950)	(57,701)	(70,043)	Income tax effect of non-GAAP adjustments[a]	(0.41)	(0.12)	(0.80)	(1.00)
Adjusted net income	$ 115,431	$ 122,681	$ 484,672	$ 437,535	Adjusted net income per share - diluted	$ 1.59	$ 1.75	$ 6.76	$ 6.23
Adjusted net income, as a percentage of revenues	29.5%	34.7%	31.6%	33.7%	Weighted-average common shares outstanding - diluted	72,451	70,092	71,651	70,239

(a) The income tax effect of the adjustments between GAAP net income and adjusted net income (non-GAAP) takes into account the tax treatment and related tax rate that apply to each adjustment in the applicable tax jurisdiction.

Reconciliation of Free Cash Flow
(in thousands)

	Three Months Ended December 31,				Twelve Months Ended December 31,			
		2024		2023		2024		2023
Net cash provided by operating activities	$	157,730	$	112,287	$	544,750	$	305,260
Capital expenditures		(16,369)		(12,069)		(51,625)		(46,555)
Free cash flow	$	141,361	$	100,218	$	493,125	$	258,705
Net cash (used in) provided by investing activities	$	(6,602)	$	(12,069)	$	(226,015)	$	5,939
Net cash used in financing activities	$	(103,659)	$	(450)	$	(118,536)	$	(13,062)

LANTHEUS™

Management Team
Led by Proven Pharmaceutical Industry Veterans

Driven by a **purpose to improve patient outcomes**, Lantheus' experienced leadership team **brings decades of expertise** in advancing innovative radiopharmaceuticals and driving scientific and commercial excellence in everything we do

Brian Markison
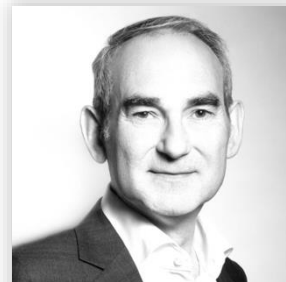CEO

Paul Blanchfield
President

Bob Marshall
CFO and Treasurer

Amanda Morgan
Chief Commercial Officer

Daniel Niedzwiecki
Chief Administrative Officer

Jean-Claude Provost, MD
Chief Science Officer

Jamie Spaeth
Chief People Officer

Previous Experience

Brian Markison	Paul Blanchfield	Bob Marshall	Amanda Morgan	Daniel Niedzwiecki	Jean-Claude Provost	Jamie Spaeth
fougera PHARMACEUTICALS INC.	Takeda	ZIMMER BIOMET	ACADIA	Weil	THERANOSTICS CONSULTING	Corium
King Pharmaceuticals	Shire		Baxter	EDWARDS ANGELL PALMER & DODGE	GE HealthCare	Sage Therapeutics
Bristol Myers Squibb	McKinsey & Company				Pfizer	Shire

Strategy Guided by Experienced, Engaged Board of Directors

Board of seasoned leaders with extensive expertise across healthcare, finance, and business management, supporting Lantheus' ability to shape the future in delivering innovative diagnostic and therapeutic solutions

Mary Anne Heino
Chairperson of the Board

Brian Markison
Director

Minnie Baylor-Henry
Director

Dr. Gérard Ber
Director

Julie Eastland
Director

Samuel Leno
Director

Heinz Mäusli
Director

Julie McHugh
Director

Dr. Phuong Khanh (P.K.) Morrow
Director

Gary Pruden
Director

Dr. James Thrall
Director

Radiopharmaceutical Leader Ready to Strengthen Capabilities at Forefront of Innovation and Patient Care

Powered by our **industry expertise**, **growing pipeline**, and **proven manufacturing and commercial platform**, we are launching **Lantheus' next phase of growth**

Pioneer with history spanning **over 65 years of leadership** in radiopharmaceuticals to positioning **Lantheus to champion the future** of this increasingly Important scientific field.

Proven success of flagship diagnostic agents with **PYLARIFY the #1 utilized PSMA PET imaging agent** that reached blockbuster status in 2024 with $1B+ in sales and **DEFINITY – #1 ultrasound enhancing agent** used in U.S. for 20+ years.

Purpose-built market-leading operations, including **advanced research**, clinical and commercial **manufacturing capabilities**, position **Lantheus** as the **premier, one-stop-shop** to address the complex demands of **radiopharmaceutical discovery**, **development and production**.

Advanced R&D engine positioned to generate steady pipeline of **diagnostics and therapeutics** that provide meaningful clinical outcomes.

Geographically diverse with multi-channel PMF network, supporting **sustained supply**, **reliability and treatment logistics** for real-time delivery, and strong **international infrastructure**, commercial footprint able to **enable growth** in attractive global markets.

Subject to closing of recently announced transactions

LANTHEUS

#1 Utilized PSMA PET Imaging Agent[1]

PYLARIFY is a radioactive diagnostic agent indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer

- with suspected metastasis who are candidates for initial definitive therapy

- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level[2]

CLEAR MARKET LEADER

LANTHEUS™

Prostate Cancer Patients May Undergo Imaging Several Times During Their Disease Journey

PSMA PET Imaging Current Addressable U.S. Market is ~445K Annual Scans or $2B+

Annual Incidence   ✳ Recurrent Disease (RD)
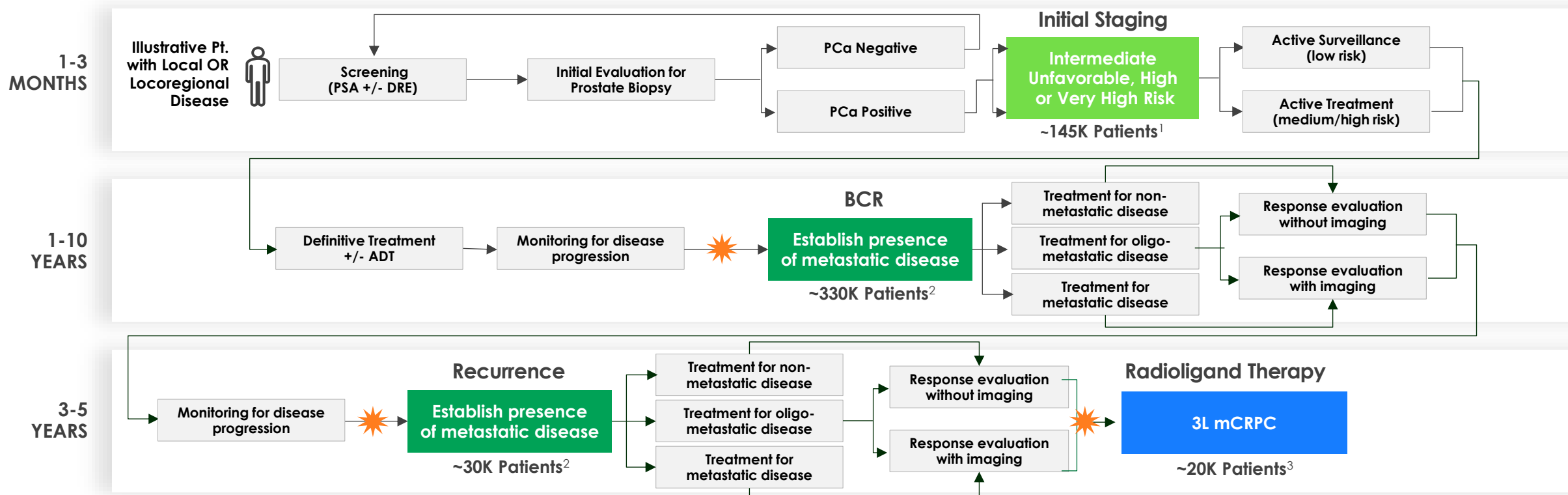
Estimated 2-3% annual growth due to increasing incidence / prevalence[4]

1. Market research interviews, survey, and analysis, Wenzel 2021 Prostate, Nezolosky 2018 J. Clin. Oncol., Agrawal 2020 JAMA.
2. Scher HI, Solo K, Valant J, Todd MB, Mehra M. 2015. Prevalence of Prostate Cancer Clinical States and Mortality in the United States: Estimates Using a Dynamic Progression Model. PloS one 10: e0139440. Based on: CDC.gov, SEER Database, NCCN.org and Axiom Primary and Secondary Market Research and Analysis, validated by Bohm Epidemiology 2020.
3. Global Data 3rd line treatment for metastatic castration-resistant prostate cancer ("mCRPC"), Lantheus primary market research informing imaging procedures performed during radioligand treatment.
4. Lantheus market research and analysis with ordering physicians, NCCN, ACS, UpToDate, SEER.

LANTHEUS

Geographically Diverse, Multi-Channel PMF Network Provides Sustained Supply and Reliability

PYLARIFY DELIVERS
Best-in-Class Patient & Customer Experience

✓ **Continue to expand our manufacturing capacity to ensure PSMA PET with PYLARIFY is *the imaging agent of choice in prostate cancer***
Working with our manufacturing partners to expand delivery windows

✓ **Additional PMFs provide geographic breadth, out-the-door time flexibility and added optionality to our existing network**
PMF partners include both commercial and academic partners

✓ **Operational enhancements, such as adding additional synthesis boxes, enable us to serve customers "on-time-in-full" at a rate of 98%+**
Demonstrates our operational excellence that we strive to deliver to all our customers

PYLARIFY Manufacturing Supported by Sizeable U.S. PMF Network –
U.S. cyclotron network already supports 2+ million FDG doses on an annual basis
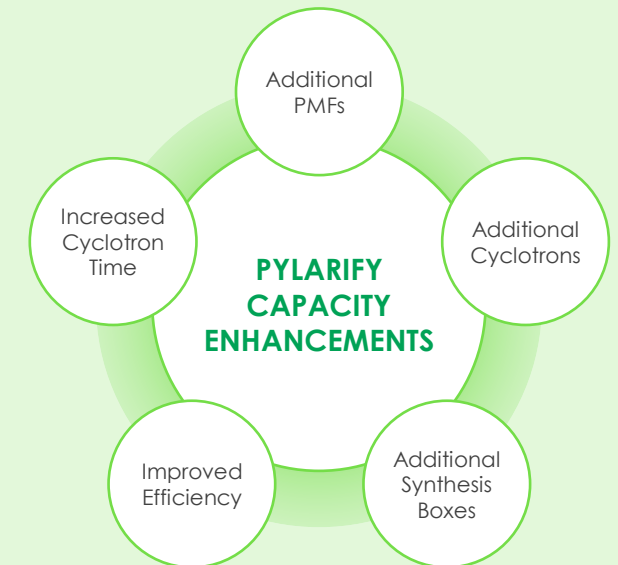
Significant Capacity per PMF
PMFs have already demonstrated the ability to produce:

40+ PYLARIFY doses per batch

Some PMFs producing:
3 batches per day; 5 days per week

90%+ of covered lives have access to PYLARIFY[2]

Contracted with 100% of our targeted academic centers[2]

PYLARIFY CAPACITY ENHANCEMENTS: Additional PMFs, Additional Cyclotrons, Additional Synthesis Boxes, Improved Efficiency, Increased Cyclotron Time

PMF = PET Manufacturing Facility.
1. IMV 2022 PET Imaging Market Summary Report; 2.Data on file.

LANTHEUS™

DEFINITY®
VIAL FOR (Perflutren Lipid Microsphere)
INJECTABLE SUSPENSION

Indicated for use in adult and pediatric patients with suboptimal echocardiograms to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border[1]

Leading U.S. Ultrasound Enhancing Agent[2]

1. DEFINITY® [package insert]. North Billerica, MA; 2.. Internal analyses and data on file;.

DEFINITY® is the #1 Utilized Ultrasound Enhancing Agent in the U.S.[1]

DEFINITY® is a trusted UEA with more than 20 years in the market

IN THE U.S.

4 OUT OF 5

contrast-enhanced echoes
are performed with DEFINITY®

**DEFINITY® HAS BEEN
INCLUDED IN MORE THAN**

3200

peer-reviewed
publications

MORE THAN
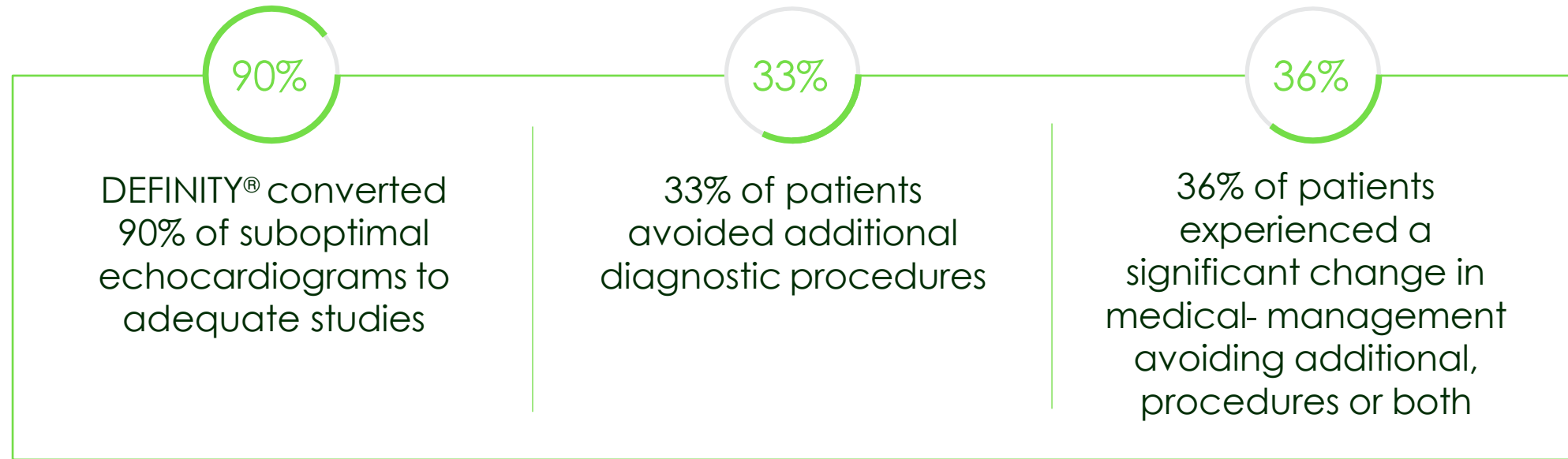
21 million

studies performed

DEFINITY® (Perflutren Lipid Microsphere) is a diagnostic ultrasound enhancing contrast agent used to opacify the left ventricular chamber and to improves the delineation of the left ventricular endocardial border in adult and pediatric patients with suboptimal echocardiograms.[2]

Unenhanced | DEFINITY®

1. Data on file, Lantheus.
2. DEFINITY® [package insert]. N. Billerica, MA: Lantheus, Inc.

LANTHEUS™

DEFINITY®
VIAL FOR (Perflutren Lipid Microsphere)
INJECTABLE SUSPENSION

DEFINITY® Reduced the Need for Additional Cardiac Imaging and Decreased the Length of a Hospital Stay[1]

90%

DEFINITY® converted 90% of suboptimal echocardiograms to adequate studies

33%

33% of patients avoided additional diagnostic procedures

36%

36% of patients experienced a significant change in medical- management avoiding additional, procedures or both

1. Kurt M, Shaikh KA, Peterson L, et al. Impact of contrast echocardiography on evaluation of ventricular function and clinical management in a large prospective cohort. *J Am Coll Cardiol*. 2009;53(9):802-810.

LANTHEUS™

DEFINITY®
VIAL FOR (Perflutren Lipid Microsphere)
INJECTABLE SUSPENSION

Glossary of Terms

AAV: Adeno-associated virus	AD: Alzheimer's Disease	AE: adverse event	ANDA: Abbreviated New Drug Application
BCR: biochemical recurrence	CCK2R: cholecystokinin-2 receptor	CLR: correct location rate	EPS: earnings per share
FAP: Fibroblast activation protein	FDA: Food and Drug Administration	GEP-NET: Gastroenteropancreatic neuroendocrine tumors	GPIB-IIIA: Glycoprotein IIb/IIIa
GRPR: Gastrin-releasing peptide receptor	ISUP: International Society of Urological Pathology	LRRC15: Leucine-Rich Repeat-Containing Protein 15	MAO-B: Monoamine oxidase B
mHSPC: metastatic hormone-sensitive prostate cancer	MCI: mild cognitive impairment	mCRPC: metastatic castration-resistant prostrate cancer	MUC16: mucin 16
NLGN3: Neuroligin 3	NPV: negative predictive value	OXTR: oxytocin receptor	PC: prostate cancer
PET: positron emission tomography	PLND: pelvic lymph node dissection	PMF: PET Manufacturing Facility	PPV: positive predictive value
PSMA: Prostate specific membrane antigen	R/P: radical prostatectomy	siRNA: Small interfering Ribonucleic acid	SSTR: Somatostatin receptor
SUVR: Standardized Uptake Value Ratio	TAM: total addressable market	TROP2: Trophoblast cell surface antigen-2	UEA: ultrasound enhancing agent