

Lantheus Investor Presentation

Building on our Foundation to Power the Future of Radiopharmaceuticals

Leerink Global Healthcare Conference 2025 March 11, 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," "building," "commitment," "continue," "could," "deliver," "drive," "expand/expansion," "expected," "growth," "guidance," "increasing," "intend", "launching," "long-term," "may," "milestone," "opportunity," "pipeline," "plan," "position," "potential," "should," "subject to," "sustained/sustainable," "target," "will," and other similar terms. Such forwardlooking 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 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 gareements 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 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 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







2026-2027
Anticipated
Product
Launches

MK-6240

F18 tau-targeted PET radiodiagnostic

NAV-4694

F18 ß amyloid-targeted PET radiodiagnostic

OCTEVY*

G68 GEP-NET PET radiodiagnostic

Cut 1 EAD targeted radiodiagnostic

PNT2003

SSTR+ GEP-NET radioequivalent therapeutic

3 Pipeline

LN1H-13633	Cu64 FAP-largeted radioalagnostic
LNTH-2401	RM2, GRPR-targeted radiodiagnostic
LNTH-2402	RM2, GRPR-targeted radiotherapeutic
LNTH-2403	LRRC15-targeted radiotherapeutic
LNTH-2404	TROP2-targeted radiotherapeutic

Key Recent Strategic Announcements*



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

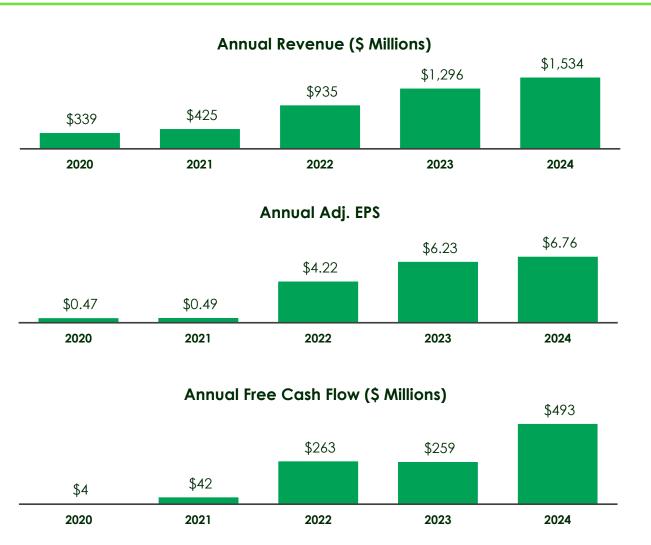


- Adds OCTEVY, a registrational-stage PET radiodiagnostic, complementary to PNT2003
- Establishes clinical and commercial radiopharmaceutical manufacturing
- Enhances early R&D capabilities

^{*}Acquisitions subject to customary closing conditions and anticipated to close 2H 2025



Continued Strong Financial Performance¹





As of December 31, 2024



\$912.8M

Cash on Hand⁴



\$750M

Available Revolving Credit



1. See slides 41 and 42 for a reconciliation of GAAP to non-GAAP financials; certain amounts may be subject to rounding. 2. Guidance provided on February 26, 2025. On a forward-looking basis, the Company does not provide GAAP income per common share guidance or net cash provided by operating activities guidance or a reconciliation of GAAP income per common share to adjusted fully diluted EPS or net cash provided by operating activities to free cash flow because the Company is unable to predict with reasonable certainty business development and acquisition-related expenses, purchase accounting fair value adjustments and any one-time, non-recurring charges, or the net effect of non-cash items. These items are uncertain, depend on various factors, and could be material to results computed in accordance with GAAP. As a result, it is the Company's view that a quantitative reconciliation of adjusted fully diluted EPS and free cash flow on a forward-looking basis is not available without unreasonable effort.3. FY 2025 guidance assumes fully diluted, weighted avg. shares outstanding of approximately 71.5M YTD, and depreciation and amortization of ~\$56M. 4. Cash, cash equivalents and restricted cash at the end of the period was \$914.5 M.

Lantheus' Journey has Driven Growth and Success Over 65 Years



LANTHEUS



1956 Founded



DuPont purchases NEN

1981



1991

DuPont forms venture with Merck called **DuPont Merck**



1998

DuPont buys Merck's interest. becomes DuPont **Pharmaceuticals**



2001

Bristol Myers Squibb Co. purchases DuPont **Pharmaceuticals**



2008

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



2015

Lantheus

IPO on Nasdaa



2020

Lantheus Holdings closes merger with **Progenics Pharmaceuticals**



In-licenses Acquires PNT2002 and Cerveau PNT2003 -Technologies two late-stage including MK-6240, radiotherapeutic novel PET imaging product agent for candidates Alzheimer's Disease

2022

TAICS



2024

Expands pipeline with three strategic transactions





RAD





Announces plans

Theraanostics and

Life Molecular

2025

to acquire

Evergreen

Imaging



CORPORATE GROWTH

FDA APPROVAL & CLEARANCE

1974 FDA Approval

FDA Approval

Xenon Xe 133 Gas 1976

Techne lite

Cardiolite

Approval

1990

FDA

1994

FDA Approval

NEUROLITE

2001

FDA Approval



2021

Approval



Clearance



2023

EMA Approval



Out licensed to Curium

2024

FDA Approval



Out licensed to **GE Healthcare**



Lantheus' Journey has Driven Growth and Success Over 65 Years



2020

Lantheus Holdings closes merger with Progenics Pharmaceuticals



Progenics

2022

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



2023

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

CER EAU

2024

Acquires Meilleur Technologies – including NAV-4694



Acquires LRRC15 and TROP2 from



Strategic investments in





2025

Announces plans to acquire Evergreen Theragnostics and Life Molecular Imaging





CORPORATE GROWTH

FDA APPROVAL & CLEARANCE

2021

FDA Approval



FDA
Clearance

PYLARIFYAI*

2023

EMA Approval



Out licensed to Curium

2024

FDA Approval



Out licensed to GE Healthcare





Leading Commercial Portfolio





4Q 2024

\$266.0M4Q 2024 Net Sales

+15.7% Growth

4Q 2024 Year-over-Year

FY 2024

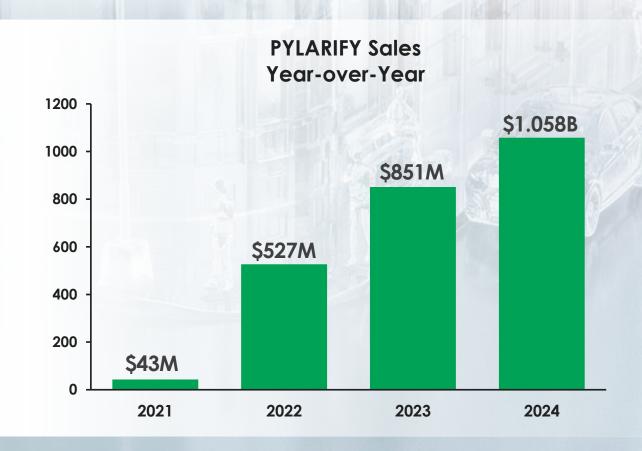
\$1.058BFY 2024 Net Sales

+24.3% Growth

FY 2024 Year-over-Year

2025 Revenue Expectation

Year-over-Year Low to Mid-Single Digit Growth



First Radiodiagnostic to Achieve BLOCKBUSTER STATUS

PYLARIFY Offers Clear Clinical Value to Patients and Healthcare Providers

Change in Intended Patient Management¹⁻³

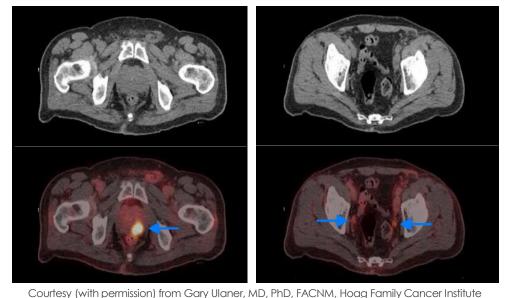


In PYLARIFY's Phase 3 pivotal study, nearly two out of three patients in the study with BCR who received PYLARIFY after negative or uninformative conventional imaging had a change in intended prostate cancer treatment

99%

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

PYLARIFY's change in intended patient management is based on 99% of enrolled patients in our CONDOR study



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 II be necessary to demonstrate whether PYLARIFY® PET/CT-directed changed in intended patient management lead to improved outcomes for patients with prostate cancer.¹

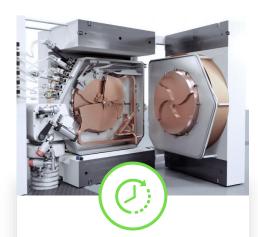
- 1. Data on file, Lantheus.
- 2. PYLARIFY® [package insert]. North Billerica, MA: Progenics Pharmaceuticals, Inc., a Lantheus company.
- 3. Morris MJ, Rowe SP, Gorin MA, et al. Diagnostic performance of 18F-DCFPyL-PET/CT in men with biochemically recurrent prostate cancer: results from the CONDOR phase 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 patientready doses "out the door"

110-minute half-life advantage

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



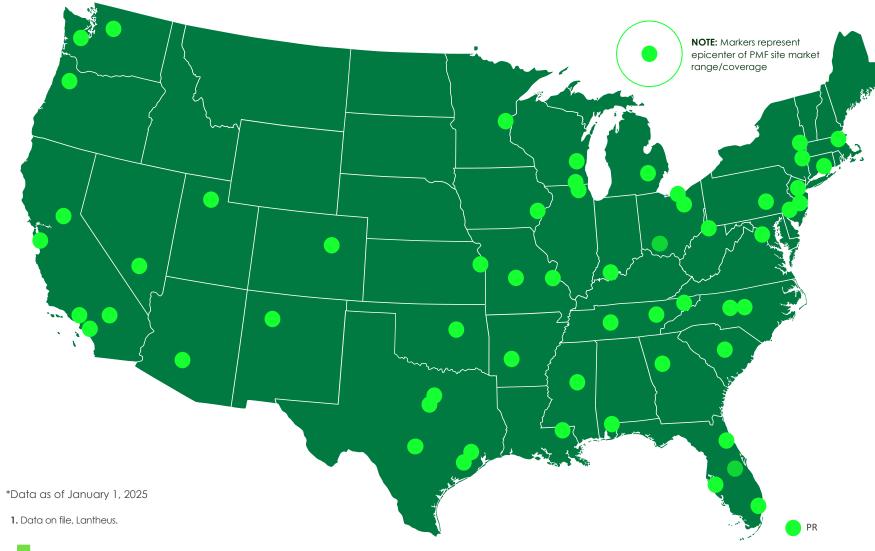
Patient is injected and scanned

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



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







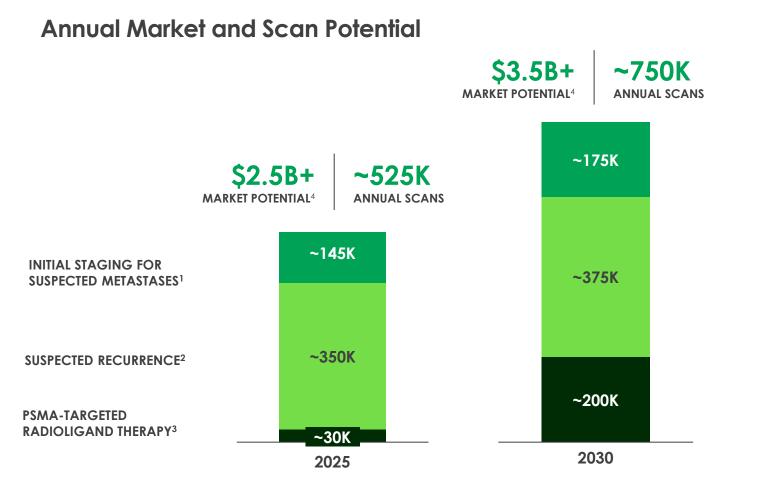
Extensive manufacturing network* with multiple radiopharmacies serving imaging centers in 48 states, District of Columbia, and Puerto Rico¹

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



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



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

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. Expanded RLT indication from 3L only to 1L, 2L & mHSPC (metastatic Hormone Sensitive Prostate Cancer). 4. Addressable market based on current management estimates, internal data and current WAC / 340B pricing.



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)

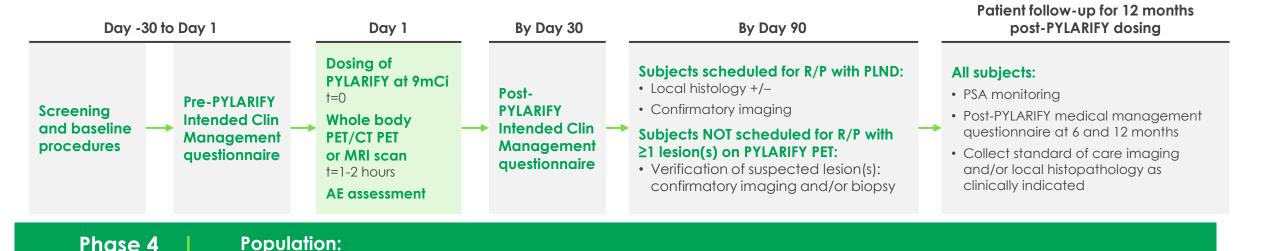
Primary Endpoint

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



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

See appendix for definition of abbreviated terms.



n = 274

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



Ida Sonni^{1,2}, Nicholas G. Nickols^{3,4}, Derace Schaffer⁵, Karl Sjöstrand⁵, Louis Montagut⁵, Aseem Anand⁵, 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, 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 Hematology-Oncology, VA Greater Los Angeles Healthcare System, Los Angeles, CA, USA; 7. Department of UsA; 7. Department of Medicine, University of California-Los Angeles, CA, USA; 7. Department of Usa; 7. Department



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.



Pt 160 - PSA 0.14 (miT0N0M1a)

0.9 cm left common iliac LN (SUVmax 9.9)

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

Pt 78 - PSA 0.02 (miT0N0M1b)

right sacrum (SUVmax 3.1)

- 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.
- <u>Current thresholds</u> for initiating PSMA PET/CT imaging in patients with BCR may need reconsideration.
- <u>Further studies are necessary</u> to refine guidelines and assess the costeffectiveness of incorporating PSMA imaging at very low PSA levels.

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







#1 Utilized Ultrasound Enhancing Agent¹

4Q 2024

\$86.2M4Q 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 2024²

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



DEFINITY improved cardiac diagnosis and streamlined patient management¹⁻³

of suboptimal echos to adequate echos³ UNENHANCED CONVERTED 90% to adequate echos³ DEFINITY

- of patients avoided additional diagnostic procedures^{3,4}
- 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.

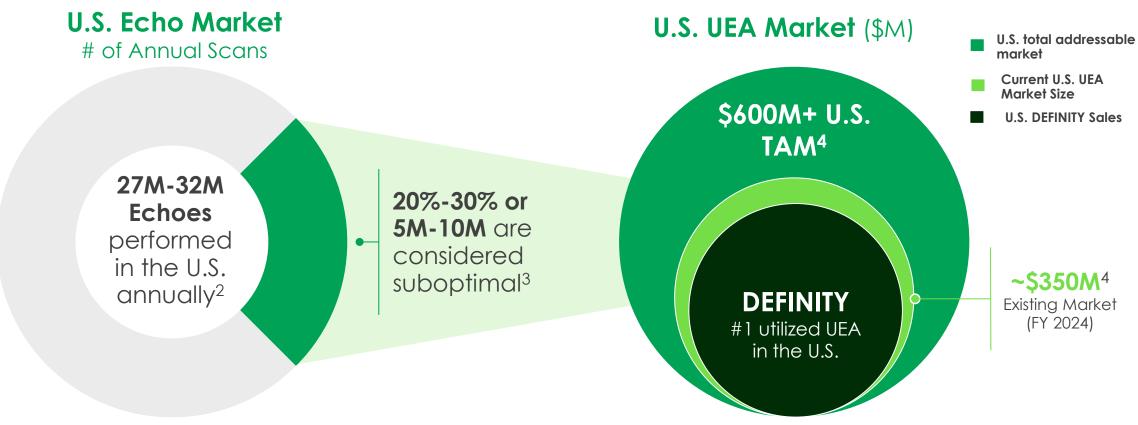
References: 1. Data on file, Lantheus. **2.** DEFINITY. Prescribing Information. Lantheus. **3.** Kurt M, Shaikh KA, Peterson L, et al. Impact of contrast echocardiography on evaluation of ventricular function and clinical management in a large prospective cohort. *J Am Coll Cardiol.* 2009;53(9):802-810. 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.





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

Significant Opportunity Remains in the Suboptimal Echo Market



- 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.





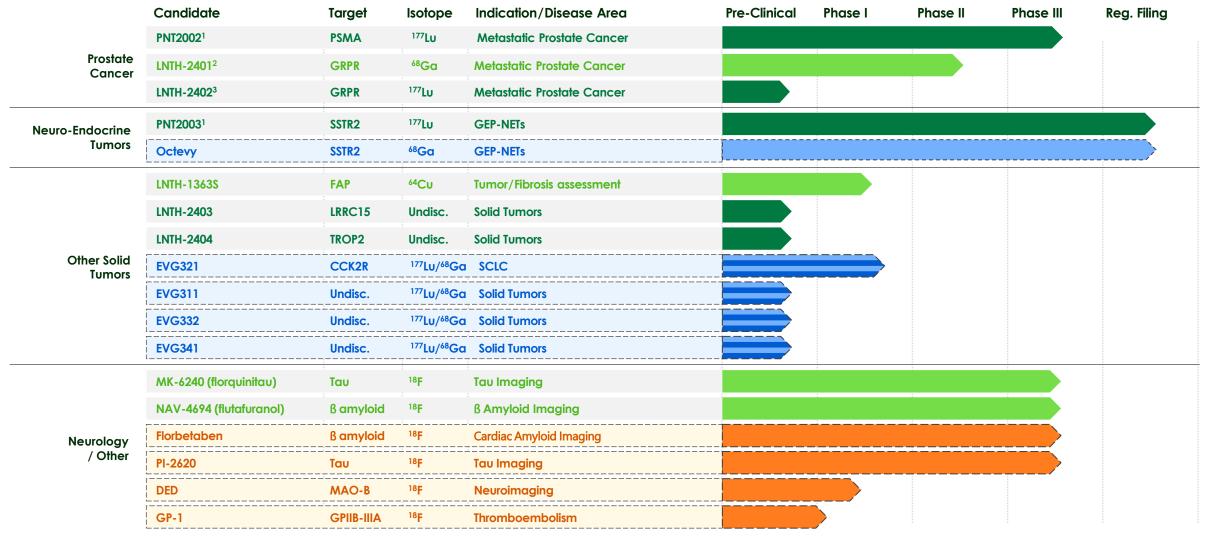
Advancing Innovative Radiotherapeutic & Radiodiagnostic Pipeline

Innovation that Makes an Impact





Includes Pipeline Assets of Life Molecular Imaging and Evergreen Theragnostics*



ANTHEUS

Diagnostic

^{*}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 ⁶⁸Ga-RM2 3. Also known as ¹⁷⁷Lu-RM2

PNT2003: Somatostatin Receptor (SSTR)-Targeted Radiotherapeutic

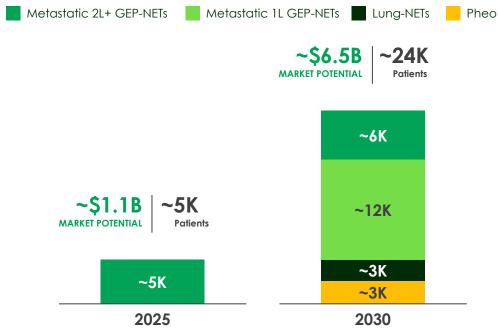
SSTR-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut and hindgut neuroendocrine tumors in adults



Anticipated to be a radioequivalent to **LUTATHERA®** (Lutetium Lu 177 Dotatate)

Potential launch in 2026²

U.S. GEP-NET Radiotherapeutic Market Annual Market Potential³

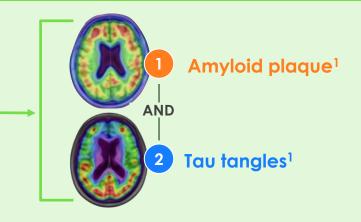


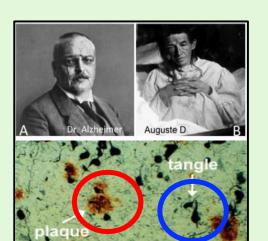
^{1.} Based on the most recent update to the FDA's online paragraph IV database listings. 2. Subject to FDA approval and positive resolution of an ongoing Hatch-Waxman litigation. 3. Factors Influencing Market Potential: Overall increase in epi population, expanding guidelines, and increased utilization of RLT within relevant patient populations. 4. Pheochromocytoma (Pheo) and Paraganglioma (Para)



Alzheimer's Disease is A Public Health Crisis

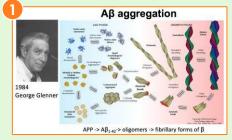
Alzheimer's disease is defined by pathological deposits of





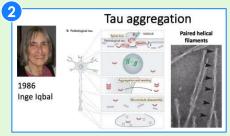
Alois Alzheimer, Auguste Deter (1906)

Hallmark pathological features of Alzheimer's disease

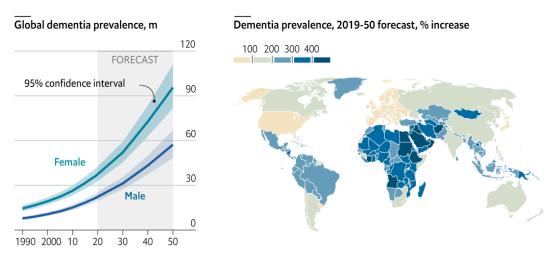


Amyloid- β plaques

Tau tangles



Alzheimer's Disease is a public health crisis



Source: "Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019", by Emma Nichols et al., *Lancet*, 2022

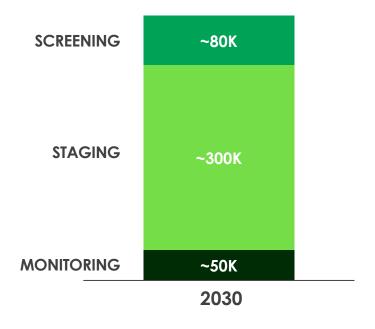
>50 million people living with dementia

1. Sheppard O, Coleman M. Alzheimer's Disease: Etiology, Neuropathology and Pathogenesis. In: Huang X, editor. Alzheimer's Disease: Drug Discovery [Internet]. Brisbane (AU): Exon Publications; 2020 Dec 18. Chapter 1. Available from: https://www.ncbi.nlm.nih.gov/books/NBK566126/ doi: 10.36255/exonpublications.alzheimersdisease.2020.ch1



The Expanding Role of Radiodiagnostics in Alzheimer's Disease





ALZHEIMER'S' ASSOCIATION



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



of ~300 dementia experts surveyed project Tau PET to add value to clinical practice⁴

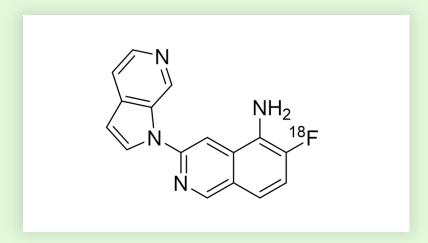
Advancing the Diagnosis of Alzheimer's Disease: Detection, Staging, and Monitoring

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 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.



MK-6240: Tau

PRODUCT DESCRIPTION & MECHANISM OF ACTION



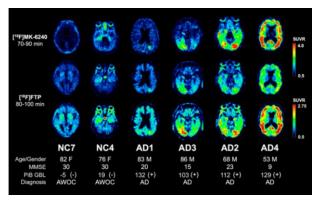
¹⁸F-MK-6240

¹⁸F-MK-6240 is a potential second-generation tau radioligand investigational PET imaging agent without appreciable off-target binding in multiple brain structures

DIFFERENTIATING FEATURES ANTICIPATED¹

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

Compared to Tauvid ¹⁸F-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}



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

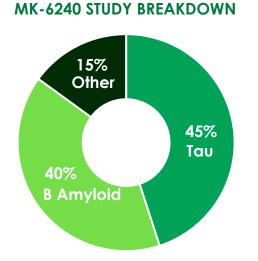
1. Gogola et al., 2022; 2. Kreisl et al., 2018; 3. Tabeshmehr, P., & Eftekharpour, E., 2023



MK-6240: Widespread Use as a Diagnostic Research Tool







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



The HEAD Study: Multicenter Longitudinal Head-to-head comparison of tau-PET Tracers¹



Washington University in Schouls Methodist BROWN

1. Lussier FZ. et al., Longitudinal multicenter head-to-head harmonization of tau-PET tracers: an overview of the HEAD study. Human Amyloid Imaging Conference, 2025.

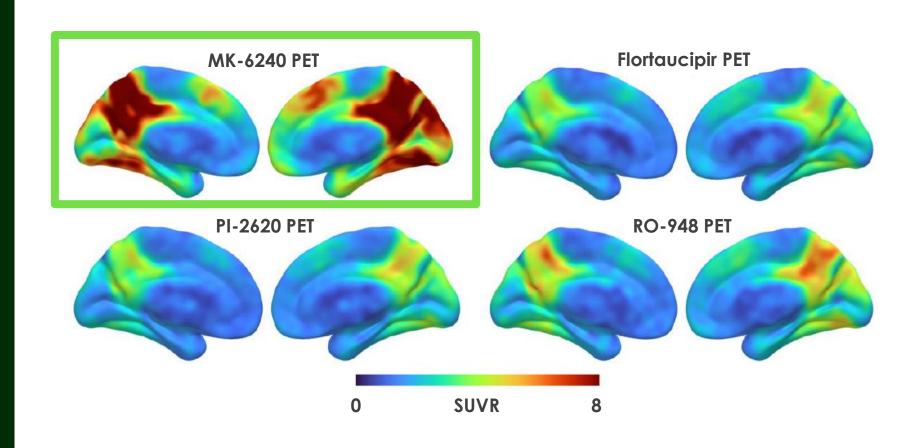


26

MK-6240 had Higher Uptake due to its Larger Dynamic Range¹

Case 2:

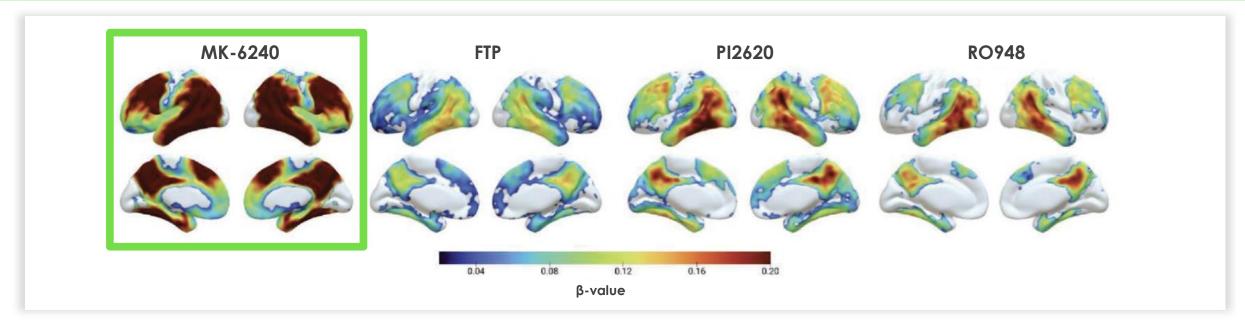
- Female
- 53 y.o.
- White
- CI Aβ+
- tau-PET acquired within 76 days



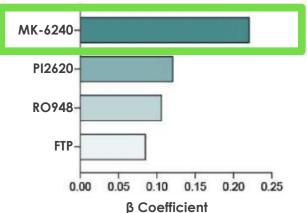
1. Lussier FZ. et al., Longitudinal multicenter head-to-head harmonization of tau-PET tracers: an overview of the HEAD study. Human Amyloid Imaging Conference, 2025.



Tau PET tracers Exhibited a Robust Association with Plasma P-Tau^{1,2}



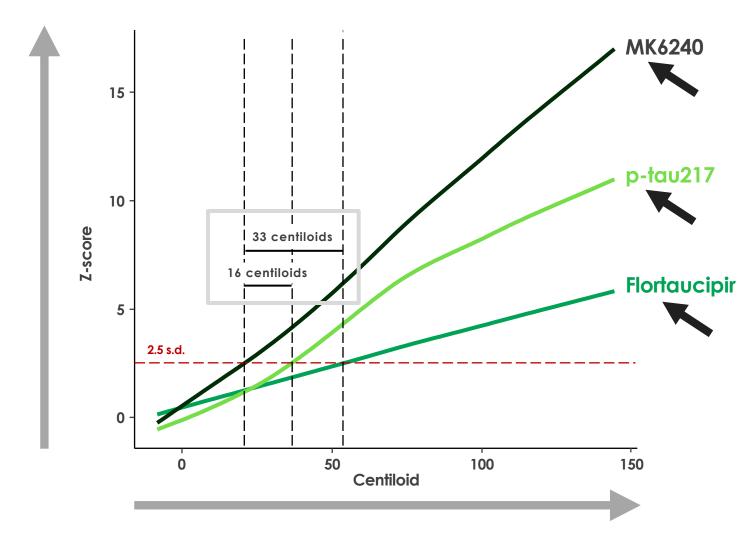
Average magnitude of the association between plasma p-tau217 and tau-PET tracers



For a subset of individuals who had all four PET tau tracers, MK-6240 showed a stronger overall association with p-tau2171



Head-to-Head Trajectories of Tau PET and Plasma p-Tau217 as a Function of Amyloid PET¹

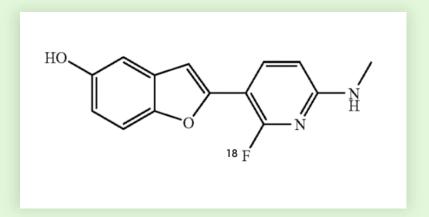


^{1.} Bellaver B. et al., Head-to-head trajectories of tau PET and plasma p-tau217 as a function of AB. Human Amyloid Imaging Conference, 2025.



NAV-4694 (flutafuranol): ß amyloid

PRODUCT DESCRIPTION



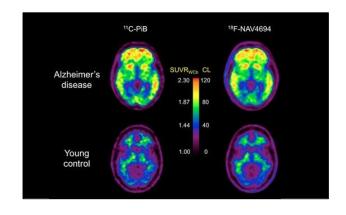
¹⁸F-NAV-4694 - flutaforanol

NAV-4694 is a potential best-in-class ¹⁸F-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}

B 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

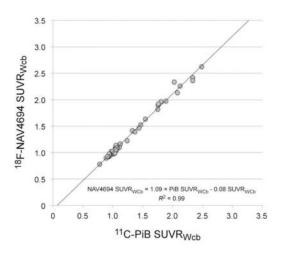
INDICATION	ISOTOPE	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	NOTES
Alzheimer's Disease	18 F					NDA filing expected in 2026

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

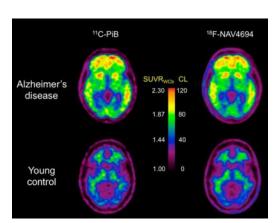
HIGHEST CONFORMANCE TO THE GOLD STANDARD^{1,3}



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 Neuracea (table 1)

NAV-4694 closely aligns to C11 PIB across the scale



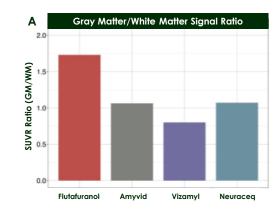
Pittsburgh Compound B (C11 PIB) is the index compound for centiloid scaling, the tool used to enable comparison of β amyloid imaging across tracers

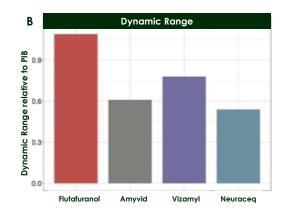
The centiloid scale anchors at 0 to normal expression of β amyloid at the low end and extends to characterize high amyloid burden at 100

TABLE 1
CENTILOID CONVERSION EQUATIONS FOR COMMONLY-USED F18 ß AMYLOID TRACERS²

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

SUPERIOR GREY MATTER/ WHITE MATTER SIGNAL RATIO AND DYNAMIC RANGE⁴

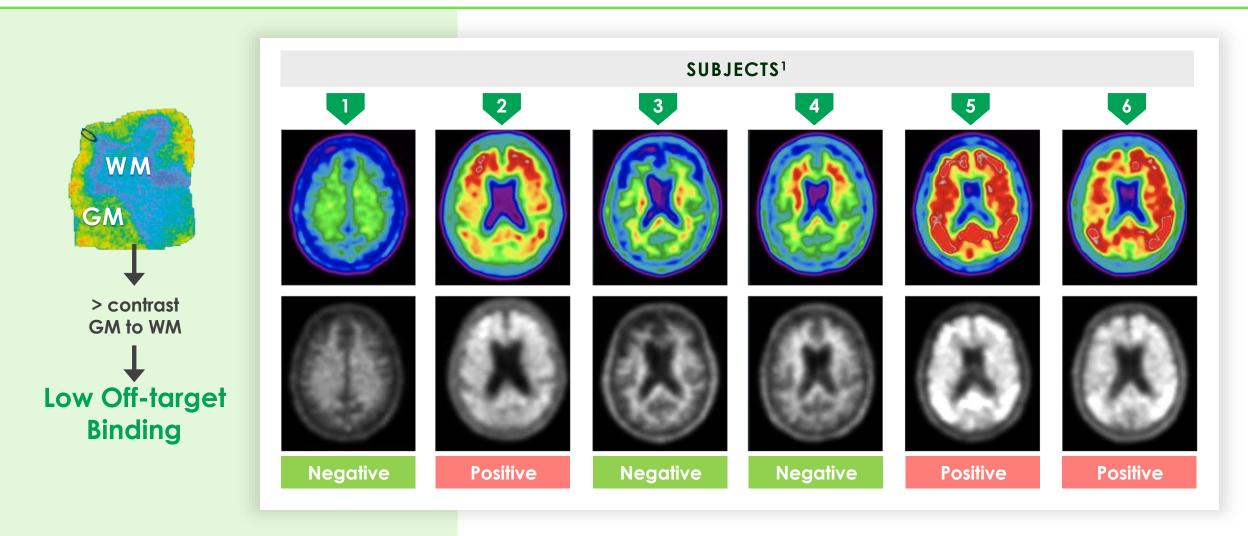




Due to these properties, **NAV-4694 generates high contrast images** that are easy to interpret by visual read and the ability to **detect low levels** of β-amyloid pathology **with high accuracy**



NAV-4694 (Flutafuranol): Potential Easy Visual Reading in Clinical Practice because of Low Off-target Binding



^{1.} Images courtesy of Dr. Tharick Pascoal, used with permission.



Potential Advantages of NAV-4694 (Flutafuranol) Second Generation Imaging Agent

	Sens	Spec	GM/WM Visual Read	F18
PiB				X
Florbetapir			×	
Florbetaben			×	
Flutemetamol			×	
Flutafuranol				

NAV-4694 (Flutafuranol) may be most suitable to clinical visual readings

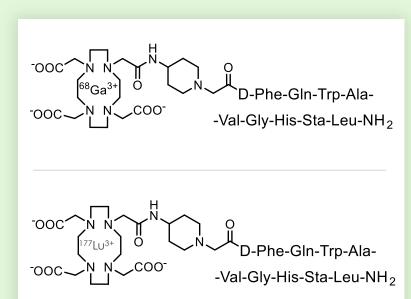
^{1.} Not based on head-to-head comparisons in all instances; patient populations and baseline characteristics may differ between studies from which data is driven. Potential advantages are derived from published data based on anticipated advantages for our investigational tracer NAV-4694.



LNTH-2401/2402: GRPR

Potential best-in-class opportunity

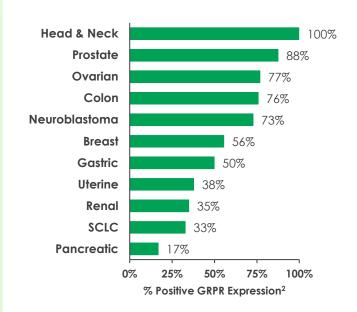
PRODUCT DESCRIPTION & MECHANISM OF ACTION



68Ga / 177Lu-LNTH-2401

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

SUMMARY OF GRPR EXPRESSION IN CANCER



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 cancers²

HIGH-LEVEL
TIMELINE

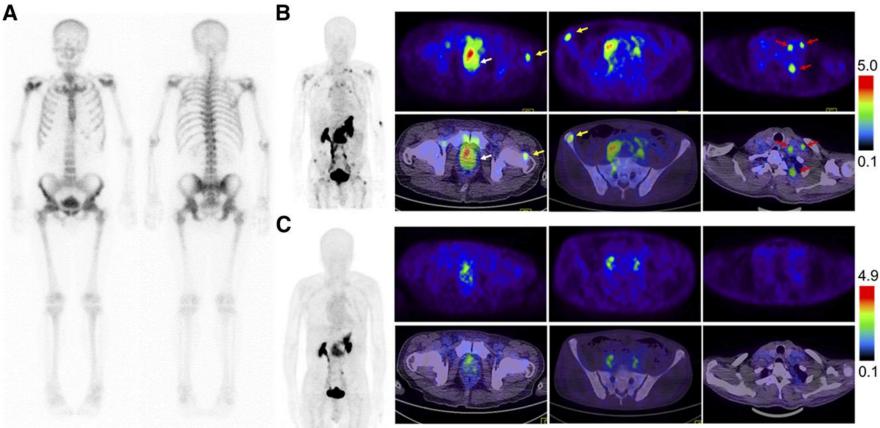
INDICATION	ISOTOPE	IND-ENABLING	PHASE 1	PHASE 2	NOTES
_	⁶⁸ Ga	LN	ΓH-2401		IND filing expected 4Q 2025
mCRPC	¹⁷⁷ LU	LNTH-2402			Phase 1 initiation planned 2026

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.



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

68Ga-RM26 PET/CT detected primary tumors, multiple lymph node involvement, and bone metastasis lesion, whereas those lesions did not significantly show up on 99mTc-MDP bone scintigraphy and showed extremely mild uptake on 68Ga-BBN PET/CT.1



A: 99mTc-MDP bone scintigraphy, B: 68Ga-RM26 PET/CT, C: 68Ga-BBN PET/CT

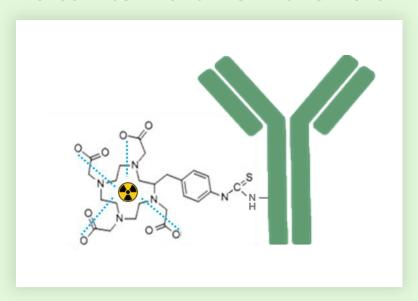
73-y-old man diagnosed as having prostate cancer (white arrow) with lymph node involvement (red arrow) and bone metastasis (yellow arrow) before prostatectomy.



LNTH-2403: LRRC15

Potential First-in-Class Therapy in a Range of Solid Tumor Types

PRODUCT DESCRIPTION & MECHANISM OF ACTION

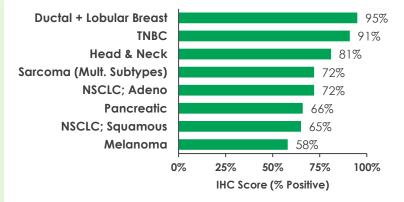


¹⁷⁷Lu-LNTH-2403

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 CANCER¹



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

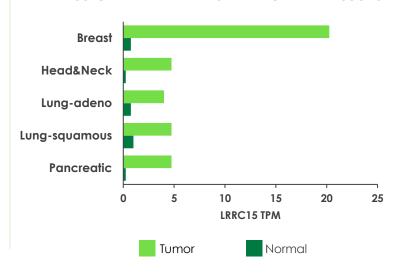
EVIDENCE FOR TARGET VALIDATION²

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



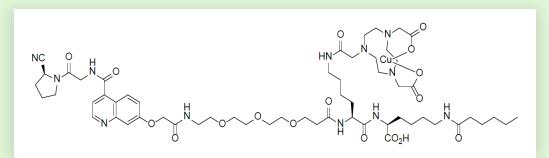
Source: Human Protein Atlas. Note: TPM = transcripts per million; IHC = immunohistochemistry. 1. Purcell et al, 2018. 2. Storey et al., 2024.



LNTH-1363S: FAP

Potential to Replace 18F-FDG Particularly in Brain, Liver, Gastro-Intestinal Cancers

PRODUCT DESCRIPTION



64Cu-LNTH-1363S

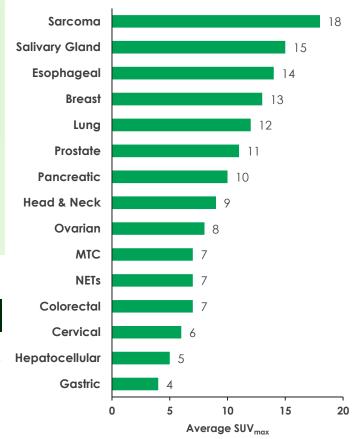
LNTH-1363S is a novel, investigational FAP-targeted, small molecule compound comprising a FAP binding domain, an albumin-binding domain for PK modulation and a chelator to contain a radionuclide

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	⁶⁴ Cu			FPI expected in 2025
Cardiac	⁶⁴ CU			
COPD/CLAD	⁶⁴ Cu			Exploratory collaborative studies
MASH	⁶⁸ Ga / ⁶⁴ Cu			in discussion
Fibrosis	Undisclosed			

68Ga-FAPI UPTAKE IN VARIOUS TUMORS1



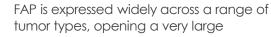
EVIDENCE FOR TARGET VALIDATION^{1,2,3}

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

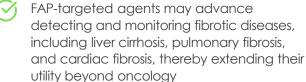
FAP is nearly absent in healthy tissues, but highly upregulated during tissue remodeling in embryogenesis, cancer, and fibrosis

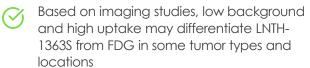
In chronic diseases, persistent activation of FAP+ fibroblasts (promoted by TGF-β) leads to excessive extracellular matrix deposition contributing to organ fibrosis in conditions like pulmonary fibrosis. cardiac fibrosis, and liver cirrhosis

DIFFERENTIATED VALUE PROPOSITION **ANTICIPATED**



tumor types, opening a very large opportunity for imaging of various cancers





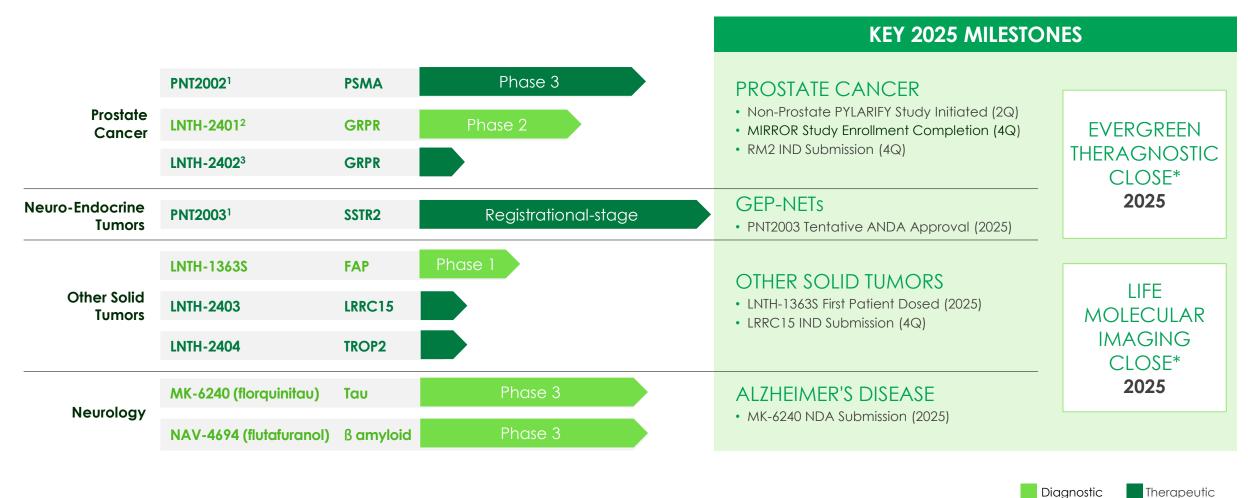
 Imaging studies with ⁶⁸Ga-FAPI-04 have demonstrated positive uptake in a wide range of tumors

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



Key 2025 Milestones

Advancing our Diversified Portfolio in High Value Markets



Diagnosiic Diagnosiic

^{1.} Collaboration with POINT Biopharma Global Inc. 2. Also known as ⁶⁸Ga-RM2 3. Also known as ¹⁷⁷Lu-RM2



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^{*} Subject to customary closing conditions.

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





Appendix

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Reconciliation of GAAP to Non-GAAP Financial Measures

(in thousands, except per share data – unaudited)

1101 (1000) INCOME	2023 36 \$ 4.65 07 0.72
	
Stock and incentive plan compensation 22,164 14,172 76,393 50,507 Stock and incentive plan compensation 0.31 0.20	0.72
Amortization of acquired intangible assets 11,846 11,308 43,807 46,440 Amortization of acquired intangible assets 0.16 0.16 (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) - (0.02)	04) (0.13)
Non-recurring refinancing related fees - 5 - 221 Non-recurring refinancing related fees	
1401116Conning 1663	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 (o) - 00,215 - 00,215	92 -
117,000 = 45,004 =	61 -
Acquisition related costs 207 107 1,555 070	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 0.01	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) (0.12)	80) (1.00)
	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,	51 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)

	Inree Mon Decem		iths Ended iber 31,		lweive Mor Decem			
		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)



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

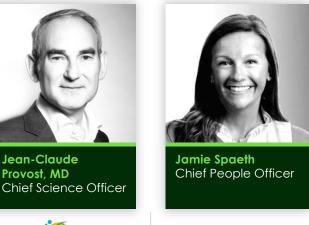


































Corium



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McKinsey & Company



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























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 marketleading 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



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Utilized PSMA PET Imaging Agent¹

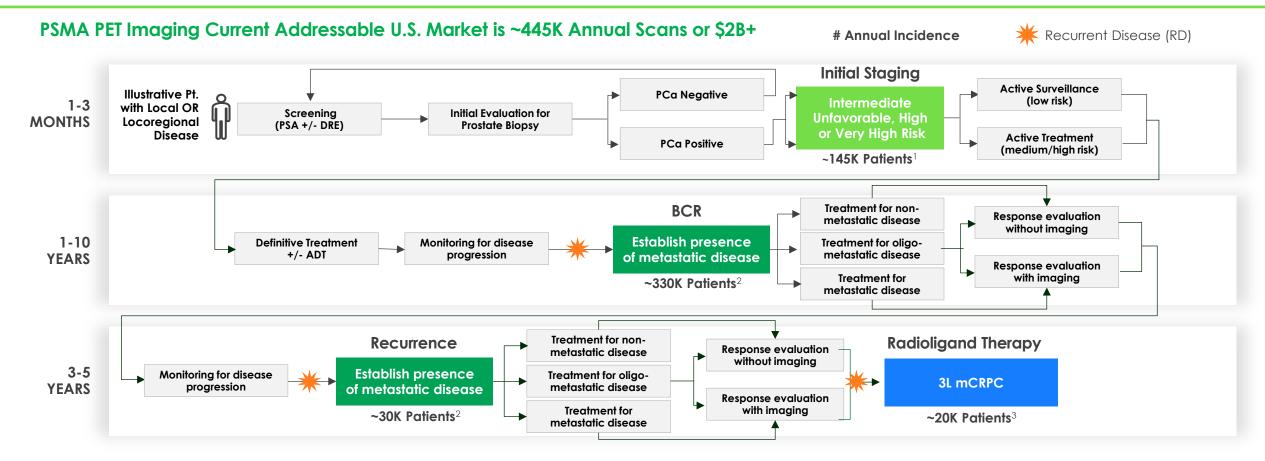


PYLARIFY is a radioactive diagnostic agent indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer

- with suspected metastasis who are candidates for initial definitive therapy
- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level²



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



Estimated 2-3% annual growth due to increasing incidence / prevalence⁴

^{4.} Lantheus market research and analysis with ordering physicians, NCCN, ACS, UpToDate, SEER.



^{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.

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:

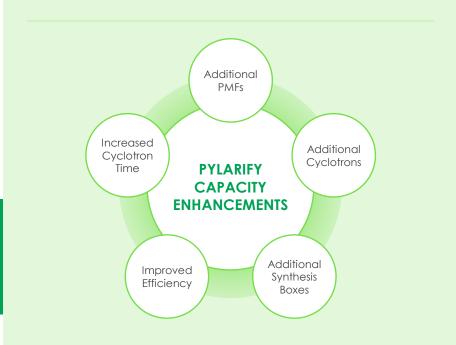
40+ PYLARIFY doses per batch

Some PMFs producing:

3 batches per day;5 days per week

90%+ of covered lives have access to PYLARIFY2

Contracted with 100% of our targeted academic centers²



PMF = PET Manufacturing Facility.

1. IMV 2022 PET Imaging Market Summary Report; 2.Data on file.



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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 border¹



Leading U.S. Ultrasound Enhancing Agent²

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

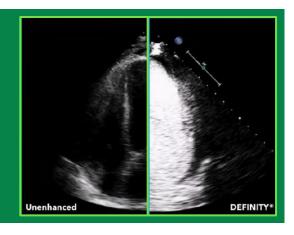
peer-reviewed publications

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



^{2.} DEFINITY® [package insert]. N. Billerica, MA: Lantheus, Inc.



^{1.} Data on file, Lantheus.

DEFINITY® Reduced the Need for Additional Cardiac Imaging and Decreased the Length of a Hospital Stay¹



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

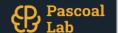
1. Kurt M, Shaikh KA, Peterson L, et al. Impact of contrast echocardiography on evaluation of ventricular function and clinical management in a large prospective cohort. J Am Coll Cardiol. 2009;53(9):802-810.





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

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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.

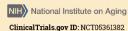
Study Design & Methods

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 . Dementia 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), Pl-2620 (45-75 mins), and R0948 (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 MK-6240 PET 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.





Funding: NIA 5 R01 AG073267



Measure Collection Status in Enrolled Participants

















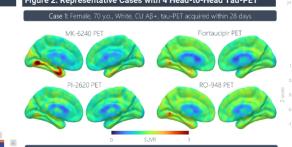


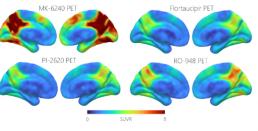
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The HEAD Study Cohort

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 APOEs4 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 Young ●CU ●MCI ●Dementia





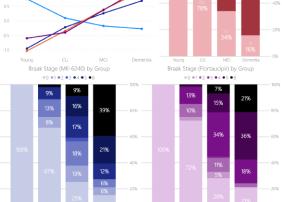


Figure 3: Clinical Characteristics of the HEAD Study Cohort

APOE4 Carrier Status - CI

ε4 alleles ●0 ●1 ●2

■ AB42/40 Ratio ■ NfL ■ GFAP ■ PTau217

64 alleles ●0 ●1 ●1

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.

■ Nanativo ■ Positivo

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

Acknowledgement:

The HEAD cohort would not have been possible without the time and commitment provided by our research participants and their partners. We would also like to thank every performance site's investigators and dedicated study members for all their contributions in the implementation, data collection, and findings in the HEAD

Lussier FZ, Povala G, Bauer-Negrini G, et al. Longitudinal multicenter head-to-head harmonization of tau-PET tracers: an overview of the HEAD study cohort. Alzheimers Dement. 2025;20(Suppl 9):e094013. Published 2025 Jan 9. doi:10.1002/alz.094013



University of Pittsburgh

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

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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 ptau217 abnormalities as a function of Aβ PET deposition. We further assessed the concordance between tau PET and plasma ptau217 positivity.



353 individuals from the HEAD cohort:

19 cognitively unimpaired young (<25 years old)

186 cognitively unimpaired elderly

148 cognitively impaired

AO DET

Methods

A β PET $\begin{cases} [^{18}F]MK6240 \\ [^{18}F]Flortaucipir \end{cases}$

- P-tau217 (AlzPath)

- Tau PET and plasma p-tau217 trajectories were modeled as functions of $\mbox{A}\beta$ 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

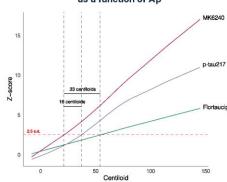


Figure 1. Robust linear regressions show MK6240 (Braak I region), Flortausipir (Braak 1 region) and plasma p-tau217 increase as a function of AB burden (n = 353), Young individuals (n = 19, < 25 years old) were used as anchors to z-scores.

Agreement between plasma p-tau217 and tau PET positivity

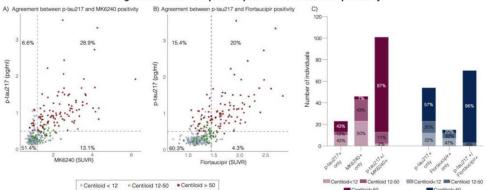


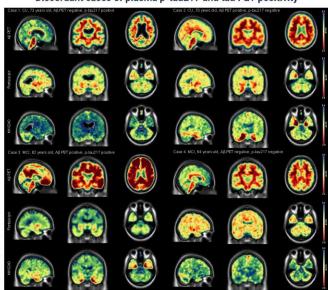
Figure 2. Agreement between plasma p-tau217 and (A) MK6240 or (B) Flortaucipir positivity. The dotted lines represent the cutoff for plasma p-tau217 and tau PET (in Braak 1 region) defined as 2.5 s.d. higher than the mean of young individuals. (C) Number of individuals according to their plasma p-tau217,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

Conclusion

MK6240 becomes abnormal at lower levels of $A\beta$ 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.

Figure 3. Case 1: cognitively unimpaired (CU), 73 years old plasma ptau217 positive individual with negative soan for AB PET (PIB), Flortaucipir and MK6240. Case 2: CU 70 years old individual plasma ptau217 negative (0.28 pyrlm inseasured in duplicate; threshold for positivity = 0.504 pyrlm) with positive AB PET (AZD4694), Flortaucipir, and MK6240. Case 3: MCI, 82 years old positive for plasma p-tau217, AB PET (PIB) and MK6240 but negative for floraucipir. Case : MCI, 64 g years old negative for plasma p-tau217, AB PET (AZD4694) and MK6240 but positive for floraucipir.

Discordant cases of plasma p-tau217 and tau PET positivity



Presented at the 2025 Human Amyloid meeting in Puerto Rico, January 2025.



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



NASDAQ: LNTH



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