eyonis™ LCS: new horizons in fighting lung cancer

Next generation AI/ML tech-based Software as Medical Device (SaMD) to help diagnose lung cancer patients at early stage

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Company Webcast

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Lung Cancer Screening

I-ELCAP study showed a 92% survival rate at 15y when diagnosed at stage 1 vs. 5% for stage 4 (1)
Lack of diagnosis accuracy is a major hurdle to screening adherence & programs implementation

Facts & Figures

Lung Cancer

- 1st cancer killer worldwide - 18% of all 2020 cancer deaths, equal to colorectal & liver cancers combined (2)
- 1.8M deaths in 2020, 2.4M projected in 2030 (2)
- A new CPT reimbursement code of $650 for quantitative CT tissue characterization in the US
- The Lung Cancer Screening TAM is $10-20bn for the US & EU and could double with Asia
- Rising frequency among never-smokers, 20% in the US & UK (3)
- Only 870K screenings performed in the US in 2021 – 6% compliance (4)

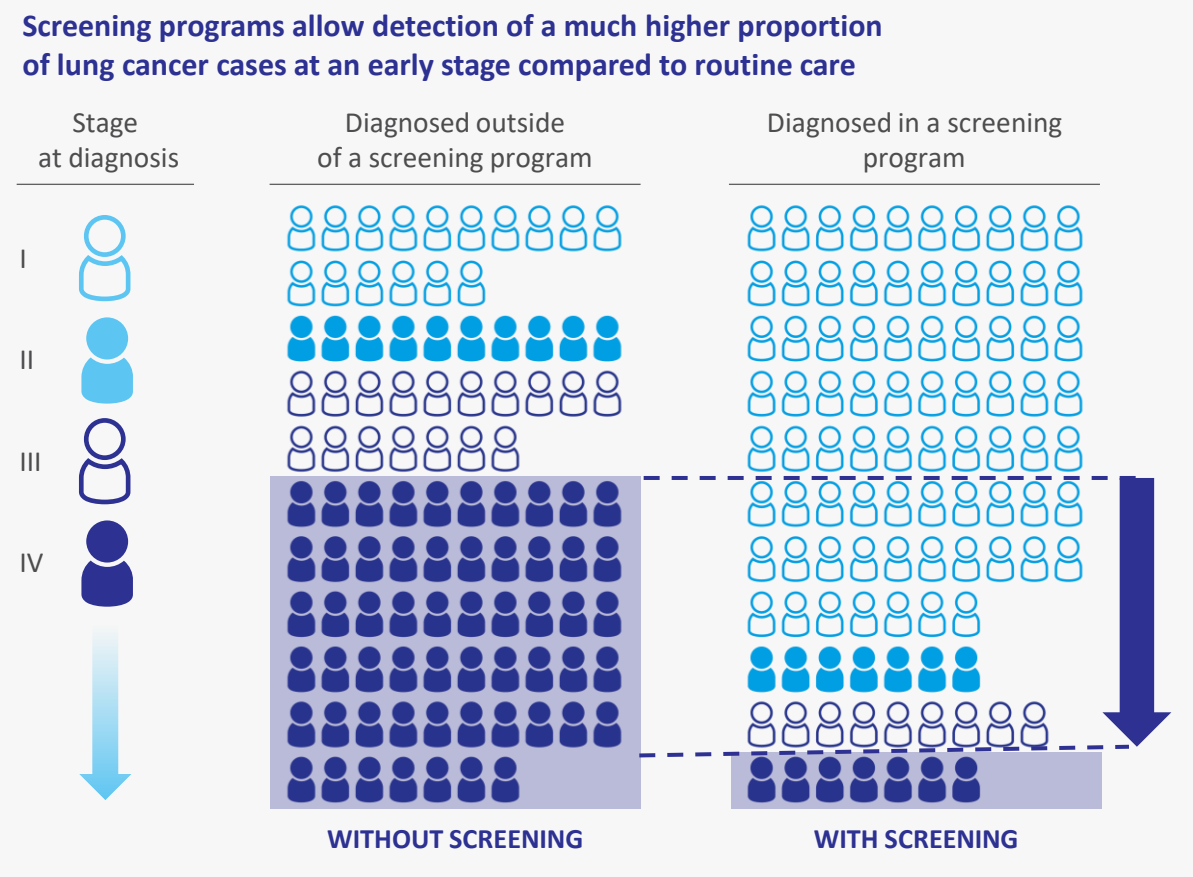
Target Population

	LCS Programs	Target population
US	Implemented - USPSTF guidelines	19M (ACR 2023 recommendations)
Europe	Implemented in Croatia & Poland - Starting in UK - Developing in IT/FR/GE/SP/NL/SW	EU T5: 22M (Est.)
Asia	Implemented in SK nationally & China regionally - Japan/Taiwan study phase	ASIA T3: 100M (Est.)

Sources:
[1] https://www.redjournal.org/article/S0360-3016(19)30110-5/fulltext
[2] Cancer Tomorrow, IARC, Global Cancer Observatory 2020 - WHO
[3] https://www.lungambitionalliance.com/our-initiatives/lung-cancer-screening-the-cost-of-inaction.htm
[4] https://nrdrsupport.acr.org/support/solutions/articles/11000093991-lcsr-state-reports

Lung Cancer Screening – the Path to Save Lives

3 landmark studies: I-ELCAP 92% survival rate at 15y when diagnosed at stage 1 vs. 5% at stage 4 – NLST & NELSON revealed stage shift with LDCT - AI LDCT can increase this trend



Adapted from Sands et al. (2021). Patient decision-making aid based on combined analysis of existing clinical trials.

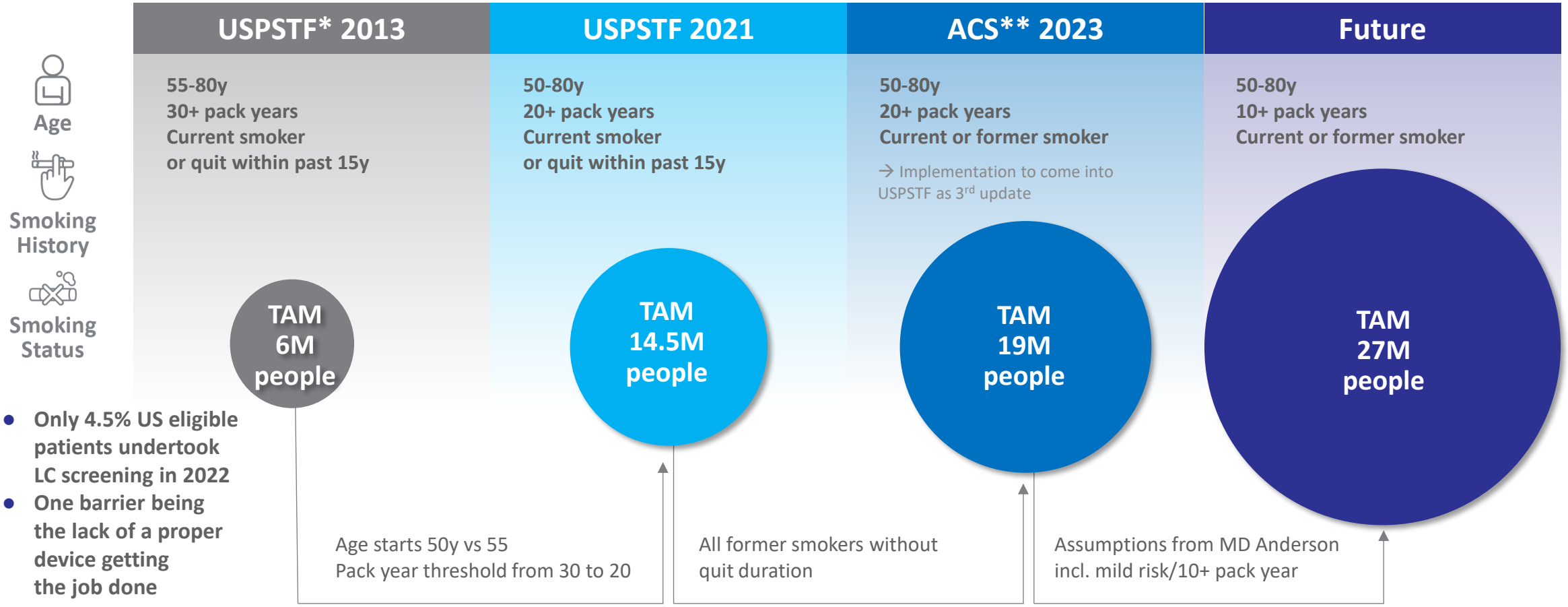
- **NELSON** trial showed LDCT screening impact: **59% cases were early-stage** vs 14% with no screening
- **24% reduction of lung cancer mortality after 10-years vs no screening**
- **NLST showed a 20% deaths decrease with LDCT screening vs chest X-Ray**

Significant stage shift leading to earlier & better patient care and lower mortality rate

NLST: *US based National Lung Screening Trial (53454 participants, 2002-2004)*
NELSON: *Dutch-Belgian Randomized Lung Cancer Screening Trial (15792 participants, 2004-2012)*
LDCT: Low Dose Computed Tomography

USA Total Addressable Market (TAM) Evolution Horizon

Lung cancer screening program in place - evolving LCS guidelines will broaden TAM



- **Only 4.5% US eligible patients undertook LC screening in 2022**
- **One barrier being the lack of a proper device getting the job done**

(*) USPSTF: United States Preventive Services Task Force
(**) ACS: American Cancer Society

Favorable US Pricing & Reimbursement Context

Existing CPT III codes for tissue characterization under CT - 0721T & 0722T
CMS payment for 2 CPTIII codes assigned to New Tech APC 1508 - Level 8 ($601 - $700)

Total Medicare Hospital payment is LDCT $107 + eyonis LCS $650

Codes CPT code	CPT description	Existing LDCT images	Hospital Outpatient Payment
71271 APC 5522	Computed tomography, thorax, low dose for **lung cancer screening**, without contrast material(s)	LDCT	$107
0721T **APC 1508**	**Quantitative CT tissue characterization**, including interpretation and report, obtained *without* concurrent CT examination of any structure contained in previously acquired diagnostic imaging Do not report 0721T in conjunction with 71271	YES	**$650**
0722T **APC 1508**	0721T **but *with* concurrent CT** examination is code 0722T Use 0722T in conjunction with 71271	NO	**$650** + $107

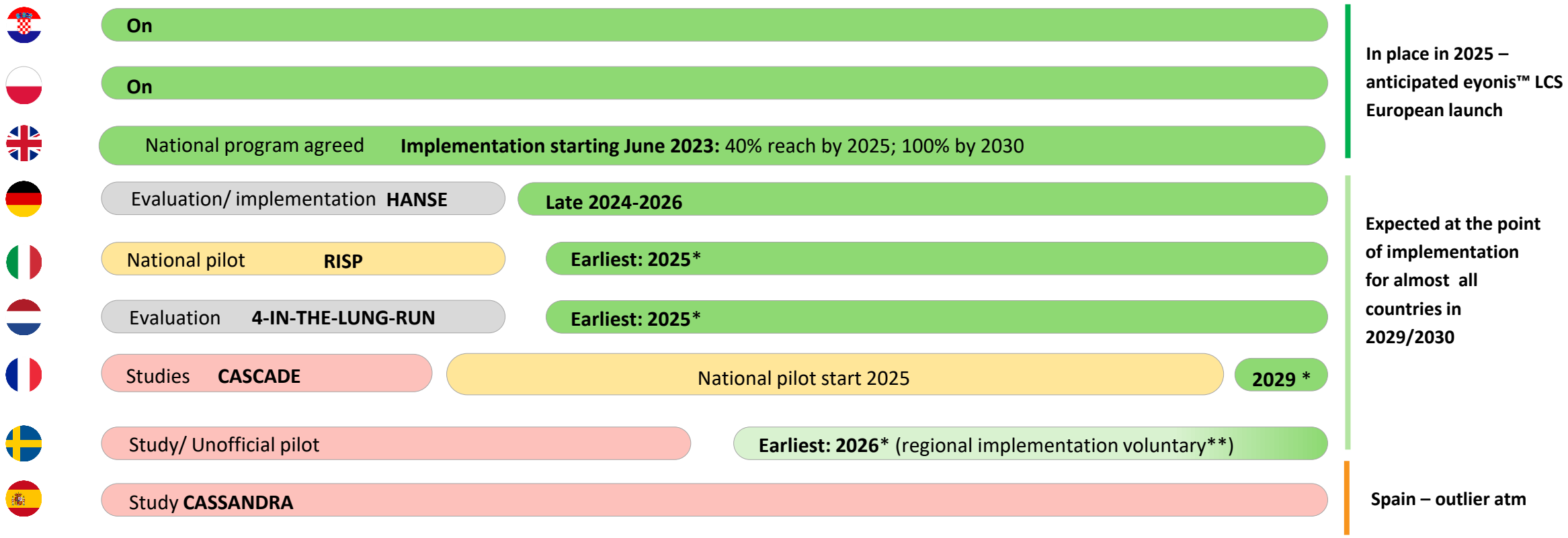
These two procedures provide an LDCT and tissue characterization & are billed on separate days

The tissue characterization is "added-on" to the LDCT & are billed on the same day

CMS CY 2023 Medicare Hospital Outpatient Prospective Payment System and Ambulatory Surgical Center Payment System Final Rule

2024 European LCS Status – 3 National Programs Started

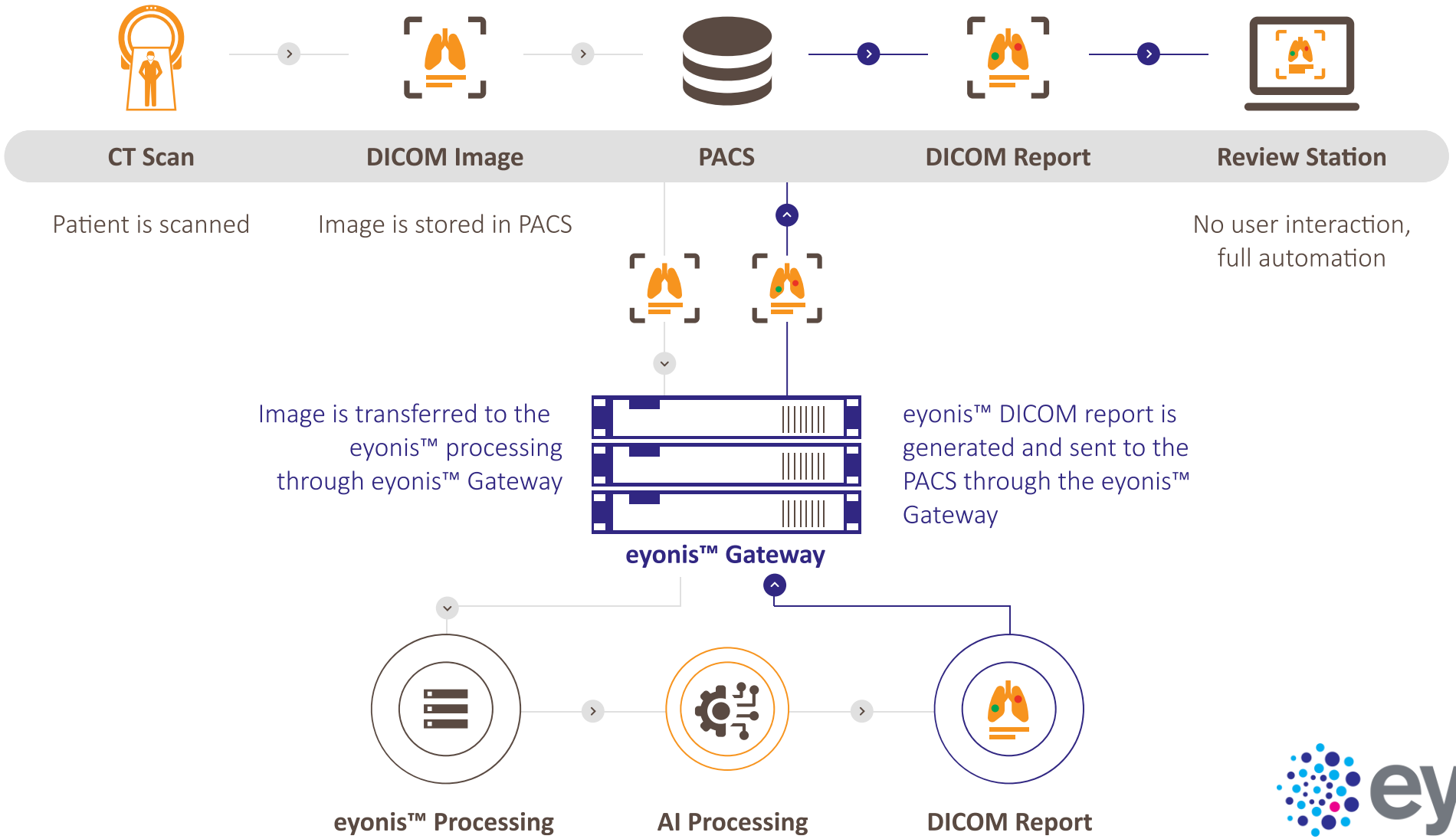
Target eligible population in Europe: 22 million people



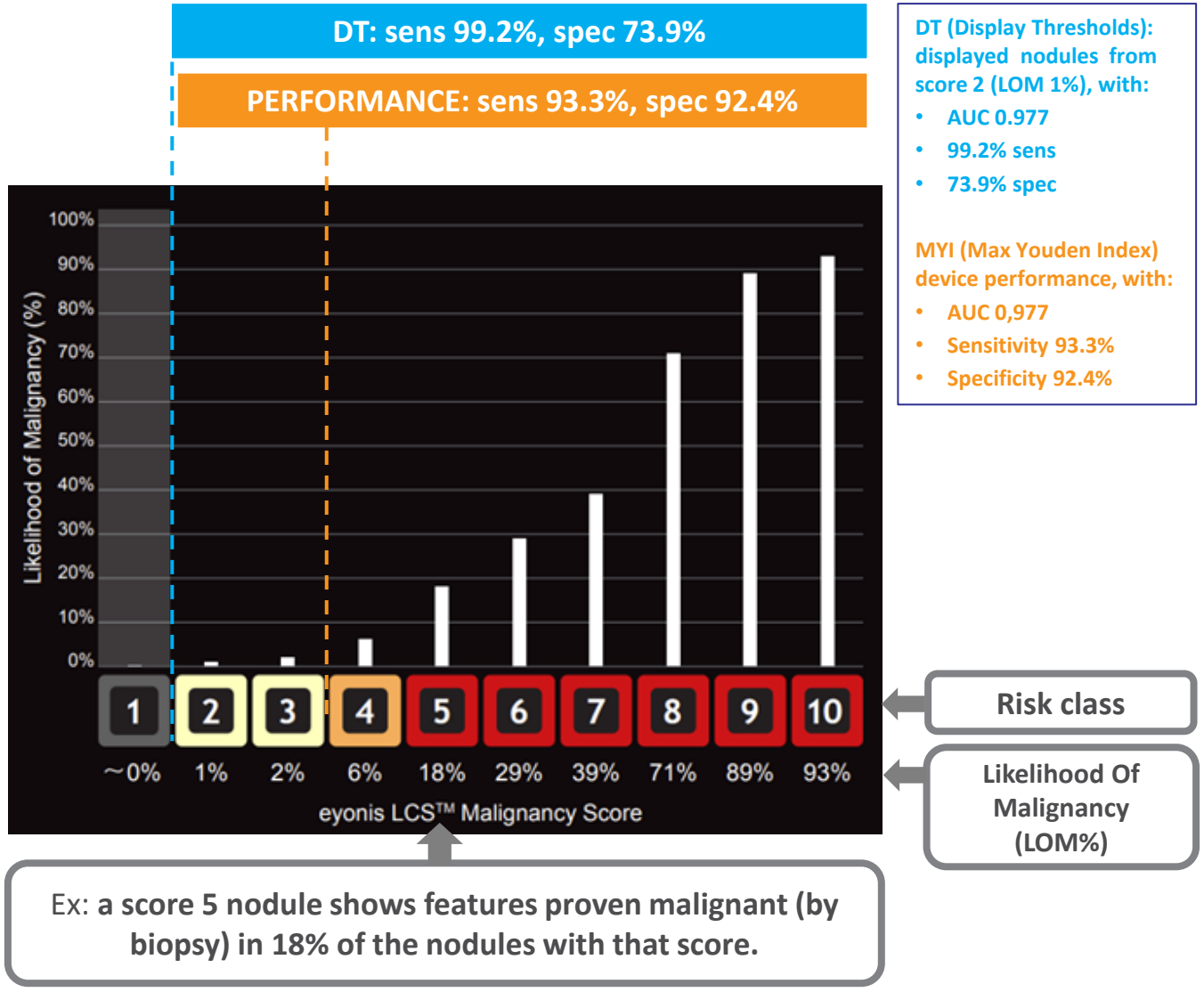
* Estimated, not based on any authority communication

** Assumed implementation rule

eyonis™ Integration in the Radiology Workflow



eyonis™ LCS Report & Malignancy Risk Score



DT (Display Thresholds): displayed nodules from score 2 (LOM 1%), with:
- AUC 0.977
- 99.2% sens
- 73.9% spec

MYI (Max Youden Index) device performance, with:
- AUC 0,977
- Sensitivity 93.3%
- Specificity 92.4%

Risk class

Likelihood Of Malignancy (LOM%)

Ex: **a score 5 nodule shows features proven malignant (by biopsy) in 18% of the nodules with that score.**

*Jonas DE, Reuland DS, Reddy SM, et al. Screening for lung cancer with low-dose computed tomography: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. doi:10.1001/jama.2021.0377

eyonis™ LCS

- **Detects benign, suspicious & malignant nodules**
- **Only shows suspicious & malignant nodules on report starting from 1% Likelihood Of Malignancy (LOM%)** so radiologists can focus on most important nodules
- **LOM% = probability of a nodule to be cancerous**
- **LOM% determined by the device ability to identify nodules** that **share statistically similar features** with **nodules known to be malignant during its training, biopsy proved (Ratio malignant nodules / total nodules identified for each score)**

- **eyonis™ LCS identifies nodule features by analyzing dimensional & complex visual features at both nodule & lung levels**
- **Standard-of-Care calculated by expert radiologists considers dimensional features only at nodule level only**

eyonis™ LCS Pivotal Standalone REALITY Study

Clinicaltrials.gov identifier: NCT0657623

A Study to evaluate the performance of eyonis™ LCS to detect, localize and characterize pulmonary nodules at baseline (first scanner of the patient) compared to the ultimate biopsy ground truth

- **Data from 5 academic centers + 2 data providers**
- **Enriched population: 342 cancers, 805 benign cases (1,147 cases in total)**
- **Objectives:**
  1. Assess device's standalone performance in characterizing positive and negative patients
  2. Assess device's standalone performance in detecting and characterizing suspicious/malignant nodules

Ground truth Generation	***eyonis™ LCS SaMD image analysis***
• 2 + 1 truthers (regular truthers - experienced radiologists + adjudicator truthers - senior radiologists), w/ all clinical data • Assess lesions' location, segmentation, type, malignancy / benign status to establish "ground truth"	• End-to-end analysis by AI/ML tech based SaMD CADe/x • Detection, localization, segmentation & malignancy score • Generate a statistical report

Statistical Analysis

Comparison of truthers ground truth VS. eyonis™ LCS SaMD output: "**How good is eyonis™ LCS**"

Primary Endpoint :

AUROC that measures eyonis™ LCS performance on patient level data > 0.8

Universal Diagnostic Performance Standards: Sensitivity, Specificity, False Positive, False Negative

Table 1. The Decision Matrix

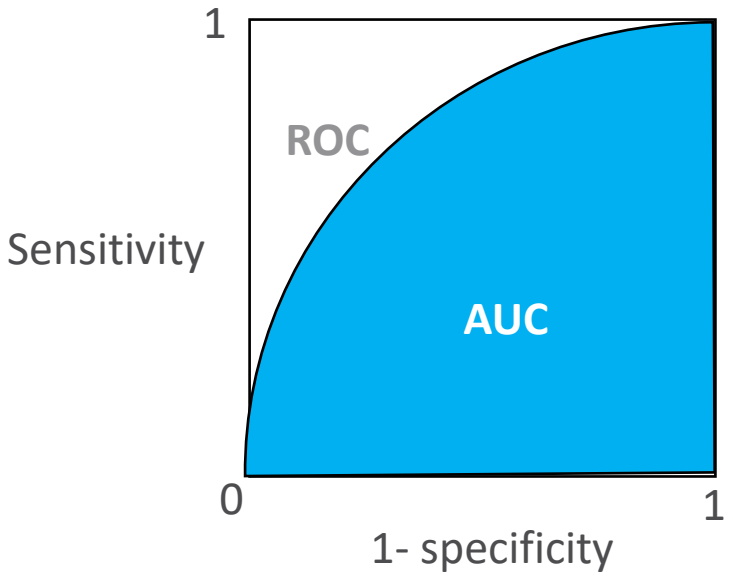
		Predicted condition	
		Test (+)	Test (–)
True condition	Disease (+)	a	b
	Disease (–)	c	d

The receiver operating characteristic curve is drawn with the x-axis as 1 - specificity (false positive) and the y-axis as sensitivity. sensitivity = a / (a + b), specificity = d / (c + d), false negative = b / (a + b), false positive = c / (c + d), and accuracy = (a + d) / (a + b + c + d).

*Korean J Anesthesiol 2022;75(1):25-36 https://doi.org/10.4097/kja.21209 pISSN 2005–6419 • eISSN 2005–7563

- **Sensitivity** is defined as the proportion of people who actually have a target disease that are tested positive
- **False Negative** (FN) refers to the proportion of people that have the disease but are incorrectly tested negative
- **Specificity** is the proportion of people who do not have a target disease that are tested negative.
- **False Positive** (FP) refers to the proportion of people that do not have a disease but are incorrectly tested positive

Universal Diagnostic Performance Standards: Area Under the Curve (AUC) & Receiving Operating Curve (ROC)



AUC (or AUROC): area below the ROC as shown in the figure

- ROC (Receiving Operating Curve) - an analytical method that is used **to evaluate the performance of a binary disease diagnostic classification method**
- ROC (Receiving Operating Curve) - a graph obtained by calculating a test sensitivity & specificity at every possible cut-off point, and plotting sensitivity against 1- specificity
- Area Under the Curve (AUC) or Area Under the Receiving Operating Curve (AUROC) quantifies overall performance of a given classification model & summarizes ROC curve in one number.

Interpreting AUC – Entire Scale from 0 to 1

Yet value scale from 0.5 to 1 – where 0.5 is meaningless and ≥ 0.9 is excellent

Table 4. Interpretation of the Area Under the Curve

Area under the curve (AUC)	Interpretation
0.9 ≤ AUC	Excellent
0.8 ≤ AUC < 0.9	Good
0.7 ≤ AUC < 0.8	Fair
0.6 ≤ AUC < 0.7	Poor
0.5 ≤ AUC < 0.6	Fail

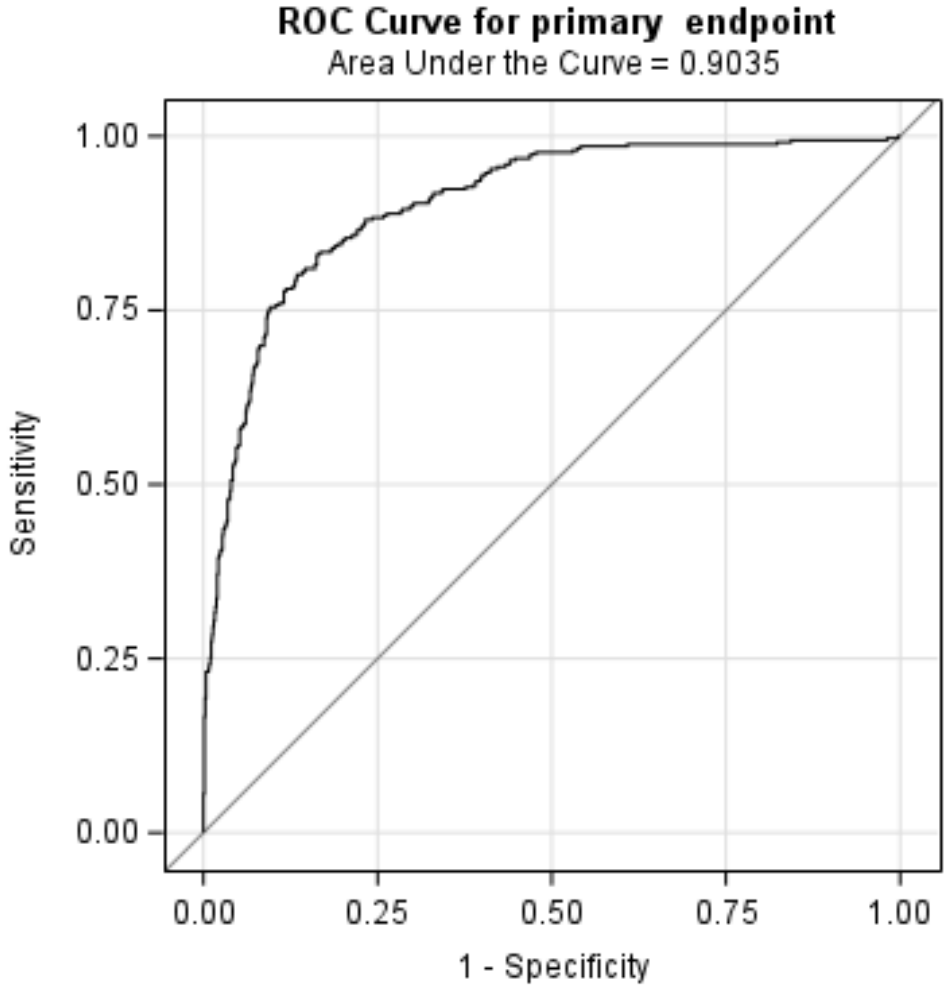
For a diagnostic test to be meaningful, the AUC must be greater than 0.5. Generally, an AUC ≥ 0.8 is considered acceptable.

*Korean J Anesthesiol 2022;75(1):25-36 https://doi.org/10.4097/kja.21209 pISSN 2005–6419 • eISSN 2005–7563

- AUC value ranges from 0 to 1, where 0.5 represents random chance, and 1 indicates a perfect classifier.
- The higher the AUC, the better the model's ability to distinguish between positive and negative instances.

REALITY Study Results: Primary endpoint met: Excellent AUC

High performance for detection & characterization of cancerous nodules in a more challenging population (enriched population)



AUC = 0.9035 [0.881-0.926], p value <0.001

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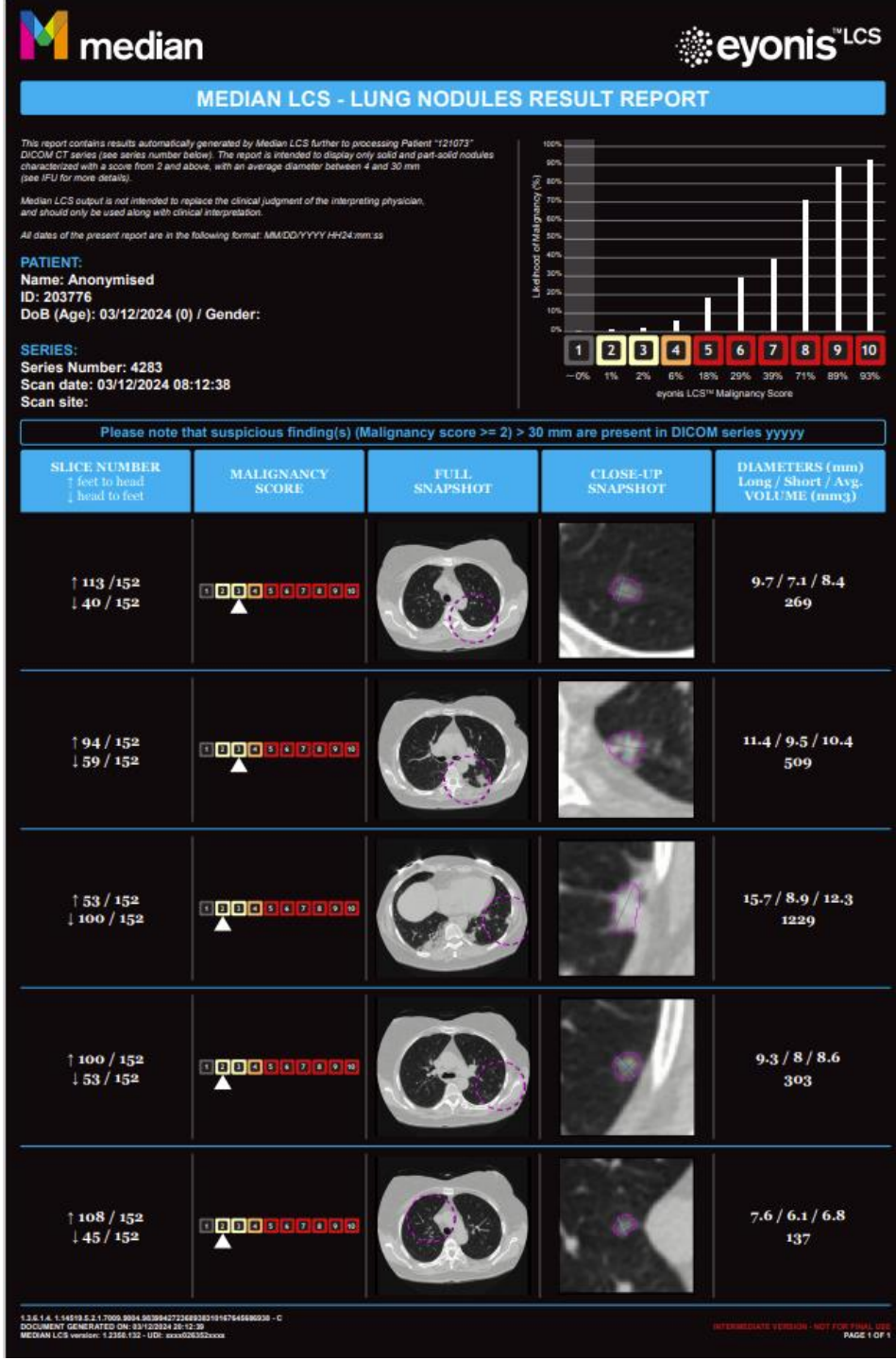
REALITY Study - All 10 objectives passed

Objective	Criteria	p-value or conclusion	Report features
Primary	**H1: AUC of ROC (patient level) > 0.8**	**Success**	Malignancy Score
Secondary	H2: Sensitivity > 70% when Specificity=70%	**<.0001 Success**	Malignancy Score
Secondary	H3: Specificity > 70% when Sensitivity=70%	**<.0001 Success**	Malignancy Score
Secondary	H4: AUC of LROC > 0.75	**Success**	Slice number “feet to head” & “head to feet” to ensure maximum compatibility with all viewers
Secondary	H5: Detection sensitivity>0.8 with average FP rate per scan<1	**Success**	Full Snapshots – Close-up snapshot
Secondary	H6: ICC>0.8 for average diameter	**Success**	Dimensional information (LA Diameter mm, volume mm3)
Secondary	H7: ICC>0.8 for long axis diameter	**Success**	Dimensional information (LA Diameter mm, volume mm3)
Secondary	H8: ICC>0.8 for short axis diameter	**Success**	Dimensional information (LA Diameter mm, volume mm3)
Secondary	H9: ICC>0.75 for Volume	**Success**	Dimensional information (LA Diameter mm, volume mm3)
Secondary	H10: Dice coefficient > 0.7	**Success**	Dimensional information (LA Diameter mm, volume mm3)



REALITY Study: Cancer Stage in Study Population

Almost 80% of cancerous cases are in Stage 1

Cancer Stage	Cancerous in REALITY
Stage 0	1 (0.4%)
Stage I	**218 (79.27%)**
Stage II	13 (4.7%)
Stage III	24 (8.7%)
Stage IV	19 (6.9%)

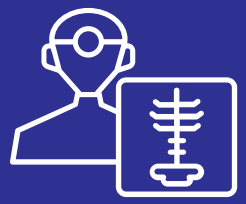
Eyonis™ LCS Could Help Improve Radiologists' Diagnosis

Expert radiologists highly trained in lung cancer screening only reach 80% sens & 76% spec

eyonis™

vs

Radiologists



TRIAL NAME	MODEL	PATIENT SIZE	SCAN TYPE	SENSITIVITY	SPECIFICITY
DANTE Infante, 2015	Human with software support	2,450	LDCT	79.5%	75.5%
LUSI Becker, 2015	Human with software support	2,028	LDCT	93.5%	62%
MILD Sverzellati, 2016	Human with software support	1,152	LDCT	68.5%	99.2%
MILD Sverzellati, 2020	Human with software support	1,151	LDCT	73.5%	99.2%
NELSON De Koning, 2020	Human with software support	6,583	LDCT	59%	95.8%
NLST Pinsky, 2013	Human with software support	26,022	LDCT	93.1%	76.5%
ITALUNG Lopes Pegna, 2013	Human with software support	1,406	LDCT	95%	26.4%
MEAN sens & spec			**LDCT**	**80.3%**	**76.4%**

2021 American Medical Association - Cochrane Library. Jonas DE, Reuland DS, Reddy SM, et al. Screening for lung cancer with low-dose computed tomography.

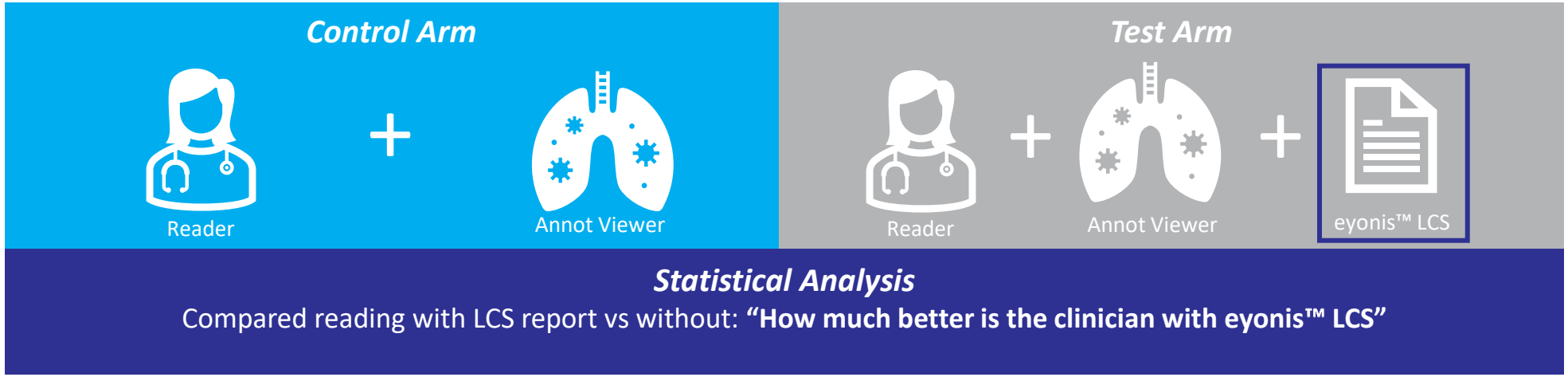
TRIAL NAME	MODEL	PATIENT SIZE	SCAN TYPE	SENSITIVITY	SPECIFICITY
Median NLST Test Sep 2023	eyonis™ LCS – Manufacturer Value	2,143	LDCT	93.3%	92.4%

Nota: Performance results obtained on different cohorts

eyonis™ LCS Pivotal RELIVE Trial

A Multi-Reader Multi-Case Trial

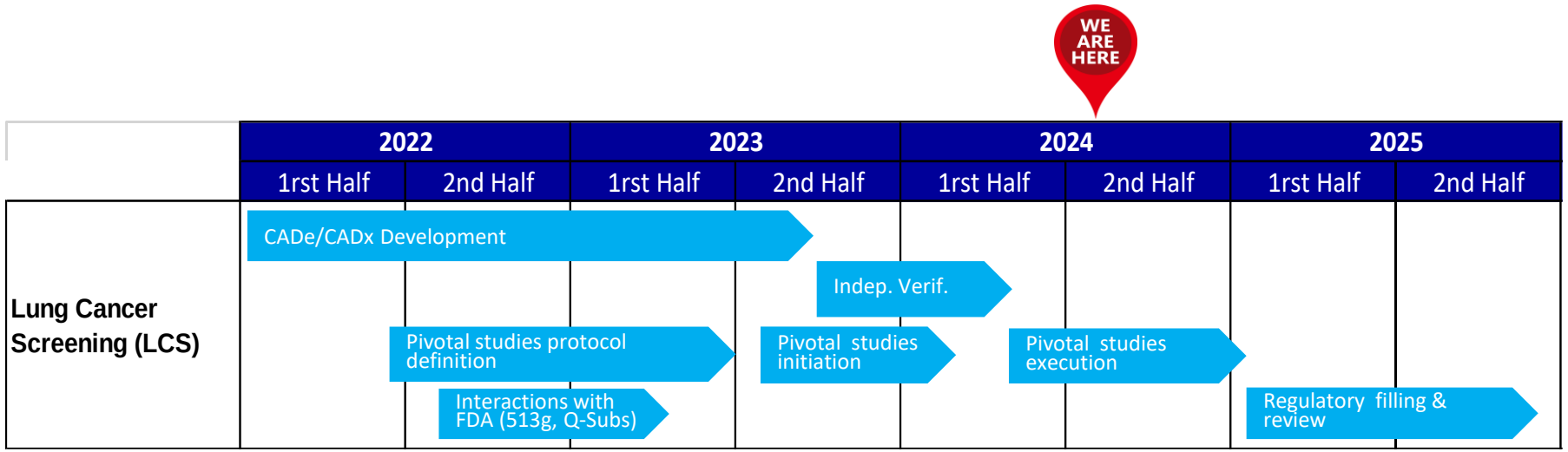
- 480 patients (160 cancers, 320 benign cases) and 16 readers
- Enriched cohort with a 1:2 distribution of cancer positive and cancer negative patients
- Paired-split-plot design
- **Objective: Demonstrate that eyonis™ improves clinician performance in analyzing LDCT lung screening scans, reducing FPs and unneeded follow-up procedures**



Primary Endpoint

Difference between with & without Median LCS in AUROC values that measures the modality performances on patient level data. Superiority with LCS report vs without to be achieved.

2024-2025 Key Milestones for eyonis™ LCS Clinical Plan



eyonis™ LCS Standalone Study Standalone - REALITY)	Release of topline study results: Q3 2024 (released)
eyonis™ LCS Multi-Reader Multi-Case Study (MRMC, RELIVE)	Release of top-line study results : Q1 2025
CADe/CADx SaMD eyonis™ LCS filing (FDA 510(k))	H1 2025
CADe/CADx SaMD eyonis™ LCS filing (CE marking)	H1 2025

2024-2025 Key Milestones for SaMD eyonis™ LCS Launch Strategy

4 key milestones for the remainder of 2024 & 2025 in complement of the clinical plan

1| Continued engagement with US KOLs pulmonologists & radiologists and initiate device trial use under research agreements

2| Engage payers with HEO-M for reimbursement discussions and reach-out to distribution partners

3| Launch Health economics studies discussions to support reimbursement code negotiation with payers

4| Prepare for setting up full US commercial organization

Median eyonis™ LCS Partnerships & Opportunities

Seven segments for partnerships and potential opportunities

PHARMA
Increase diagnosed patients for drug treatment
Overcome Pharma efficiency challenge & accelerate drugs development

MEDICAL DEVICES
Increase diagnosed patients to drive surgical intervention and radiation treatments

LIQUID BIOPSY
Offer best in class cancer continuum of care from early detection to therapy monitoring

median eyonis™

- Partnership visibility/Brand equity
- Product development (Tech or funds)
- Network/KOLs
- Distribution/Customer base/Revenue generation

BIG TECH
Support faster development & deployment thru Cloud solutions & GPS computing power enablers technology & business connections

AI SaMD
Leverage product capabilities
Expand product portfolio

RADIOLOGY /IMAGING
Address deployment & integration challenges

MARKET PLACES
Provide a discovery, distribution & monetization channel with users

eyonis™ LCS - Next Steps

1

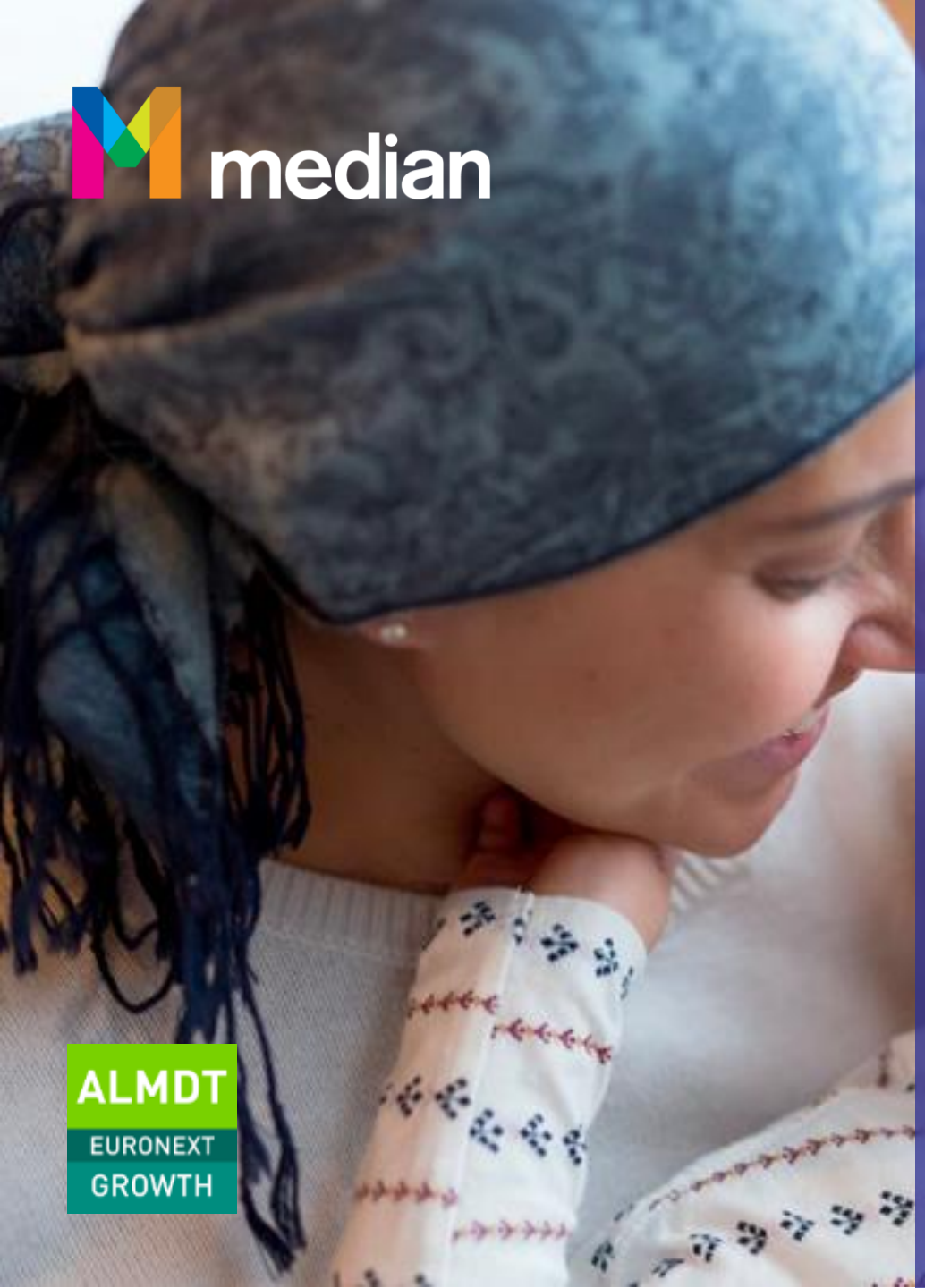
Complete pivotal RELIVE study, file and obtain health authorities clearances

2

Sign distribution partnership agreements

3

Roll out launch plan and start revenue generation in H2 2025 in the US



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ALMDT
EURONEXT
GROWTH

Our Core Values

Leading innovation with purpose
Combine the spirit of innovation with our passion and conviction to help cure cancer and other debilitating diseases.

Committing to quality in all we do
Be dedicated to quality in everything we do. Quality begins with us and we are committed to it.

Supporting our customers in achieving their goals
Listen to the needs of our customers and help make their goals our goals through our innovation, imaging expertise, superior services, and quality solutions.

Putting the patient first
There is a person at the other end of the images we analyze who is counting on us to do everything we can to help make them healthier.

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