

Practical Assessment of Liver Fat for NAFLD-NASH



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INVESTOR PRESENTATION -MAY 2022

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ENDRA Life Sciences: Investment Highlights

PROPRIETARY SCALABLE PLATFORM

- Thermo Acoustic Enhanced Ultrasound (TAEUS®) uses radio frequency pulses to create sonic waves
- TAEUS differentiates tissues similar to MRI but at 50x lower cost,¹ at the point of patient care
- Potential to address multiple unmet clinical needs, and generate diverse revenue streams
- TAEUS CE mark received in Europe, and FDA De Novo request planned for Q3 2022 in the U.S.

MULTI-BILLION DOLLAR MARKET

- First TAEUS indication focused on NAFLD-NASH with no practical diagnostic tools
- 1.8 billion people² affected with excess liver fat. \$12.5 billion global market opportunity³

EXTENSIVE PATENT PORTFOLIO: DEFENSIVE & OFFENSIVE VALUE

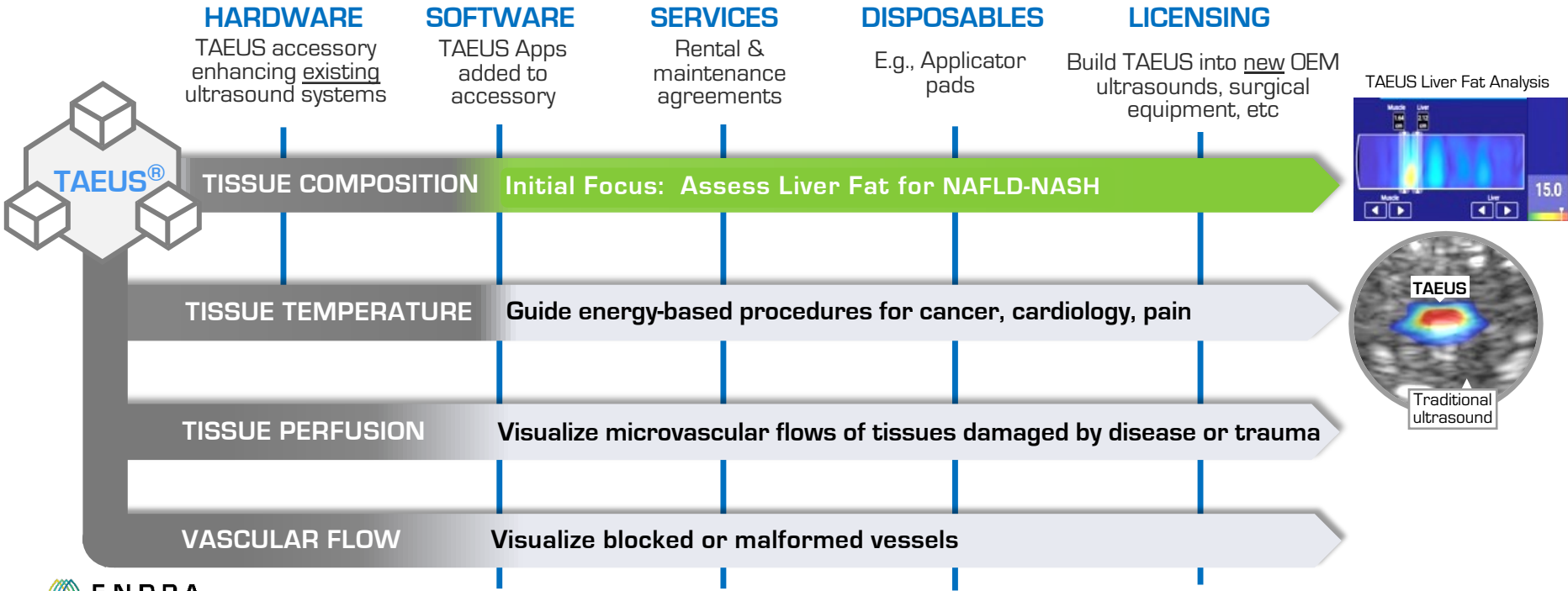
- 90 internally-developed global IP assets,⁴ including 46 issued patents.

CAPITAL-EFFICIENT OPERATING MODEL

- Small ENDRA team + world-class technical, clinical and commercial partners

TAEUS[®] Platform Evolution¹ & Business Model

START WITH LIVER-FOCUSED ACCESSORY & SOFTWARE ENHANCING EXISTING ULTRASOUND SYSTEMS,
THEN SCALE WITH ADDITIONAL CLINICAL APPLICATIONS & REVENUE STREAMS



ENDRA's 1st Target: Large Unmet Need in NAFLD–NASH Diagnostics

RAMPANT DISEASE, APPROACHING THERAPIES ... BUT NO PRACTICAL DIAGNOSTIC TOOLS

Liver Disease: NAFLD–NASH

Accumulation of fat (>6%) in liver

1.8 billion people affected.¹

Linked to obesity, diabetes, genetics

Can progress asymptotically to liver fibrosis, cirrhosis, cancer

Increased risks with NAFLD^{2,3}

- Cardiovascular disease: 1.6x
- Chronic kidney disease: 1.2x

Annual U.S. medical costs >\$100B⁴

Diagnostic Gap

Currently no practical diagnostic tools:

- **MRI:** \$2M–\$3M, 5 tons, not point-of-care, concentrated in urban areas
- **Liver biopsy:** Invasive, painful

1st Therapies Near

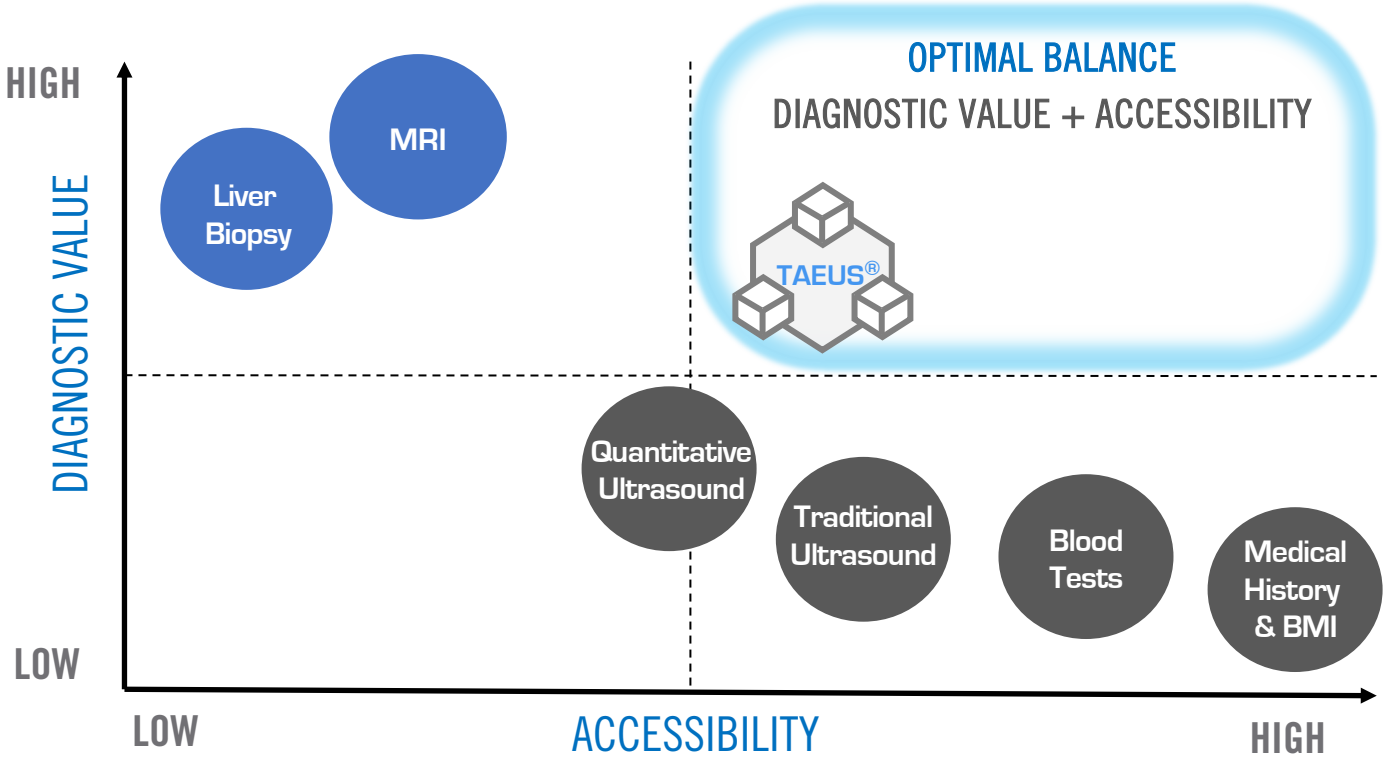
Advent of first **targeted pharma therapies** for NAFLD-NASH increases need to identify & monitor patients

~50 drugs in development⁴ including ~30 in Phase II–III⁵

Many target fat metabolism⁵

Assessing Liver Fat of 1.8 Billion NAFLD–NASH Patients

NO CURRENT TOOL HAS BALANCED DIAGNOSTIC VALUE + ACCESSIBILITY



ENDRA's TAEUS[®]: Enhancing Traditional Ultrasound

RADIO FREQUENCY PULSES CREATE SONIC WAVES THAT QUANTITATE LIVER FAT FRACTION



Illustration of TAEUS probe



Screen shot of TAEUS measurement

TAEUS is not yet approved for sale in the U.S.

TAEUS PROCEDURE

- As little as 15 minutes of user training; easy-to-interpret results
- Locate liver with any traditional B-mode ultrasound
- Apply & activate TAEUS probe; each scan takes 1.5 seconds
- ✓ ENDRA completed first TAEUS human feasibility study (n=19), validated against MRI-PDFF. **Sensitivity 0.88 Specificity 0.82 AUROC 0.91 @ MRI-PDFF 6% steatosis**
- ✓ CE mark received in Europe
- FDA De Novo request planned for Q3 2022

TAEUS[®] Liver Application: Targeting High-Value Segments

CLINICIANS & DRUG DEVELOPERS BOTH STRUGGLE WITH MRI & BIOPSY LIMITATIONS

CLINICIANS

IMAGING, LIVER, METABOLISM

Radiology

~100,000 clinicians

Gastro-Hepatology

~45,000 clinicians

Endocrinology, Primary Care

~300,000 clinicians

PHARMACEUTICAL COMPANIES & CRO's

TRIAL RECRUITMENT

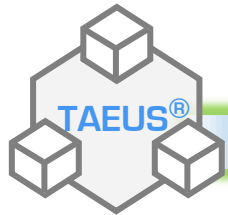
Reduce
**Screening
Failure Rates**
which routinely
run at **55%** in
NASH studies¹

TRIAL EXECUTION

Measure liver fat
more frequently,
monitor changes
between MRI's
and biopsies²

COMMERCIALIZATION

Support front-
line clinical
identification &
monitoring of
target patients
with therapy







Identify & monitor patients with liver fat, non-invasively & cost-effectively

ENDRA Partners

SUPPORTING TECHNICAL, CLINICAL & COMMERCIAL DEVELOPMENT OF TAEUS

Value to ENDRA

	Partner's Role	Build Clinical Evidence	Refine Technology	Commercial Support
	8 TAEUS clinical evaluation sites (4 EU, 3 U.S., 1 China)	●	●	●
	Ultrasound leader, supporting ENDRA intros to GE customers			●
	Pharma companies piloting TAEUS for drug trial screening	●		
	Academic lab developing TAEUS artificial intelligence capabilities		●	

Commercializing TAEUS Liver: 3 Core Elements



TARGET CLINICIANS @LOCAL LEVEL

Small ENDRA team + partners



Europe & U.S.

Distributors



E.g., Vietnam

DRIVE AWARENESS, INTEREST & TRIAL

Clinical conferences, "lunch & learn" events
Online education & marketing → 4000+ CRM names



BUILD CLINICAL EVIDENCE IN TARGET MARKETS

Leverage as reference sites supporting commercialization



Europe

U.S.

China

Anticipated Milestones: ENDRA Liver Application

2022

- ✓ Sign high-value China partnership with Shanghai General Hospital
- ✓ Achieve clarity on U.S regulatory strategy
 - Submit De Novo request in Q3 2022
- ✓ Strengthen intellectual property portfolio
 - Collect TAEUS clinical evidence from global research partners
 - Ramp commercialization efforts & drive sales in Europe
 - Forge new alliances with drug developers and med-tech OEMs

ENDRA Financial Information: March 31, 2022

Cash	\$7.1M
• Q2 ATM ¹ gross proceeds	\$7.8M
Common Shares Outstanding	44.6M ¹
Fully Diluted Shares Outstanding	55.1M
Management / Director Ownership ²	16.0%

¹ ATM: At-The-Market facility. ATM sales (April 1-May 12, 2022): 18.6M shares and \$7.8M gross proceeds

² Based on fully diluted shares, assumes full vesting and exercise of all options.

Refer to ENDRA's SEC filings for audited financial details

Leadership & Advisors

MANAGEMENT



Francois Michelin

Chairman & CEO

20+ years in med-tech

GE Healthcare, Smith & Nephew, Biomet



Michael Thornton

CTO

15+ years med-tech

Founder, Enhanced Vision Systems (sold to GE)



Renaud Maloberti

CCO

20+ years in med-tech. 12 years in ultrasound

FujiFilm, BK Medical, GE Healthcare



Amy Sitzler

VP Engineering

20 years in engineering & quality at GE Healthcare



Irina Pestrikova

Senior Director, Finance

10 years financial reporting, modeling and analysis
ENDRA, Wells Compliance

INDEPENDENT DIRECTORS

Sam Gambhir, MD, PhD

In Memoriam: 1962-2020

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Stanford University

Michael Harsh

Chief Technology Officer
(Ret.), GE Healthcare

Anthony

DiGiandomenico

Co-founder, MDB Capital

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Allen Institute for AI

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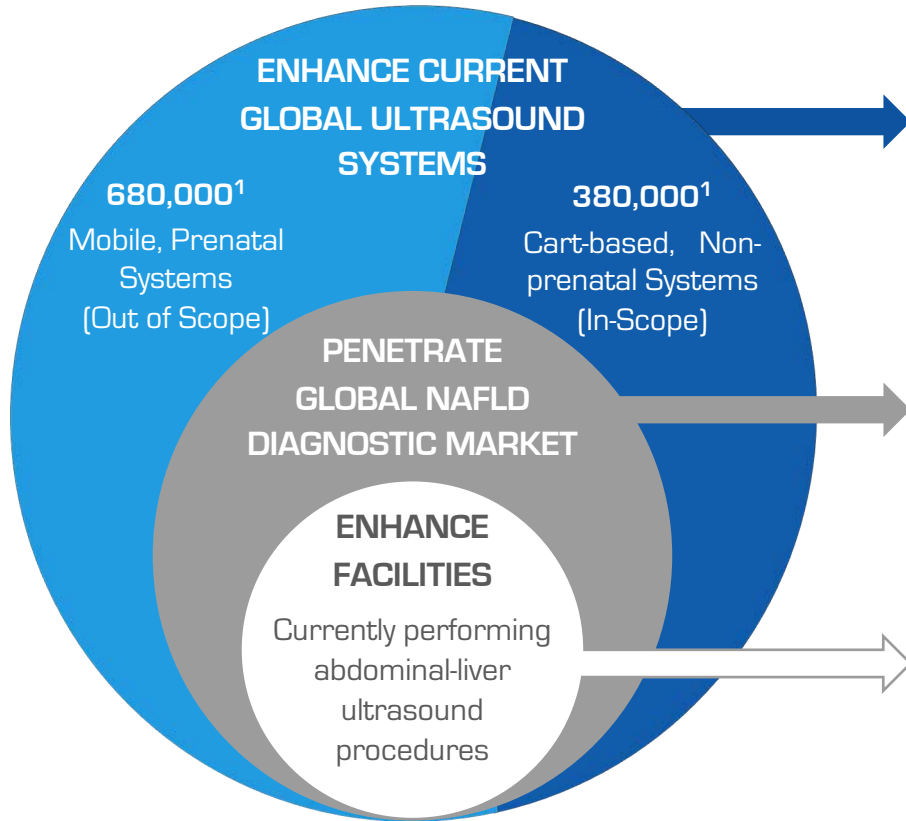
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APPENDIX

See more. Do more. Live better.®

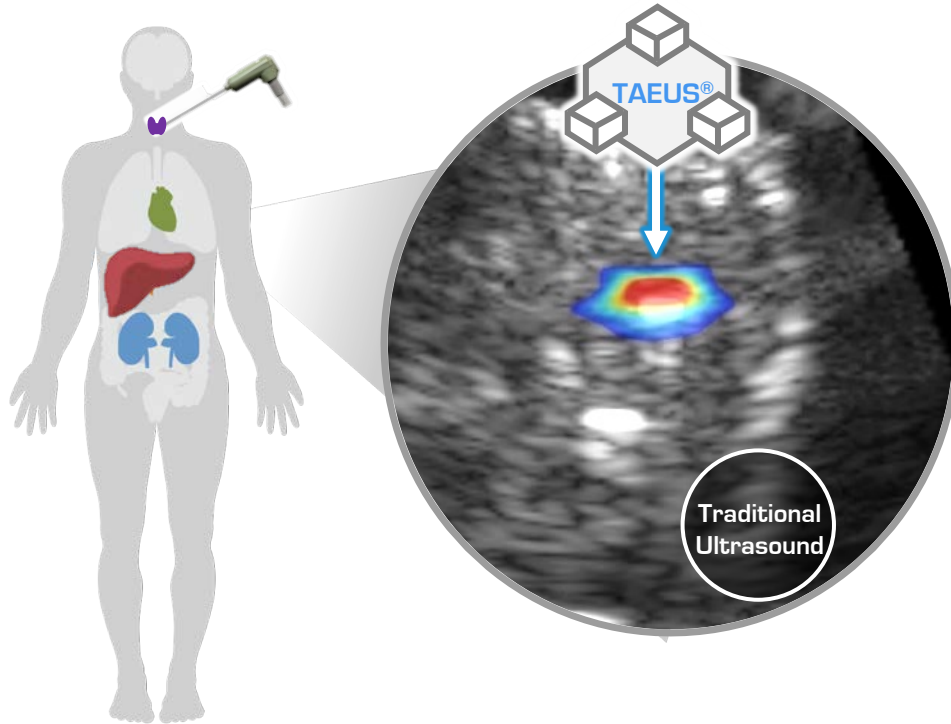
Addressable Markets for TAEUS Technology: 3 Approaches



- **\$19 billion market²** = Enhance installed base of 380,000 cart-based ultrasound systems (best target for TAEUS accessory) x \$50K TAEUS accessory (liver & future applications)
- Upside: + ENDRA services + disposables + licensing
- **\$12.5 billion market (2020)** calculated from trends in liver disease, evolution of diagnostic technologies (laboratory, imaging, invasive), supplier pricing & sales, provider & procedure trends.
- Source: Grandview Research, 2020: *Liver Disease Diagnostics, Market Estimates & Trend Analysis 2020 -2027*, page 34
- **\$1 billion market** = ~20,000³ global facilities (i.e., hospitals, specialty centers, private practices) x 1 unit TAEUS liver @\$50K
- Upside: + Facilities buying more than 1 TAEUS unit
+ New ultrasound adopters: E.g., Endocrinology
+ ENDRA services, disposables, licensing

Future TAEUS Application: Guidance of Energy-Based Therapies

SHOW HEAT OR COLD SIGNATURE OF THERMO-ABLATIVE PROCEDURES FOR CANCER, CARDIOLOGY, PAIN



THERMO-ABLATIVE PROCEDURES

- 5+ million procedures annually¹ growing at 15%¹ CAGR, driven by aging-related diseases: cancer, pain, cardiology
- Current surgical guidance tools are inaccurate or impractical: Printed guidelines or expensive MRI

“Doctors aren't always sure where the (thermo-ablative) energy is going. They could hit a vessel or another heat-sink in the body and the academic models fall apart and treatment is ineffective.”

Jonathan Rubin, MD PhD
Head for Ultrasound & Abdominal Interventional Radiology (Retired),
The University of Michigan

TAEUS Liver: Expected Clinical & Economic Value to Stakeholders

BUILD TAEUS ON TOP OF EXISTING LIVER ULTRASOUND PROCEDURES; POTENTIAL 9 MONTH TAEUS PAYBACK

HEALTHCARE PROVIDERS

PAYERS

PATIENTS

Patient presents with one or more of the following:

- **Abnormal liver function** (blood tests): ALT, AST
- **Abdominal symptoms:** Pain, nausea, vomiting, trauma, appetite loss, weight loss
- **Risk factors for liver disease:** Obesity, alcohol use, diabetes, hepatitis B/C, jaundice, high-cholesterol, autoimmune disorders, polycystic ovary syndrome
- **Incidental findings** from other exams (e.g., renal calculi)

Medical necessity established for ultrasound examination

Existing Ultrasound Procedures

Clinician assesses liver with in-office traditional ultrasound:

- Liver attenuation, echogenicity, volume
- Abnormal hepatic blood vessels (e.g., portal vein), varices
- Abnormal masses (cysts, tumors), fluid collection, gallbladder pathology, biliary dilatation
- **Procedure coded as CPT 76705**
Ultrasound abdominal, single organ, limited. Hospital Outpatient & Physician Payment Estimate:¹
\$137 - \$338

TAEUS Procedure

Clinician offers optional (patient self-pay) TAEUS liver scan² for ~\$35³

Patient Value

- Stays on exam table ~5 mins longer
- Receives additional NAFLD information w/o invasive biopsy or expensive & time-consuming MRI
- Submits TAEUS receipt to Medical Savings Account as permitted

Clinician Payback (illustration)

- \$50,000 TAEUS purchase
- @ 35 patients per week
- w/ \$35 patient self-pay
- = TAEUS breakeven ~ 40 weeks

TAEUS procedure expected to be coded as CPT 76999: *Unlisted ultrasound procedure.* Hospital Outpatient & Physician Est. Payments: \$0 - \$210⁴

Education & Reimbursement

1. Clinician submissions of TAEUS 76999 claims with procedure details (time, equipment used, clinical value) helps to educate payers on new TAEUS test
2. Growth of (separate) published clinical evidence further supports TAEUS clinical & economic value and encourages medical societies (e.g., AASLD) to adopt TAEUS as standard of care for NAFLD-NASH assessment
3. **Over time, items 1 & 2 influence payers to cover TAEUS as a separate reimbursed procedure**

Liver Fat Measurement Tools: Relative Performance & Accessibility

Liver Fat (Steatosis) Test	AUROC ¹	Sensitivity ²	Specificity ³	Diagnostic Value (liver fat)	Accessibility (Affordability, Safety, Ease-of-Use)	Other Considerations
Liver Biopsy	Historical Gold Standard for NASH Diagnosis			++	--	<ul style="list-style-type: none"> Measurement variability due to pathology interpretation Invasive. Requires surgical training.
Blood Tests (E.g., ALT) <small>Lemoine, 2019 (J Acquir Immune Defic Syndr; 80(4))</small>	0.88	0.91	0.77	+	+	<ul style="list-style-type: none"> Low relative AUROC & specificity vs. other tests Susceptible to non-NASH related diseases
Magnetic Resonance Imaging (MRI) <small>Imajo, 2016 (Gastroenterology;150(3))</small>	0.98	0.90	0.93	+++	--	<ul style="list-style-type: none"> Becoming Gold Standard for research studies Not practical for daily clinical practice. Costs \$2M-\$3M. Slow & Complex, not point-of-care. Limited access. Patient restrictions; hip replacements, obesity, tattoos....
Thermo Acoustic Enhanced Ultrasound (TAEUS®) <small>ENDRA, 2019 (Robarts Feasibility Study; endrainc.com)</small>	0.91	0.88	0.82	++	+++	<ul style="list-style-type: none"> Ease of use: ~15 mins training. 1.5 secs/scan. Point-of-care. Works with any B-mode ultrasound. Low cost: ~\$50K Strict quantitative measurement. Accurate, repeatable
Qualitative Ultrasound: B-Mode <small>Paige, 2017(AJR; 208)</small>	0.81	0.61 - 0.89	0.70	--	+++	<ul style="list-style-type: none"> Broadly available, easy to use, point-of-care and safe. Not recommended for low to medium fat level (<25%) High level of training. Variable results, operator dependent
Quantitative Ultrasound: Backscatter, Attenuation, Elastography <small>Lin, 2015 (Clinical Gastroenterology & Hepatology;13) Paige, 2017(AJR; 208) Causey 2018 (Hepatology; 67(4)) Eddowes, Deeks, Newsome 2019 (Gastroenterology)</small>	0.70 - 0.95	0.75 - 0.87	0.70 - 0.91	+	+	<ul style="list-style-type: none"> Varied AUROC, sensitivity & specificity Cumbersome techniques, some require use of phantom Expensive, high level of training Variable results, Operator dependent

¹ **AUROC** (Area Under Receiver Operator Curve): Measures the relationship between sensitivity and specificity as the Reference threshold changes (E.g., MR liver fat threshold of 6%, 10%, 15%, Etc).

² **Sensitivity:** The percentage of people correctly identified as having liver fat above the reference threshold (E.g., 6%).

³ **Specificity:** The percentage of people correctly identified as NOT having liver fat above the reference threshold (E.g., 6%).

Sources & Assumptions

PAGE 3

- 1 \$50K ENDRA device estimated price compared to \$2.5M MRI price
- 2 Journal of Hepatology, 2019 Vol. 70. *Non-alcoholic fatty liver disease – A global public health perspective* Zobair M. Younossi. Page 533 "global prevalence of NAFLD in the general population has been estimated to be 25%" [x 7.3 billion population in 2015] = 1.8 billion people with NAFLD
- 3 Grandview Research, 2020: *Liver Disease Diagnostics, Market Estimates & Trend Analysis 2020-2027*
- 4 IP Asset: filed patents, issued patents and pending patent applications

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- 1 Journal of Hepatology, 2019 Vol. 70. *Non-alcoholic fatty liver disease – A global public health perspective* Zobair M. Younossi. Page 533 "global prevalence of NAFLD in the general population has been estimated to be 25%" [x 7.3 billion population in 2015] = 1.8 billion people with NAFLD
- 2 NAFLD risk profiles from 2021 Korean Association for the Study of the Liver (KASL) treatment guidelines. Dr. Cho Yong-kyun, head of KASL NAFLD treatment guidelines revision committee, and professor at the Kangbuk Samsung Hospital's Internal Medicine Department
- 3 *Cardiovascular Risk in Non-Alcoholic Fatty Liver Disease: Mechanisms and Therapeutic Implications* Claudio Tana. Int'l Journal of Environmental Research & Public Health, Aug 2019
- 4 Hepatology, The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. Younossi, Blissett, Henry, Stepanova, Racila, Hunt, Beckerman, 2016
- 5 ENDRA estimate based on information from clinicaltrials.gov

PAGE 8

- 1 *Unique Insights Gained From Multiple NASH Studies, Overcoming Key Challenges to Design and Execute More Efficient Clinical Trials*. COVANCE-LABCORP CSCVMER002-0919, 2019
- 2 ENDRA is proposing TAEUS technology as an add-on tool to drive clinical trial efficiencies, not (yet) as a replacement of MRI or biopsy for endpoint measurement

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- 1 ENDRA estimate of 2020 worldwide ultrasound units in use, based on GlobalData MediPoint, 2014 report indicating 800,000 units growing at 4%-5% CAGR.
- 2 Addressable market includes TAEUS accessory & software, for liver and other TAEUS clinical applications. Addressable market estimate does not include TAEUS licensing, disposables or service.
- 3 Global estimate of 20,000 healthcare facilities performing abdominal-liver ultrasound scans including:
 - 9,000 U.S facilities: Based on 2017 U.S Medicare Provider Utilization and Payment Data: Physician and Other Supplier public use files from CMS (sites performing CPT 76705 procedures). 2017 facilities grossed up 3% CAGR to estimate 2019 facilities.
 - 11,000 European & Asian facilities: Based on ENDRA internal estimate of non-US facilities, derived from US facilities and installed base of ultrasound systems in global use.

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- 1 ENDRA estimate derived from Grand View Research, *Global Radiofrequency Ablation Devices Market, Segment Forecast to 2020*, Oct. 2014. Note: Procedure volumes are for RF ablation procedures only. Procedure volumes are larger when including other energy-based ablation technologies such as microwave, cryotherapy and HIFU.

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- 1 Estimated payment range for CPT76705 includes Medicare vs. Private Insurance, and hospital and physician fees. Source: Medicare Fee Schedules (HOPD and Physician) and Kaiser Family Foundation (www.kff.org)
- 2 Once TAEUS receives FDA clearance
- 3 Suggested patient self-pay of \$25 to \$50. Pricing determined by healthcare provider
- 4 Estimated payment range for assorted applicable procedures coded under CPT 76999, including Medicare and Private insurance payments, including hospital and physician fees. ENDRA's TAEUS is not expected to immediately secure reimbursement. Source Medicare Fee Schedules (HOPD and Physician) and Kaiser Family Foundation (<https://www.kff.org>)