

The logo icon consists of two interlocking loops, one orange and one light blue, forming a stylized infinity symbol or a continuous path.

ALVA 10

MOVING DIAGNOSTICS TO THE FOREFRONT OF PRECISION MEDICINE



Problem statement in Precision Medicine

Alva10: a solution to the problem

Diagnostics in Precision Medicine Case Studies

Case Study #1 – Opioid Use Disorder

Case Study #2 – Lung Cancer

Case Study #3- Liver Disease

POLLING QUESTION #1



What is your level of familiarity with the term 'Precision Medicine'?

- 1) First time hearing it
- 2) Have been to a few talks
- 3) Working knowledge - we use this at our company
- 4) We're looking to implement it but don't know where to begin
- 5) Expert – I could give this talk!

PROBLEM: "IMPRECISION MEDICINE" EXPENSIVE FOR EMPLOYERS TODAY



10 of the highest-grossing drugs in the U.S. **fail** to improve the symptoms and outcomes of the majority of patients for which they are prescribed. **Blue** represents the patients who benefit.

Diagnostic tools can determine which drug is right for which patient.



1. Adaptation of Nature Graphic, 2015 Schork, N. Personalized Medicine: Time for one-person trials.

DECREASING WASTED DRUG SPEND MUST BE ACHIEVED INDICATION BY INDICATION



All drugs are developed as targeted therapies, but a lack of diagnostics in the market today to identify patients that will/will not respond to these drugs in each individual indication before they are taken/paid for creates millions in wasted drug spend.

Popular High Spend Drugs	Indication	Response Rate Ranges
Humira Pen	Rheumatoid Arthritis, Psoriatic Arthritis, Crohn's, Ankylosing Spondylitis Psoriasis Ulcerative colitis	36-40% 71-78% 7-9%
Enbrel	Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis Psoriasis	40-46% 37%
Stelara	Psoriatic Arthritis, Crohn's Disease, Ulcerative Colitis Psoriasis	17-28% 66-76%
Dupixent	Atopic dermatitis	32-35%
Jardiance	Glycemic control in diabetes	23-32%
Trulicity	Decrease risk of cardiovascular death Glycemic control in diabetes	OR 0.86 34%
Biktarvy	HIV-1 treatment	89-92%
Vyvanse	ADHD Binge Eating Disorder	50-60% 25%
Eliquis	Deep Vein Thrombosis, Stroke, Pulmonary Embolism	HR 0.45 - 82

DIAGNOSTICS ARE THE SOLUTION TO THE “IMPRECISION MEDICINE” PROBLEM



Drug Response

All drugs are target therapies (not just in oncology), but there are a few diagnostic tests to identify responders vs. non-responders. Drug response rates hover around 30% across disease areas, meaning that 70% of drug costs are wasted on non-response.



Disease Risk & Recurrence

In many disease areas, especially cancer, patients stay on long term therapies without knowing if there is benefit to remaining on therapy, despite side effects and cost. Depending on the disease, 20-60% of patients could be safely removed from therapy.



Adverse Events

Patients suffer more than 10 million adverse events in response to drugs every year, most due to metabolic and genetic factors which can be determined ahead of prescription.



Accurate Diagnosis

Major neurodegenerative diseases including Alzheimer’s, Parkinson’s and MS frequently take years to accurately diagnose, which misses an opportunity to treat ahead of progression.

IF DIAGNOSTICS ARE THE SOLUTION, WHY HAVEN'T WE SOLVED OUR 'IMPRECISION MEDICINE' PROBLEM YET?



"It's all about the money."
- Joe Jackson

J. Pers. Med. **2014**, 4, 163-175; doi:10.3390/jpm4020163

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Article

Personalized Medicine's Bottleneck: Diagnostic Test Evidence and Reimbursement

Joshua P. Cohen * and Abigail E. Felix

"Diagnostics account for less than 5 percent of reimbursable healthcare costs while guiding more than 65 percent of clinical decisions. The keys to precision medicine are massively undervalued."

DIAGNOSTICS' VICIOUS CYCLE



Company

- Develops promising biomarker or tool
- Raises funds from Investors to run clinical trial
- Conducts clinical trial and obtains CPT code for diagnostic
- Submits evidence dossier with clinical trial information to payer

Payer

- Determines in most cases that clinical evidence insufficient for coverage and deems diagnostic "experimental and investigational"
- Provides inadequate reimbursement leading to minimal physician adoption

Investors

- Refuse to fund additional studies without knowing threshold for coverage

• **! Company shuts down = Diagnostic unavailable for patients**

Inadequate Evidence



Non-Coverage



No Capital



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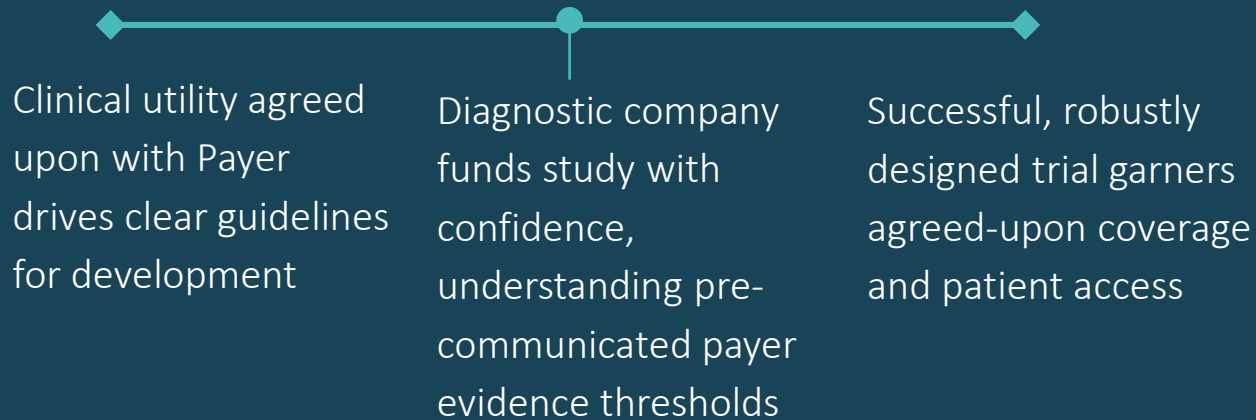
Case Study #2 – Lung Cancer

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VIRTUOUS INSTEAD OF VICIOUS CYCLES



We partner payers and diagnostic companies to develop new generation of diagnostics with high clinical utility, validity, and coverage.



“Healthcare is confounding. In no other industry can the customer not give the supplier their vendor requirements.”

– Pharmacy Director, Blues Plan

Clinical Utility



Evidentiary Threshold



Reimbursement



All healthcare payers benefit from a diagnostic strategy

Commercial TPAs	Medicare
Full-risk providers	Local MACs
Re-insurers	Medicaid agencies

Our diagnostic analysis has enabled payers to:

- Improve effectiveness of pharmacy + medical spend
- Identify top opportunities for reducing ineffective therapeutic spend in multiple disease areas
- Provide solutions:
 - Identify existing diagnostics/technologies/toolsOR
 - Derive and develop new tools

ALVA10 Difference

We work with payers and healthcare tool innovators in tandem to create value across the precision medicine ecosystem



Incorporates payer feedback during development to ensure build-for-purpose tools



Allows transparent, interactive agreement on economic impact



Reduces resources to review/implement technologies with insufficient clinical utility/validity



Improves outcomes, optimizes care, reduces sick days, increases member retention

ENABLING SAVINGS IN HIGH COST AREAS THROUGH EARLY ADOPTION OF DIAGNOSTICS



Payers' strategic approaches to cost of care have benefitted from diagnostics in a variety of ways.

Some of these approaches may also work for employers.

- Pilot Programs
 - Diagnostics used in pilot programs to prove out lower cost of care or care pathway implementation
- Data Development Programs
 - Early and preferred access to approved diagnostics in order to track improved outcomes/cost savings
 - Data generated can lead to broader coverage of the diagnostic
- Investment
 - Employer VC arms investing in diagnostics
- Commissions
 - Developing diagnostics fit-for-purpose to meet payers' financial and clinical needs

LEVERAGING WHAT HAS WORKED FOR PAYERS INTO AN APPROACH THAT WILL BENEFIT EMPLOYERS



Employers are payers too!

Employers should also be educated on Precision Medicine and how/where to look for maximally impactful solutions to high spending

Chronic disease areas are exhibiting a Renaissance of diagnostic development, which is key for lowering costs precisely in those areas where few levers currently exist:

- Oncology applications
- Autoimmune diseases (RA, psoriasis, UC, etc.)
- Opioid Addiction (OUD), substance abuse)
- Nonalcoholic Steatohepatitis (NASH)
- Women's Health
- Heart Failure, Stroke

AGENDA



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POLLING QUESTION #2



What is your level of familiarity with the field of Opioid Use Disorder/Opioid Addiction?

- 1) First time hearing it
- 2) Have been to a few talks
- 3) Working knowledge - we have this challenge at our company
- 4) We're looking to implement a strategy for this but don't know where to begin
- 5) Expert – I could give this talk!



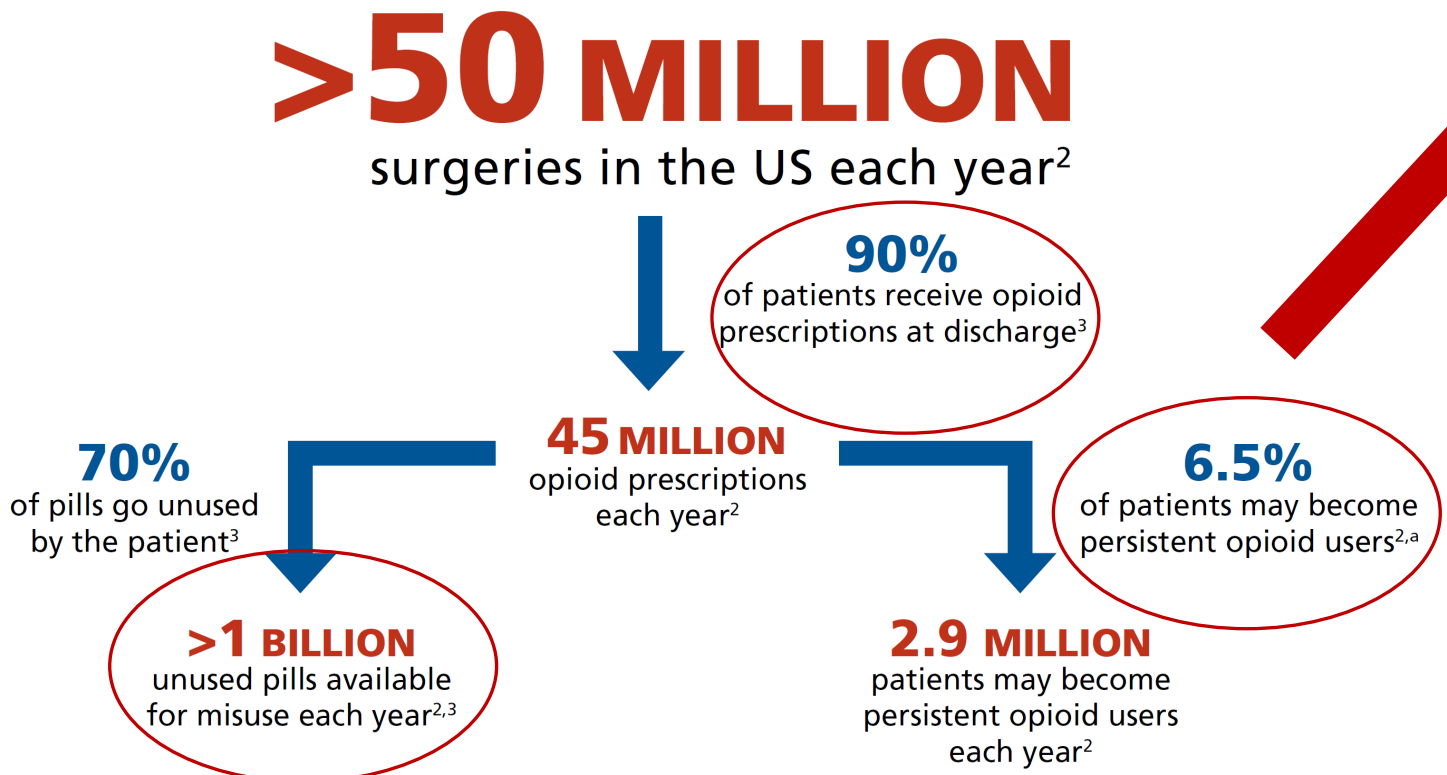
RESEARCH

The Economic Burden of Opioid Abuse: Updated Findings

Noam Y. Kirson, PhD; Lauren M. Scarpati, PhD; Caroline J. Enloe, BS; Aliya P. Dincer, BS; Howard G. Birnbaum, PhD; and Tracy J. Mayne, PhD



Midwest Business Group on Health
The Source for Leading Health Benefits Professionals



- Real world, claims data analysis of 9,342 matched abuser/nonabuser pairs were analyzed.
- Costs: Relative to nonabusers, abusers had significantly higher annual health care resource utilization, leading to \$14,810 in per-patient incremental annual health care costs.
- Inpatient (+ \$2,880), outpatient (+ \$3,906), and rehabilitation (+ \$2,324) costs were all higher in abusers.

OPIOID USE DISORDER: PRESCIENT MEDICINE



90% of US spending on opioid epidemic is spent on treatment, while only 10% spent on prevention. Current methods for determining which patients are likely to become OUD are highly subjective and usage is spotty. Opioid addiction has a high genomic component that can be leveraged to prevent addiction before it begins.

Prescient Medicine LifeKit Predict

- First and only genomic test to garner FDA breakthrough designation (approval pending)
- Test stratifies patients entering elective surgery into 'high risk' and 'low risk' for OUD
- Non-invasive; cheek swab sample
- 16 gene signature

LifeKit Predict represents dramatically new way to avoid opioid use in vulnerable patients



Elective surgeries are huge risk for opioid exposure – OUD prevalence in these populations ranges from 3-10x national average



OUD costs ~14K annually⁸ in incremental costs to manage, while opioid Rx post surgery costs employers \$5-7K



1 in 16 Rx leads to chronic opioid use; 48 hour turnaround means pain management plan gets adjusted before surgery begins + opioids get prescribed



Only Precision Medicine solution in Opioid Use Disorder

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POLLING QUESTION #3



What is your level of familiarity with the field of Tumor Profiling for Lung Cancer?

- 1) First time hearing it
- 2) Have been to a few talks
- 3) Working knowledge - we have this challenge at our company
- 4) We're looking to implement a strategy for this but don't know where to begin
- 5) Expert – I could give this talk!

DX OPPORTUNITY IN LUNG CANCER



The opportunity for Precision Medicine in lung cancer is to identify the specific genetic mutations that drive that patient's tumor, so that they can take a single drug to act on that gene pathway, instead of chemo/radiation on the entire body. These drugs are more effective, with fewer side effects – and the patients live longer.

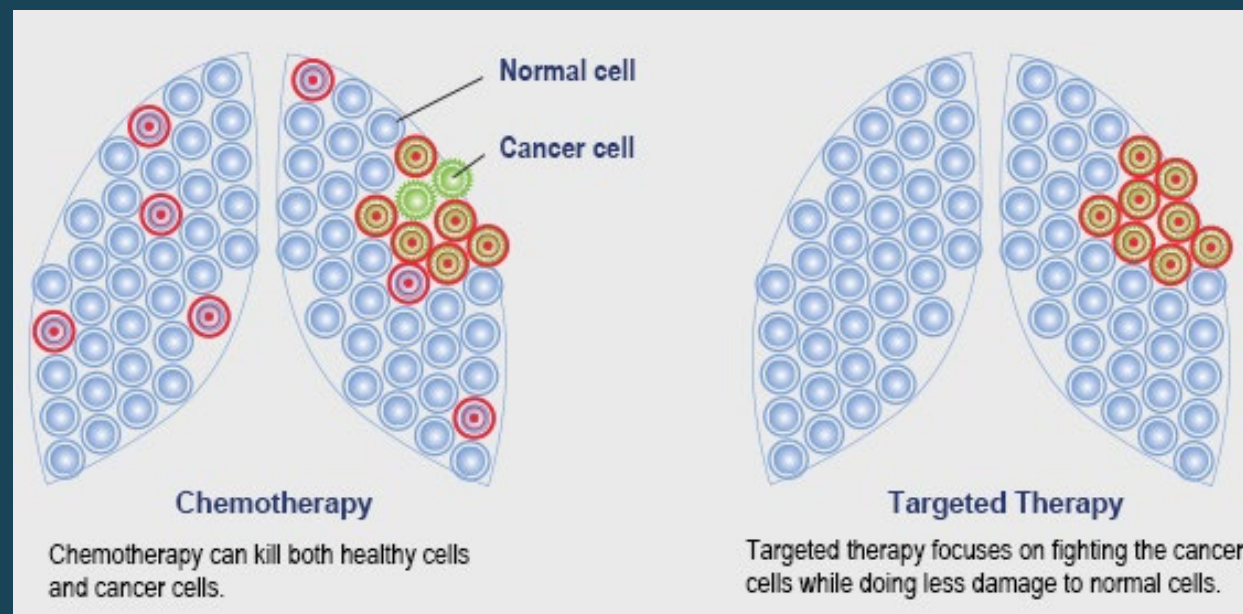
Lung cancer is the second most prevalent cancer among men and women in the US, and is leading cause of cancer deaths

- 84% of all lung cancers are non-small cell lung carcinoma (NSCLC)

57% NSCLC diagnosed in late stage (III-IV) due to lack of symptoms and screening²

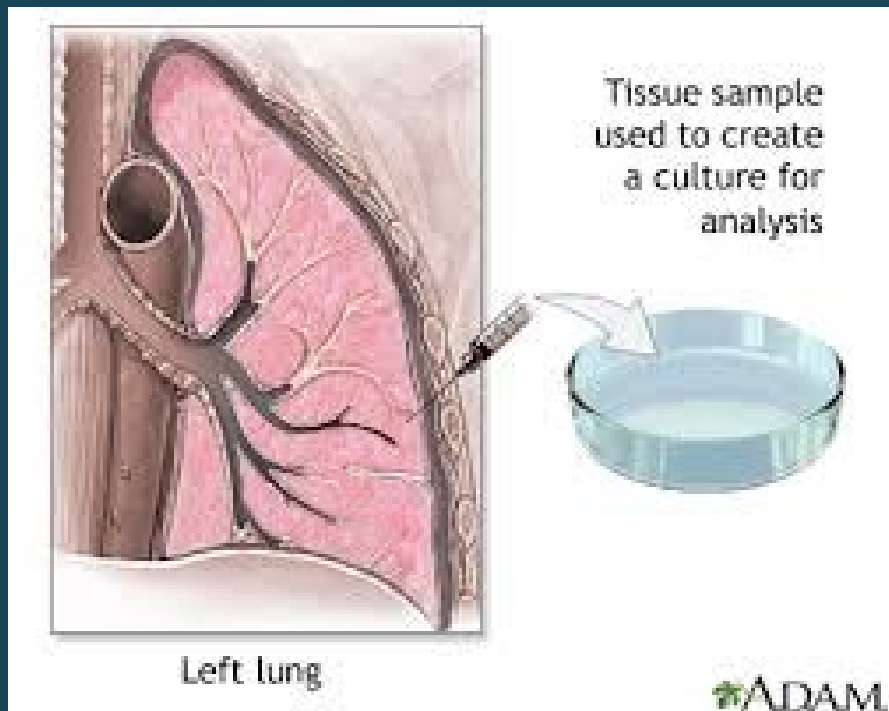
Development of targeted molecular therapies

- Improved median overall survival from an avg. of 20 mos. to upwards of 50 mos. for some drugs



Source: Republished from Boehringer Ingelheim (BI), *Lung Cancer in Non-Smokers*, 2016.

TISSUE BIOPSY VS LIQUID BIOPSY



VS



- Tissue biopsies cost \$8K on average, \$37K with 30% Adverse Event rate
- In 31% of cases, tissue sample is not obtainable while fast action needed

- Simple blood test available anywhere, costs \$250
- Turnaround time for testing is ~9 days, vs 20 for tissue

LIQUID BIOPSY MUTATION DETECTION: RESOLUTION BIOSCIENCE



More than 70% of lung cancer is diagnosed too late for surgery to be curative. Tissue biopsies have historically been used to identify driver mutations and assign targeted therapies that yield better outcomes, but with high cost and low access.

Resolution Bioscience ctDx Lung panel

- Only panel based on Next-Gen Sequencing technology specifically developed for circulating tumor DNA (ctDNA) as sample type
- 'Liquid Biopsy' blood sample based panel
- Optimally designed for clinical utility (23 genes)
- PLA code 0176U, covered by Medicare
- LabCorp distribution network

Liquid biopsy technology opens door for widespread Precision Medicine in cancer



Multiple peer-reviewed publications on clinical validity, including prospective clinical utility publication with Memorial-Sloan Kettering¹. Accuracy comparable to tissue.



Liquid biopsy is key for cost savings



Utility study¹ showed that in 31% of cases, tissue sample is not obtainable while fast action needed.



Technology broadly applicable outside of NSCLC; can lead transition from tissue

AGENDA



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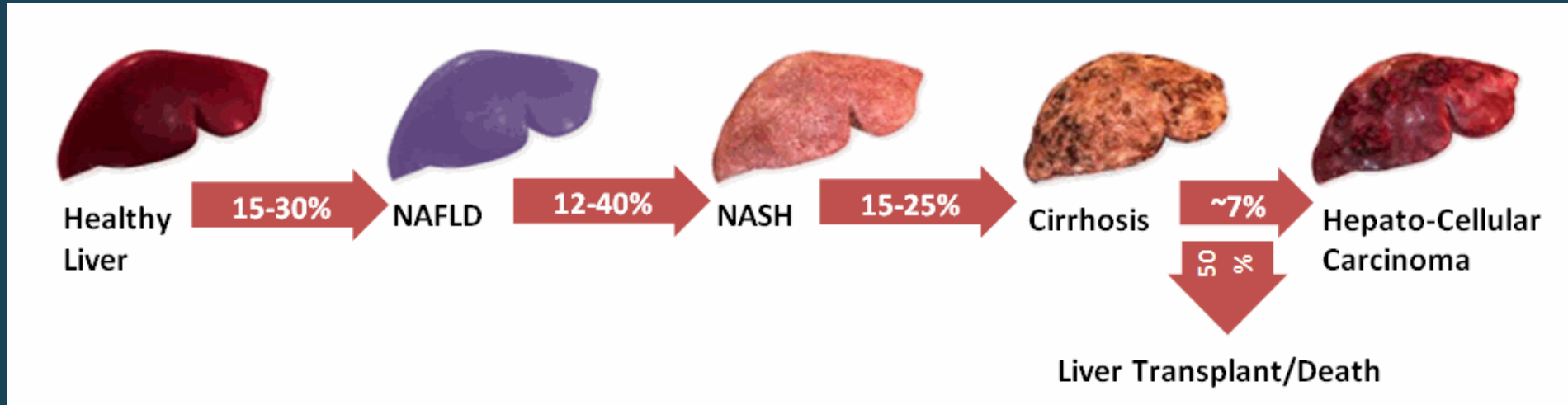
POLLING QUESTION #4



What is your level of familiarity with the field of NASH?

- 1) First time hearing it
- 2) Have been to a few talks
- 3) Working knowledge - we have this challenge at our company
- 4) We're looking to implement a strategy for this but don't know where to begin
- 5) Expert – I could give this talk!

NASH – THE SILENT LIVER DISEASE



- Increased weight gain & high BMI can lead to excessive fat accumulation in the liver
- Associated with obesity, diabetes, hyperlipidemia, hypertension, metabolic syndrome
- No drug treatment is currently approved for NASH
- 50 drugs are in the drug development pipeline; first anticipated approval in late 2021
- Only way to definitively diagnose NASH today: expensive, invasive liver biopsy

NASH – THE WORLDWIDE EPIDEMIC

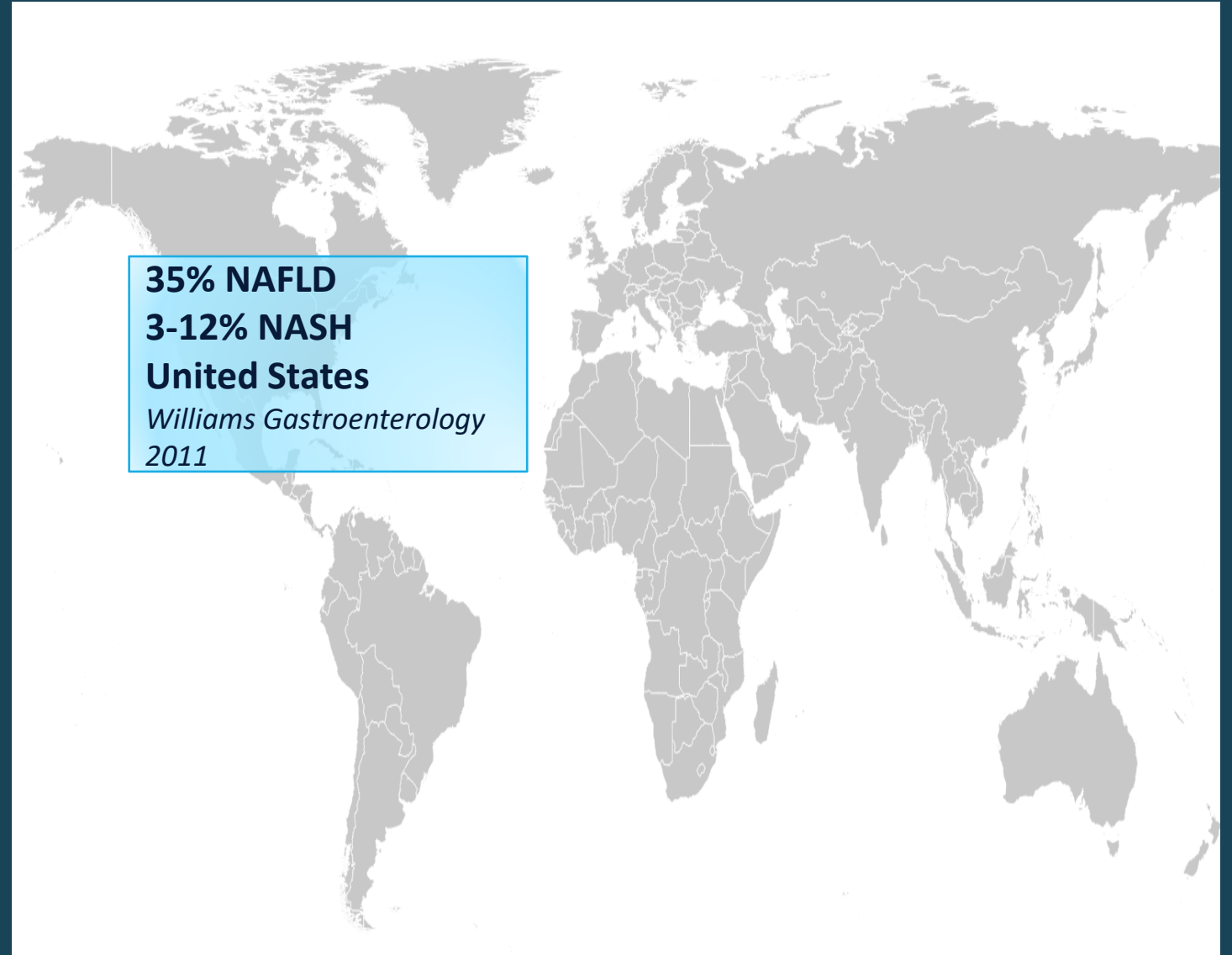


Global prevalence of NAFLD
>25% of adult pop

10% of NAFLD patients will
develop NASH, but no Dx exists
now to determine when

Is now **most common cause of
liver transplants** in the U.S.

Market-spend is anticipated to
reach **>\$25B by 2025**.





3-12% of US population has this fatty liver condition¹¹, which is heavily tied with metabolic disease. First FDA approved drugs expected 2021, opening this market for pharma.

Alva10 leading way on optimized diagnostic pathway that:

- Will differentiate between NAFLD (pre-NASH) and NASH itself
- Will include low cost non-invasive diagnostics upfront, saving higher cost diagnostics for more nuanced clinical questions
- Will accurately determine the stage of advanced fibrosis, for which first NASH drugs will be indicated

Non-invasive diagnostics are a necessity in face of oncoming NASH drugs



High Negative Predictive Value (NPV) can restrict use of over-utilized and costly/risky liver biopsies today



NASH drug approvals will begin in 2021-2022; 50 drug pipeline expected to be \$20B market by 2030



Urgent need to improve upon 'flawed gold standard' that liver biopsy represents today, or risk over-spending



Quick, non-invasive procedures enables diagnostics to act as prior authorization criteria for NASH drugs



THANK YOU!

Questions, Discussion