



**ThermoFisher**  
SCIENTIFIC

## Pioneer the Path to Precision Genomics with Ion Torrent Next-Generation Sequencing

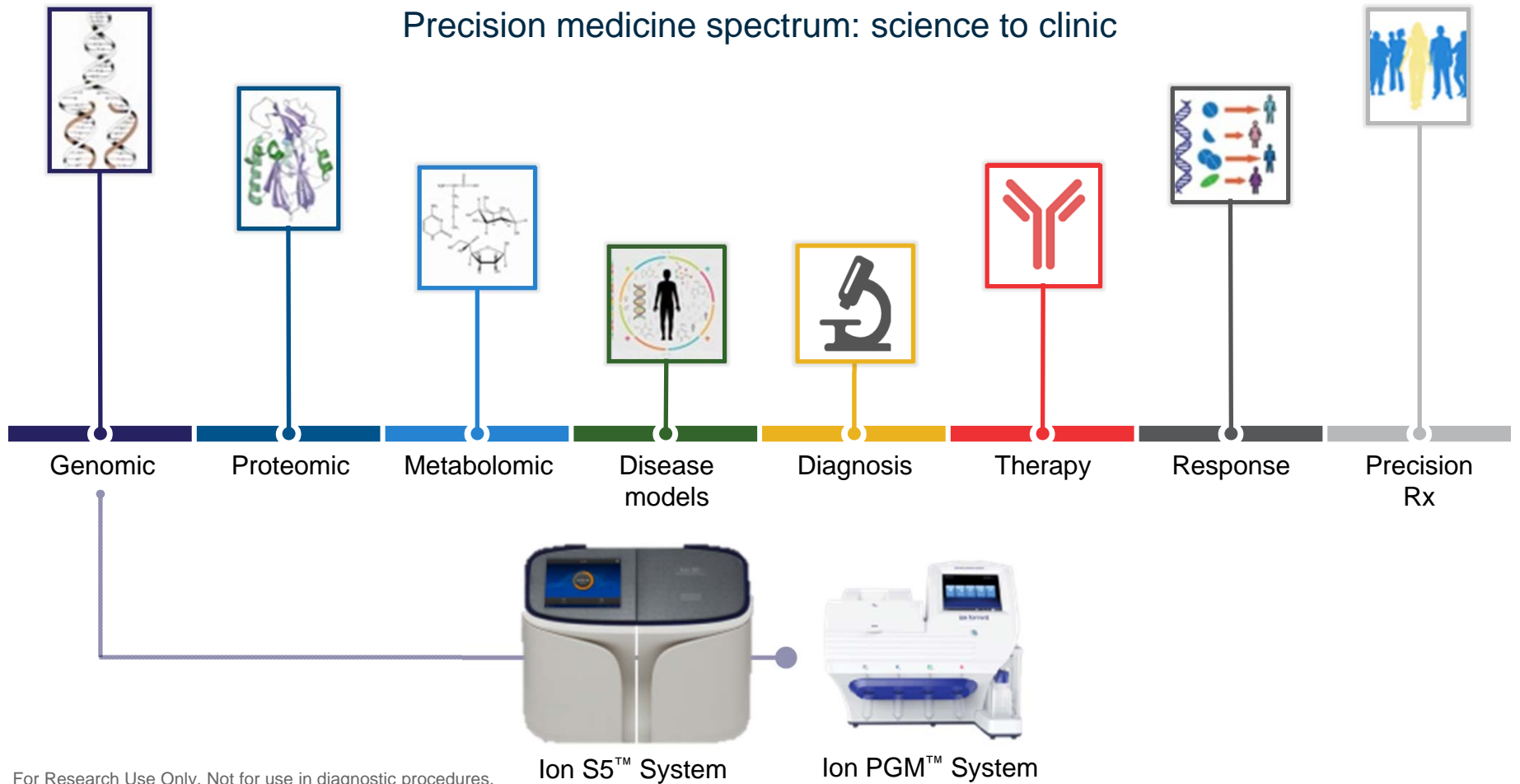
Asia Chang  
Sr. Director Product Management, Oncology  
2016/10/28

The world leader in serving science

# Ion Torrent NGS Research Tools—Helping to Advance Progress Toward Precision Medicine



Precision medicine spectrum: science to clinic



For Research Use Only. Not for use in diagnostic procedures.

# Simplest and Fastest Workflow



**Simple**



**Scalable**



**Supported**



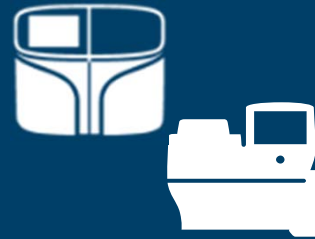
**Fast**

Ion AmpliSeq™  
technology

Ion Chef™  
System

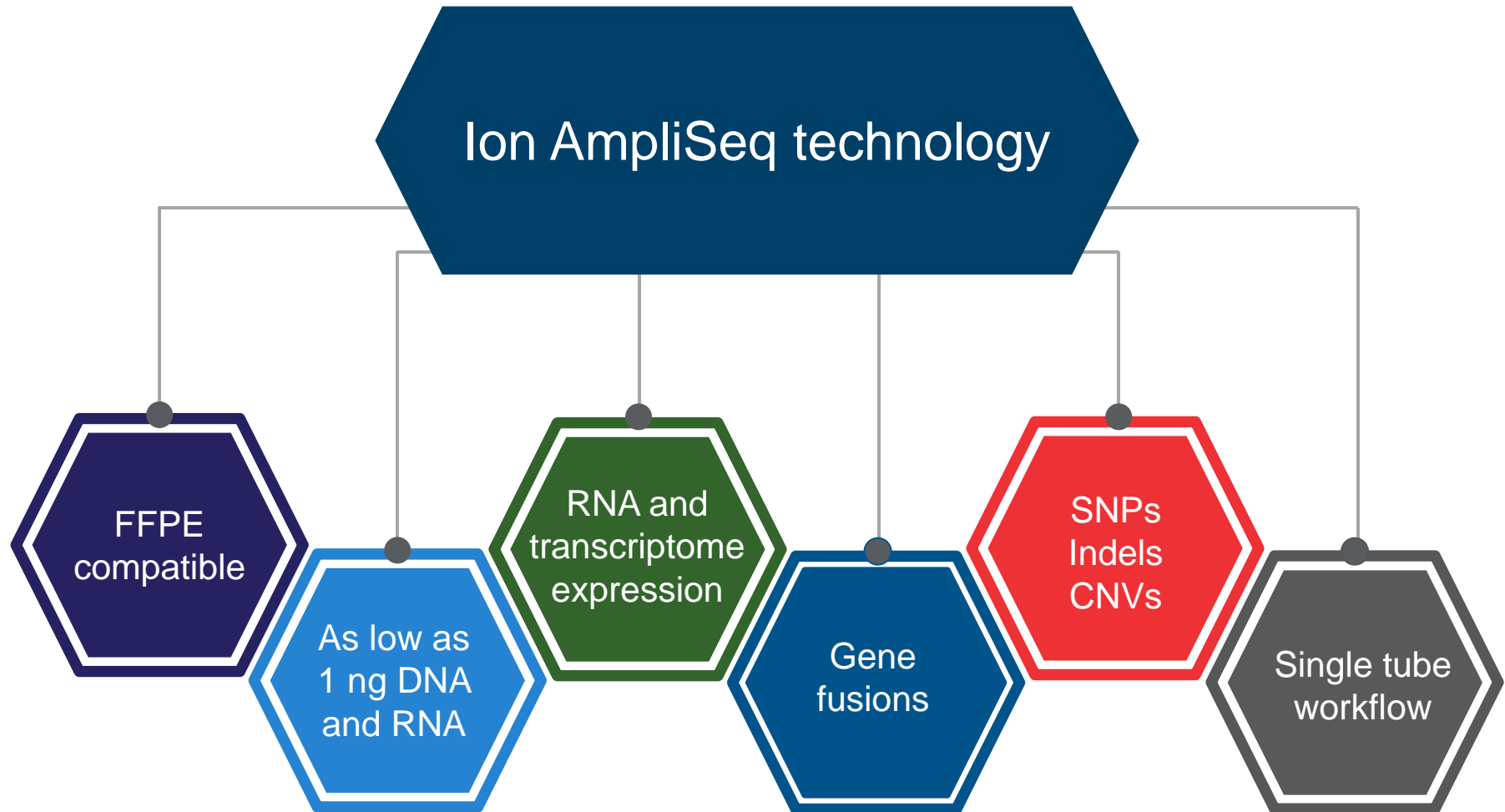
Ion S5™ System  
Ion PGM™ System

Ion Reporter™  
software



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# The Foundation of Ion Torrent NGS Solutions for Oncology Research

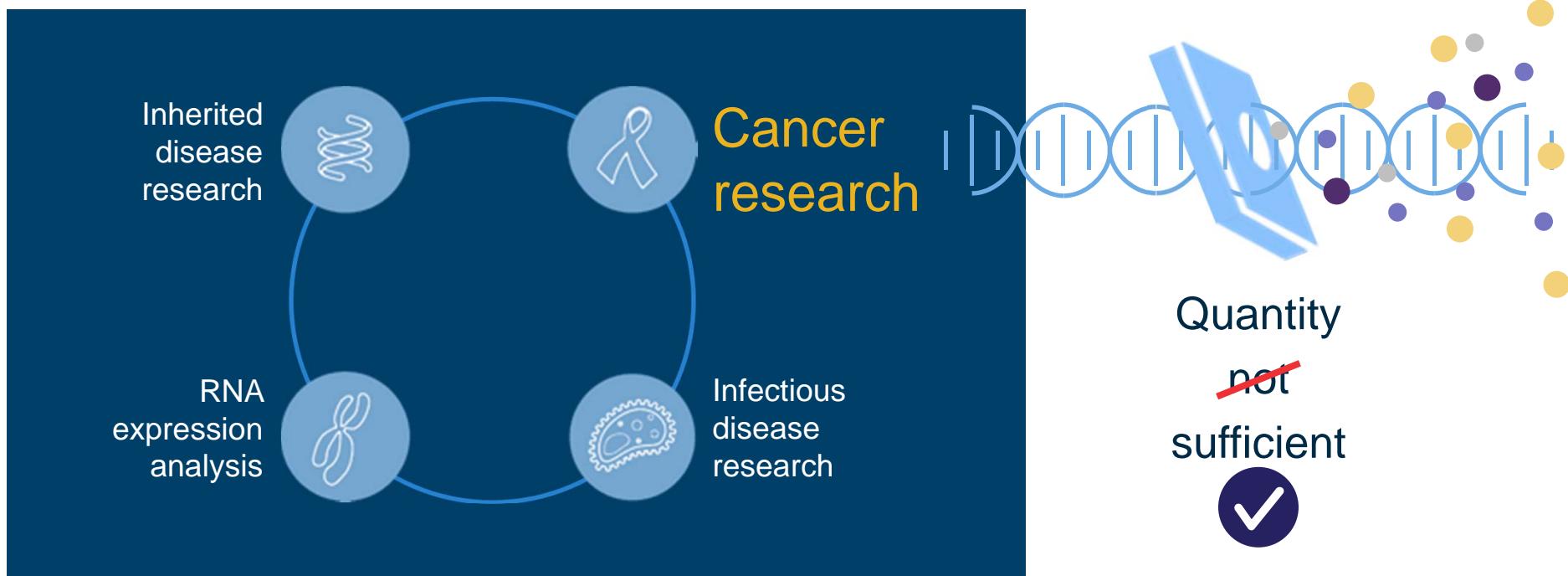


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## Multiple Application Areas, Unlimited Panel Options

Low sample input and formalin-fixed, paraffin-embedded (FFPE) compatibility make Ion AmpliSeq technology an excellent tool for cancer research applications.



# Our Portfolio for Cancer Research Founded on Ion AmpliSeq Technology

Discovery

Translational  
research

Routine research  
sample analysis

## Ion AmpliSeq Panels

- Predesigned panels
- Flexible custom panels using Ion AmpliSeq™ Designer

### Welcome to Ion AmpliSeq Designer

The primer design tool to create custom, ultrahigh-multiplex primer pools for Ion Semiconductor Sequencing.

Sign In

or

Register new account

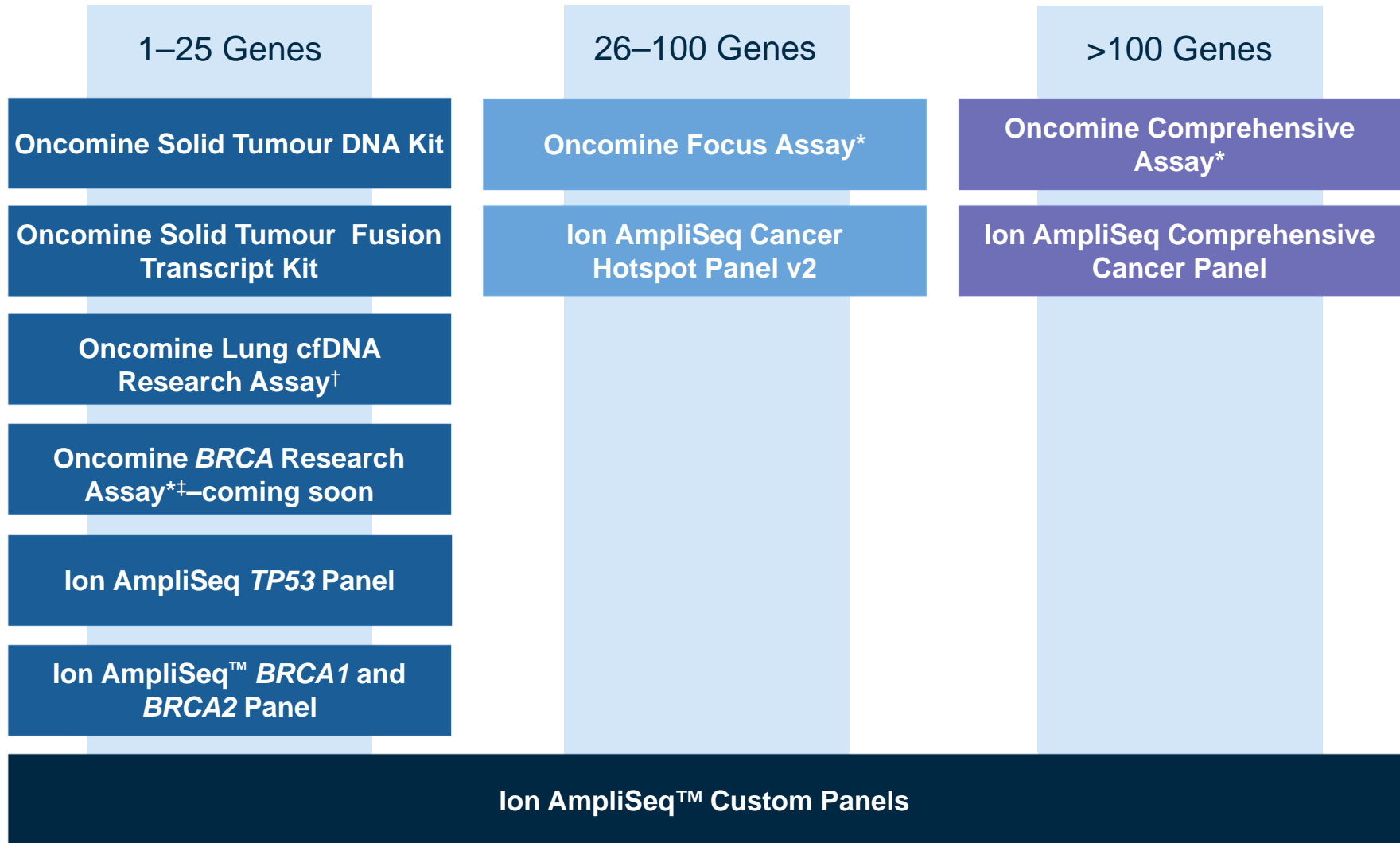
## OncoPrint Assays

- Curated content
- Optimized protocols based on validation with clinical research samples
- Enhanced manufacturing QC and bioinformatics
- Dedicated field support



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# Ion AmpliSeq and OncoPrint Products—Options for Oncology Research

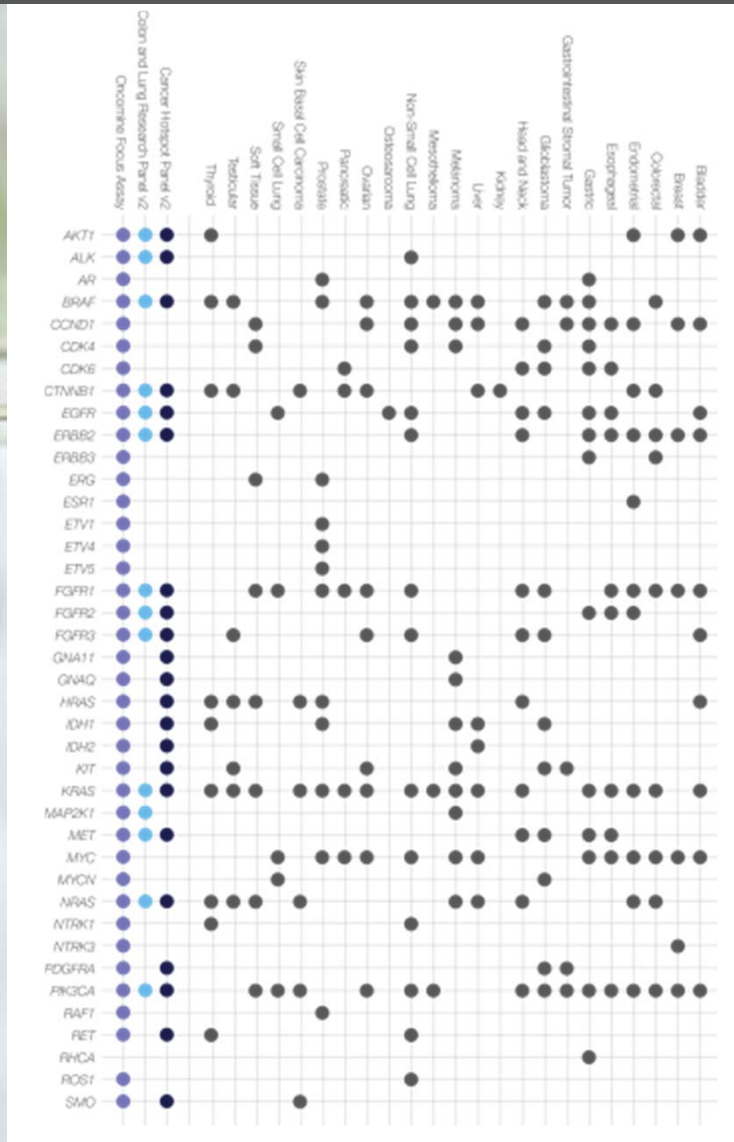


\* Based on AmpliSeq technology

† Based on Tag Sequencing technology

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# Select Your Assay



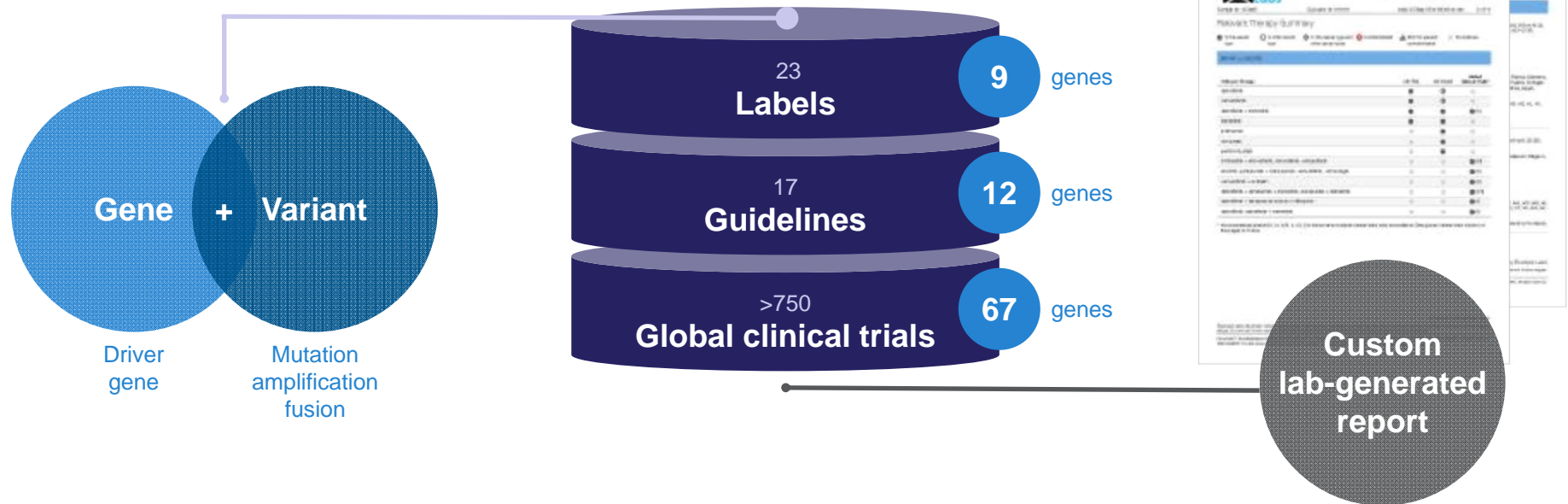
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# Uncover More with OncoPrint Knowledgebase Reporter

- The OncoPrint Knowledgebase Reporter offers associated evidence for labels, guidelines, and clinical trials
- Customizable reports help simplify your data results



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# OncoPrint Knowledgebase Reporter—Custom Lab-Generated Report

## Relevant therapy summary for research purposes

Relevant Therapy Summary

In this cancer type  
  In other cancer type  
  In this cancer type and other cancer types  
  Contradicted  
  Both for use and contradicted  
  No evidence

**BRAF p.(V600E) c.1799T>A**

Relevant Therapy	US-FDA	US-NCIN	EMA	ESMO	Global Clinical Trials*
vemurafenib	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/> (1)
dabrafenib	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/> (1)
dabrafenib + trametinib	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/> (1)
cobimetinib + vemurafenib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/> (1)
trametinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
regorafenib	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (1)
plimometab	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
selumetinib	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
plimometab + selumetinib	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>

## Variant summary table

example Labs

123 Street  
City, State USA 00000  
Tel +1 000-000-0000  
email@example.com  
www.example.com

Sample ID: 12345    Operator ID: 01010101    Date: 03 Nov 2015 23:53:19 PM    2 of 82

Variant Summary

Sample Cancer Type: Breast Cancer

In this cancer type  
  In other cancer type  
  In this cancer type and other cancer types  
  Contradicted  
  Both for use and contradicted  
  No evidence

Gene Variant	US-FDA	US-NCIN	EMA	ESMO	Global Clinical Trials
ERBB2 amplification	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>

## Current global clinical trials

Current Global Clinical Trials Information

Global Clinical Trials information is current as of 2016-03-01. For the most up-to-date information regarding a particular trial, search [www.clinicaltrials.gov](http://www.clinicaltrials.gov) by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers'.

**BRAF p.(V600E) c.1799T>A**

<p><b>NCT01739764</b></p> <p>A Phase IV, PostMarketing, Open-Label, Extension (Follow-up) Study of Vemurafenib in Patients With BRAF V600 Mutation-Positive Malignancies Previously Enrolled in an Adjuvant Vemurafenib Protocol</p> <p>Cancer type: Melanoma</p> <p>Variant class: BRAF V600 mutation</p>	<p><b>Other identifiers:</b> 123451, 2014-0494, CANC - 3028, EudraCT Number: 2012-002144-80, Extensioe (follow-up) Study, 0028399, NCI2013-01190, RL43324.931.13, PER-061-15, R5ac-2012-0300, Trial/TroveID-177020, UKCRN ID: 18400, USMAVVM</p> <p><b>Population segments:</b> Line of therapy N/A, Stage IV</p> <p><b>Phase:</b> IV</p> <p><b>Therapy:</b> vemurafenib</p> <p><b>Countries:</b> Belarus, Bosnia and Herzegovina, Brazil, Canada, Croatia, Cyprus, Egypt, Germany, Greece, Hungary, Israel, Italy, Netherlands, New Zealand, Portugal, Republic of Korea, Romania, Russian Federation, Serbia, South Africa, Spain, United Kingdom, United States</p> <p><b>US States:</b> AL, CA, IA, IL, MA, NY, PA, TX, WA</p> <p><b>US Contact:</b> Hoffmann-La Roche Contact Reference Study ID Number: 0028399   888-652-6720; <a href="mailto:genetechclinicaltrials@druginfo.com">genetechclinicaltrials@druginfo.com</a></p>
<p><b>NCT01990248</b></p> <p>Zel55: A Prospective Observational Safety Study of Patients with BRAF-V600 Mutation-positive Unresectable or Metastatic Melanoma Treated with Vemurafenib (Zelboraf)</p> <p>Cancer type: Melanoma</p> <p>Variant class: BRAF V600 mutation</p>	<p><b>Other identifiers:</b> CP24402, HELIOS ID HRC [004 021], NCRN 530/Zel55, ROCHE ZEL55, Trial/TroveID-195632, UKCRN ID13625, ZEL55</p> <p><b>Population segments:</b> First line, Second line or greater/Refractory/Relapsed, Stage IV, Stage IV</p> <p><b>Phase:</b> IV</p> <p><b>Therapy:</b> vemurafenib</p>

## Current US-FDA information

Current US-FDA Information

In this cancer type  
  In other cancer type  
  In this cancer type and other cancer types  
  Contradicted

US-FDA information is current as of 2015-04-01. For the most up-to-date information, search [www.fda.gov](http://www.fda.gov).

**BRAF p.(V600E) c.1799T>A**

<p><b>cobimetinib + vemurafenib</b></p> <p>Cancer type: Melanoma    Label as of: 2015-11-10    Variant class: BRAF V600E mutation</p> <p><b>Indications and usage:</b></p> <p>COTELLIC™ is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib.</p> <p>Limitation of Use: COTELLIC™ is not indicated for treatment of patients with wild-type BRAF melanoma.</p> <p><b>Reference:</b></p> <p><a href="http://www.accessdata.fda.gov/drugatfda_docs/label/2015/20141490401.pdf">http://www.accessdata.fda.gov/drugatfda_docs/label/2015/20141490401.pdf</a></p>	<p><b>dabrafenib + trametinib, trametinib</b></p> <p>Cancer type: Melanoma    Label as of: 2015-11-20    Variant class: BRAF V600E mutation</p> <p><b>Indications and usage:</b></p> <p>MEKINIST™ is a kinase inhibitor indicated, as a single agent or in combination with dabrafenib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA approved test.</p> <p>Limitation of use: MEKINIST is not indicated for treatment of patients who have received prior BRAF-inhibitor therapy.</p> <p><b>Reference:</b></p> <p><a href="http://www.accessdata.fda.gov/drugatfda_docs/label/2015/20141490401.pdf">http://www.accessdata.fda.gov/drugatfda_docs/label/2015/20141490401.pdf</a></p>
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# Exciting Menu Expansion for Oncology Research in Development



## Peripheral monitoring/cell-free DNA research

**Oncomine Lung cfDNA  
Research Assay<sup>†‡</sup>**

**New!**

**Oncomine™ Breast  
cfDNA Research Assay<sup>†‡</sup>**

**Coming soon**

**Oncomine™ Colon  
cfDNA Research Assay<sup>†‡</sup>**

**Coming soon**

## Immune response gene expression research

**Oncomine™ Immune Response Research Assay\***

**Coming soon**

\* Based on AmpliSeq technology

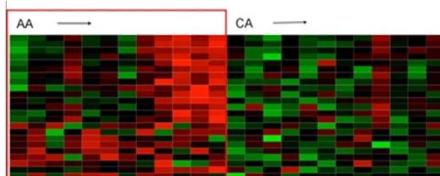
† Based on Tag Sequencing technology

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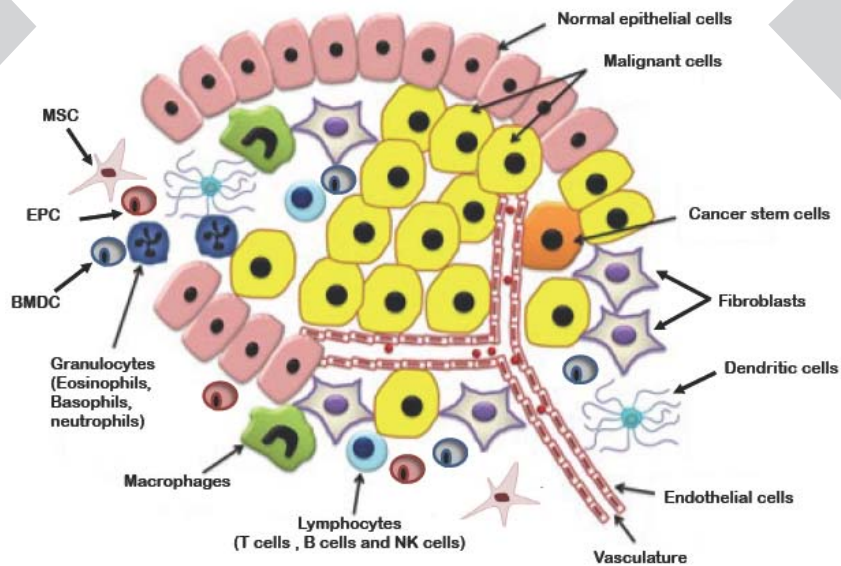
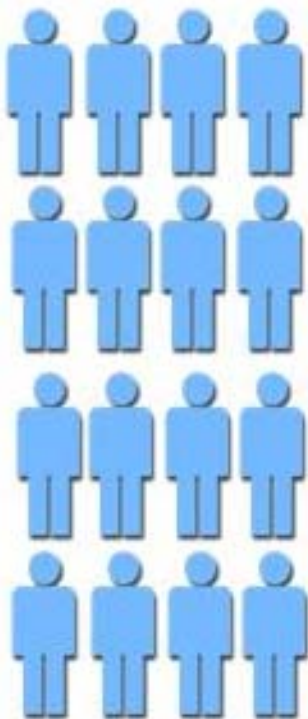


# OncoPrint™ Immune Response Research Assay\*

## OncoPrint™ Immune Response Research Assay\*



- Tumor Infiltrating Lymphocyte level
- Low expressors



Potential to respond



Low chance of responding



# OncoPrint Flagship Assays for Cancer Research

## OncoPrint Comprehensive Assay

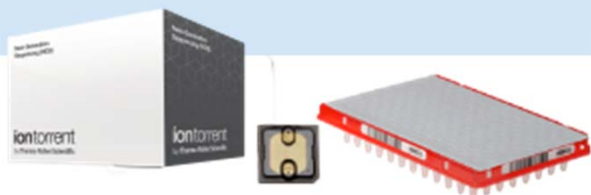
143 Genes

### NCI-MATCH Clinical Trial

For more information, refer to:

<http://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/nci-match>

<http://www.cancer.gov/research/key-initiatives/precision-medicine>



## OncoPrint Focus Assay

52 Genes

In development: multi-gene NGS companion Dx test

In cooperation with pharma partners



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# NCI-MATCH Trial—Molecular Analysis for Therapy Choice

Technology chosen for study:  
Ion PGM System and OncoPrint Comprehensive Assay\*

## Objectives:

- Study the effectiveness of genomics-informed targeted treatment strategies
- Demonstrate the use of a standardized NGS assay and platform across multiple independent clinical sequencing sites
- Use **one standardized test** for stratification into **many clinical trials**

<http://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/nci-match>  
<http://www.cancer.gov/research/key-initiatives/precision-medicine>

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# NCI-MATCH Trial—Overview

## Protocol and selected technology:

- Phase I: 3,000 samples stratified in 10 treatment arms
- Using Thermo Fisher Scientific assay >4,000 variants across 143 genes
- Testing at 4 central laboratories using a robust, standardized protocol



- 192 active sites
  - 2/3 community hospitals
  - 1/3 academic institutions

● 796 approved sites

## Collaboration:

- Partnership between NCI and multiple pharma companies

<http://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/nci-match>

# NCI-MATCH—Interim Evaluation

## Phase I results published June, 2016

- **795 samples submitted in the first 3 months**
  - Far surpassing original estimate of 50 samples/month
- Of 739 core needle biopsies, **87% were successfully sequenced**
  - Industry standard ~80% success rate
  - Of the 13% not sequenced, a high percentage were necrotic and devoid of any viable nucleic acid material
- Of the **optional fine-needle aspirate (FNA) samples** submitted, **97% were successfully sequenced**
- **Phase II will require submission of FNA samples and is projected to increase the sequence success rate from 87% to 98.6%**

<http://ecog-acrin.org/nci-match-eay131-researchers>

# NCI-MATCH Trial Update, June, 2016: Next Steps

The MATCH trial has resumed after a planned pause for interim scientific analysis. Based on high interest and success, the scope for Phase II has significantly increased.

- **Expanding to 24 treatment arms**
  - Originally 10 treatment arms
- **Expanding enrolment to 5,000**
  - Originally 3,000
- **Increasing testing capacity by adding Ion S5™ XL systems\***
  - Was 50 samples/month—now, 100 samples/week
  - Turn around time: sample-to-results in 14 days
- Phase II study is projecting a 23% match rate
- FNA samples (optional in Phase 1) are now required to address the high percentage of core biopsies found necrotic and devoid of any viable material

\* The Ion S5 XL System is For Research Use Only. Not for use in diagnostic procedures.



# Our Ion Torrent NGS Platforms



Ion PGM System

- Minimal sample input
- Fast turnaround times
- Small panels, microbial genomes



Ion Chef System

- Automated library prep, template prep, and chip loading
- 30-minutes total set up time for library and template prep



Ion S5 System

- Simple set up <15 min
- Plug-and-play reagents
- Scalable throughput

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## Our Vision for the Future

A photograph of a young woman with dark hair, wearing a white lab coat, smiling warmly at the camera. She is in a laboratory setting, with shelves of equipment and supplies visible in the background. The lighting is bright and professional.

In development, a universal  
companion diagnostic test

# Our Vision for the Future: A Universal Diagnostic (Dx) Product

## Universal means:

- At product launch: one CDx validated for selection of therapy A, B, & C
- In the future: new clinical trials validate the same CDx for more therapies, D, E, F

## Oncomine Universal Dx Test

One companion diagnostics (CDx) test  
multiple and increasing drug indication



## One test

**Many** answers to inform patient management decisions and indication of multiple treatments

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A Mission We Are Proud of



We enable our customers to make the world healthier, cleaner, and safer.

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