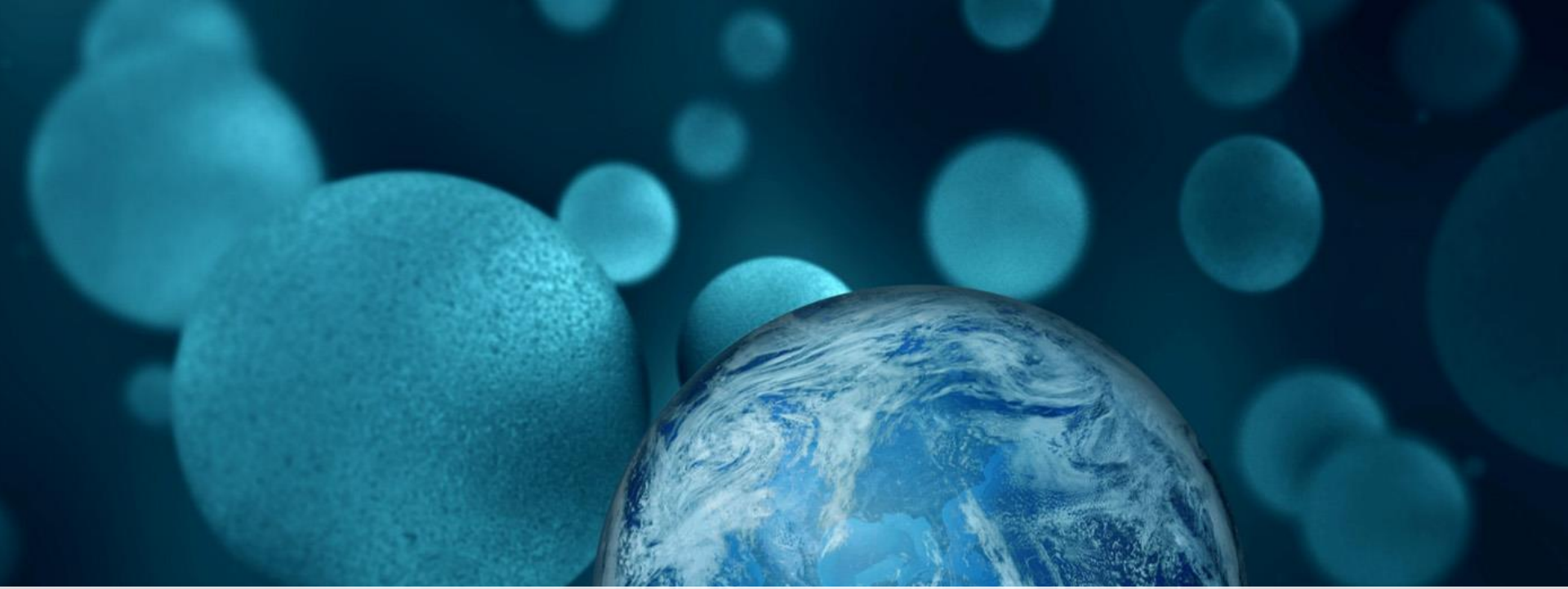


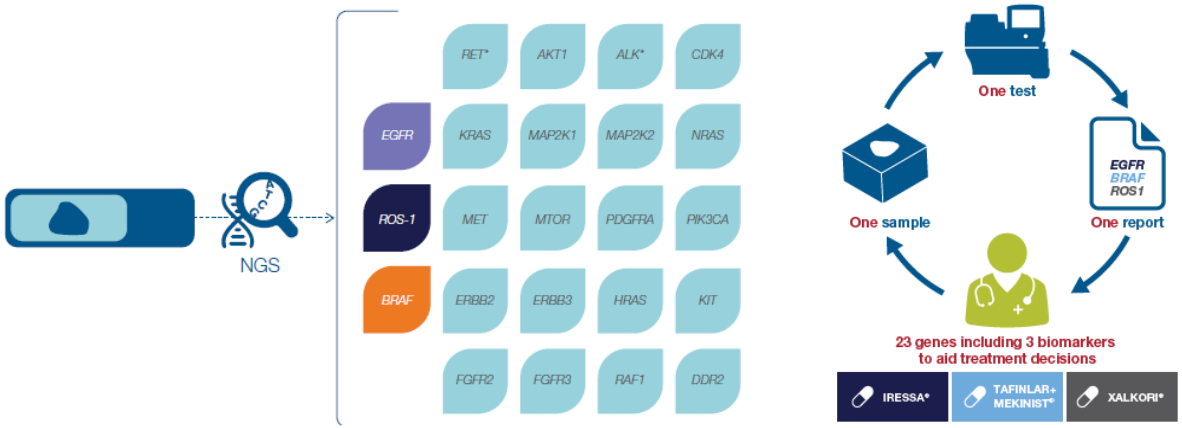
ThermoFisher SCIENTIFIC

NGS CDx submission experience

Lynne McBride
Director of Regulatory and Clinical
October 6, 2017

The Ion Torrent™ Oncomine™ Dx Target Test

Oncomine Dx Target Test, *in vitro* diagnostic (IVD) approved by FDA for NSCLC for 3 CDx markers and the analytic reporting of (23 genes, 369 variants, including, DNA and RNA)



The first targeted next-generation sequencing (NGS) *in vitro* diagnostic (IVD) test for non-small cell lung cancer (NSCLC), with the reporting of multiple biomarker results for **multiple targeted therapies** from **one sample** within **four days**, minimizing the risk of depleting tissues and requiring additional biopsy

For *in vitro* diagnostic use.

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Intended Use

The Oncomine™ Dx Target Test is a qualitative *in vitro* diagnostic test that uses targeted high-throughput, parallel-sequencing technology to detect sequence variations in 23 genes in DNA and RNA isolated from formalin-fixed, paraffin- embedded tumor (FFPE) tissue samples from patients with non-small cell lung cancer (NSCLC) using the Ion PGM™ Dx System.

The test is indicated to aid in selecting NSCLC patients for treatment with the targeted therapies listed in Table 1 in accordance with the approved therapeutic product labeling.

Table 1 List of variants for therapeutic use

Gene	Variant	Targeted therapy
BRAF	BRAF V600E	Tafinlar® (dabrafenib) in combination with Mekinist® (trametinib)
ROS1	ROS1 fusion	Xalkori® (crizotinib)
EGFR	L858R, Exon 19 deletions	Iressa™ (gefitinib)

Results other than those listed in Table 1 are indicated for use only in patients who have already been considered for all appropriate therapies (including those listed in Table 1). Safe and effective use has not been established for selecting therapies using this device for the variants in Table 1 in tissue types other than NSCLC.

Intended Use con't

Analytical performance using NSCLC specimens has been established for the variants listed in Table 2.

Table 2 List of variants with established analytical performance only

Gene	Variant ID/type	Nucleotide change
KRAS	COSM512	c.34_35delGGinsTT
KRAS	COSM516	c.34G>T
MET	COSM707	c.3029C>T
PIK3CA	COSM754	c.1035T>A

The test is not indicated to be used for standalone diagnostic purposes, screening, monitoring, risk assessment, or prognosis.

Prior to submission:

- 11 formal pre submission documents implemented
- Several face to face meetings and many TC meetings associated with pre submission documents
- 16 development studies
- 27 analytical validation studies
- 5,500 data runs
- 6 external study sites implemented

- Bi monthly informal meetings made available to review status and questions prior to first module submitted and ending prior to approval.
  - Held on an as needed basis

During submission

- 4 modules (manufacturing, SW validation, analytical validation, clinical validation)
  - 733 Volumes in total (across 4 modules)
  - 226,000 pages for the original 4 modules
- Multiple addendums
- 3 manufacturing sites inspected
- 2 external test sites inspected
- 1 instrument 510(k)
- During submission, as needed calls to address questions
- Formal responses submitted against one deficiency letter

All within 12 months