



# KINNATE

B I O P H A R M A

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RAF Clinico-Genomic Landscape Study

November 2021

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# RAF Clinico-Genomic Landscape Study Executive Summary

Genomic Landscape Study conducted in collaboration with Guardant Health (GuardantINFORM™ ) focused on characterizing the prevalence of patients with advanced & metastatic solid tumors bearing BRAF Class I, II and III alterations as identified via liquid biopsy

Key findings include:

- Among the nearly 6,000 patients identified in GuardantINFORM™ as having BRAF alteration-positive cancers across all tumor types, **approximately 55% were found to be harboring Class II and III alterations**
  - Suggests that Class II and III alterations, across patients with advanced and metastatic solid tumors, may be higher than prior publicly disclosed datasets have identified\*
  - When looking across the most common tumor types (NSCLC, Melanoma and Colorectal Cancer (CRC)), approximately 65%, 20% and 30% of oncogenic BRAF alterations, respectively, are BRAF Class II & III
  - In addition to NSCLC, melanoma and CRC, BRAF Class II & III alterations are also detected at substantial rates in other common and rare tumor types such as prostate, breast, duodenal adenocarcinoma, renal pelvis urothelial carcinoma, cholangiocarcinoma
- Currently, patients with Class II and III BRAF alterations have no available targeted therapies and represent a significant and potentially greater unmet clinical need than previously understood
  - The 2020 sales for the 3 approved products for Class I BRAF alterations were US\$1.8B
  - Liquid biopsy-based screening may increase the identification of Class II & III alterations in cancer patients, pointing to a potentially larger need for therapies that target not only Class I, but also Class II & III alterations

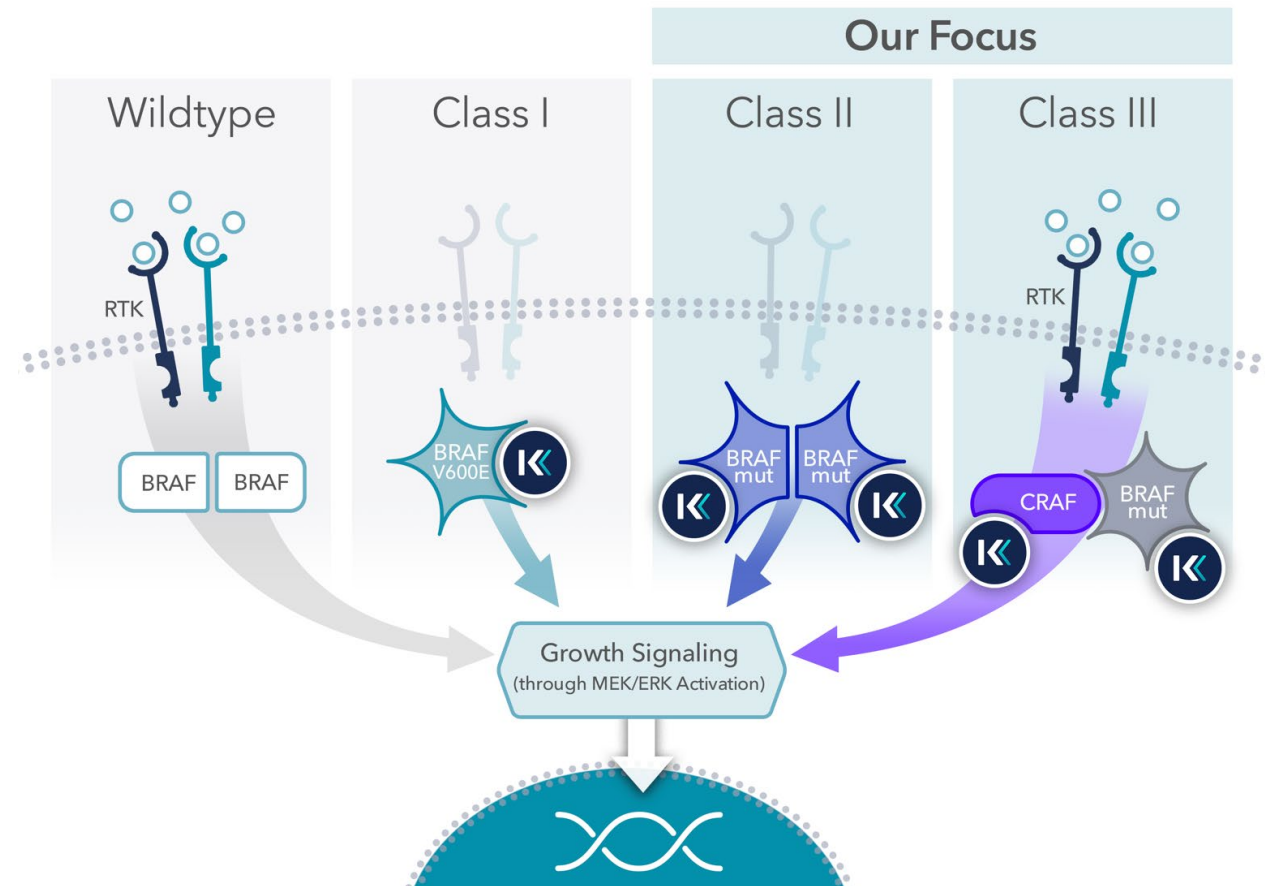
The study will also assess real-world clinical outcomes stratified by BRAF Class and by treatment which will be presented at a future date



# BRAF Class II & III Alterations Define Distinct Patient Populations

These Patients have no Approved Targeted Therapies and Poor Clinical Outcomes

- Patients with BRAF Class I alterations, represented by BRAF<sup>V600E/K</sup>, can be treated with approved RAF inhibitors vemurafenib, dabrafenib & encorafenib
- BRAF Class II & III alterations include SNVs, Indels & gene fusions, and activate MAPK signaling by BRAF homodimer (Class II) or BRAF/CRAF heterodimer (Class III) formation
- Patients with BRAF Class II & Class III BRAF alterations have no available targeted therapies & represent a significant unmet clinical need
- Kinnate's approach targets dimer signaling in these patient populations while minimizing MAPK pathway rebound in normal wild type RAF signaling



# RAF Genomic Landscape Study Design and Objectives

- Kinnate's collaboration with Guardant utilizing GuardantINFORM™ to **understand the real-world occurrence, characteristics & outcomes of patients with oncogenic BRAF alterations across solid tumors**
- GuardantINFORM™ combines de-identified longitudinal clinical information and genomic data collected from the Guardant360® liquid biopsy test which has been provided to more than 175,000 patients to date in the United States. Over 80% of the patients are linked to treatment and procedural data
- Guardant360® is a commercial 73 Gene DNA panel optimized for analysis of ctDNA (liquid biopsy)

## Key Study Objectives:

### 1. Determine Occurrence Rates

- Calculate the occurrence rates of BRAF Class I, II, III alterations in advanced solid tumors

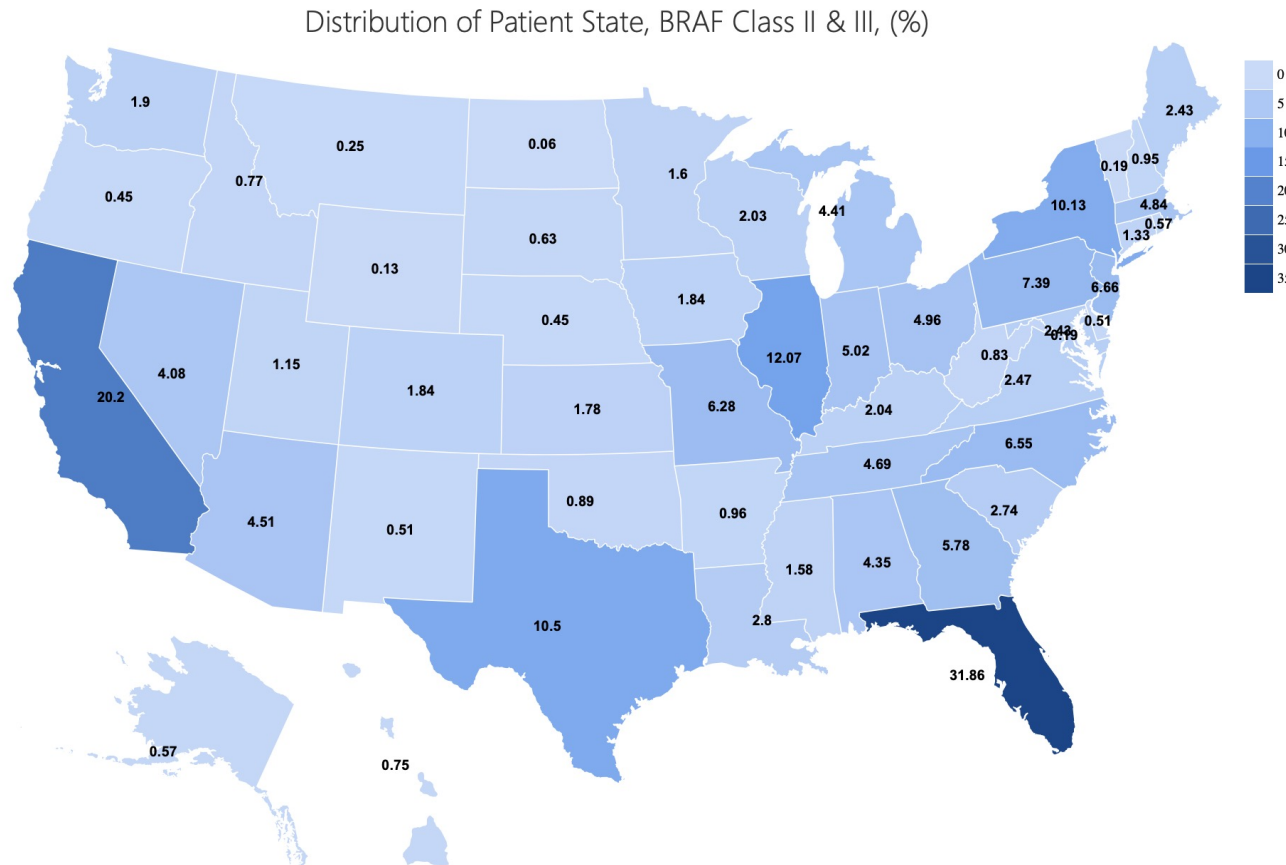
### 2. Explore Relationships Between BRAF Class, Patient Characteristics and Outcomes

- Characterize attributes of **patients & tumors** bearing BRAF Class I, II or III alterations
  - Patient Demographics (Location, Age, Sex, Smoking Status)
  - Cancer Treatments
  - Co-occurrence with other mutations
- Real world outcomes

**Preliminary analysis is focused on the occurrence rates of BRAF Class I, II, III alterations (SNV's & Indels)**

# Demographics of Patients Bearing BRAF Class I, II or III Alterations

GuardantINFORM™ identified nearly 6,000 patients with BRAF Alteration-positive cancers



Patient demographics by BRAF class, across all cancer types

Parameter		BRAF Class			
		Class I	Class II	Class III	
<b>Age</b>	n	2,643	1,524	1,622	
	Mean	64.90	68.93	67.47	
	SD	12.94	10.65	11.80	
	Median	66	69	68	
	Min	16	23	16	
	Max	85	85	85	
<b>Gender</b>					
	Female	Frequency	1,396	718	802
		Percent (%)	52.82	47.11	49.45
	Male	Frequency	1,247	806	820
Percent (%)		47.18	52.89	50.55	
<b>Vital Status</b>					
	Unknown/ Still Alive	Frequency	1,540	865	923
		Percent (%)	58.27	56.76	56.91
	Date of Death Known	Frequency	1,103	659	699
Percent (%)		41.73	43.24	43.09	
<b>Smoking Status</b>					
	Ever Tobacco Product User	Frequency	1,140	869	851
		Percent (%)	43.13	57.02	52.47
	Unknown	Frequency	1,503	655	771
Percent (%)		56.87	42.98	47.53	

Note: Patients with multiple BRAF alterations across functional classes (I/II/III) were excluded from the demographic summary.

- Patients with BRAF Alteration-positive cancers originate from all states in the U.S.
- Age distribution & gender balance are broadly similar across all 3 patient Populations (BRAF Class I, II & III)

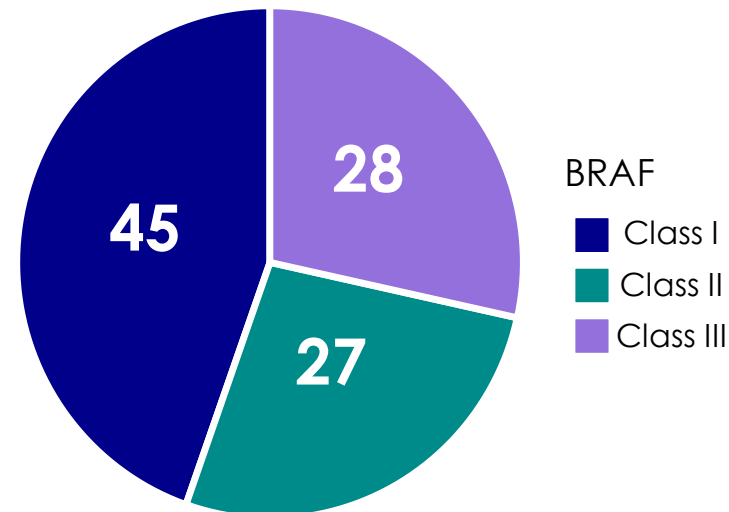


# Pan-Cancer Prevalence of Patients Bearing BRAF Alterations

## Majority of oncogenic BRAF alterations (~55%) are Class II or III

Guardant360<sup>®</sup> analysis of ~143,000 ctDNA positive samples from cancer patients with advanced or metastatic disease

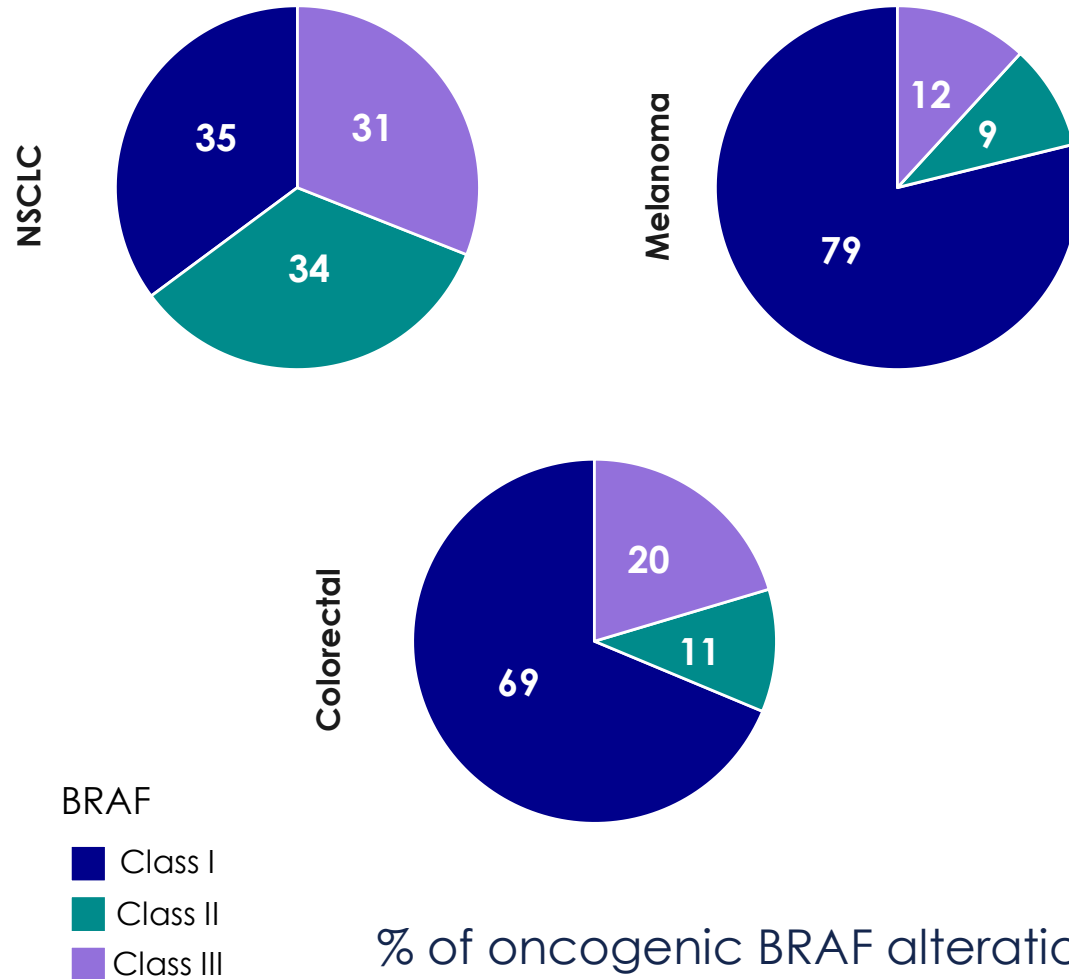
- 2.2% of ctDNA positive patients had BRAF Class II or III



% of Oncogenic BRAF Alterations

Across all tumor types, liquid biopsy analysis in GuardantINFORM<sup>™</sup> identified that the majority of patients with BRAF alterations have Class II & III alterations versus previous public sources based on smaller sample set showed a minority

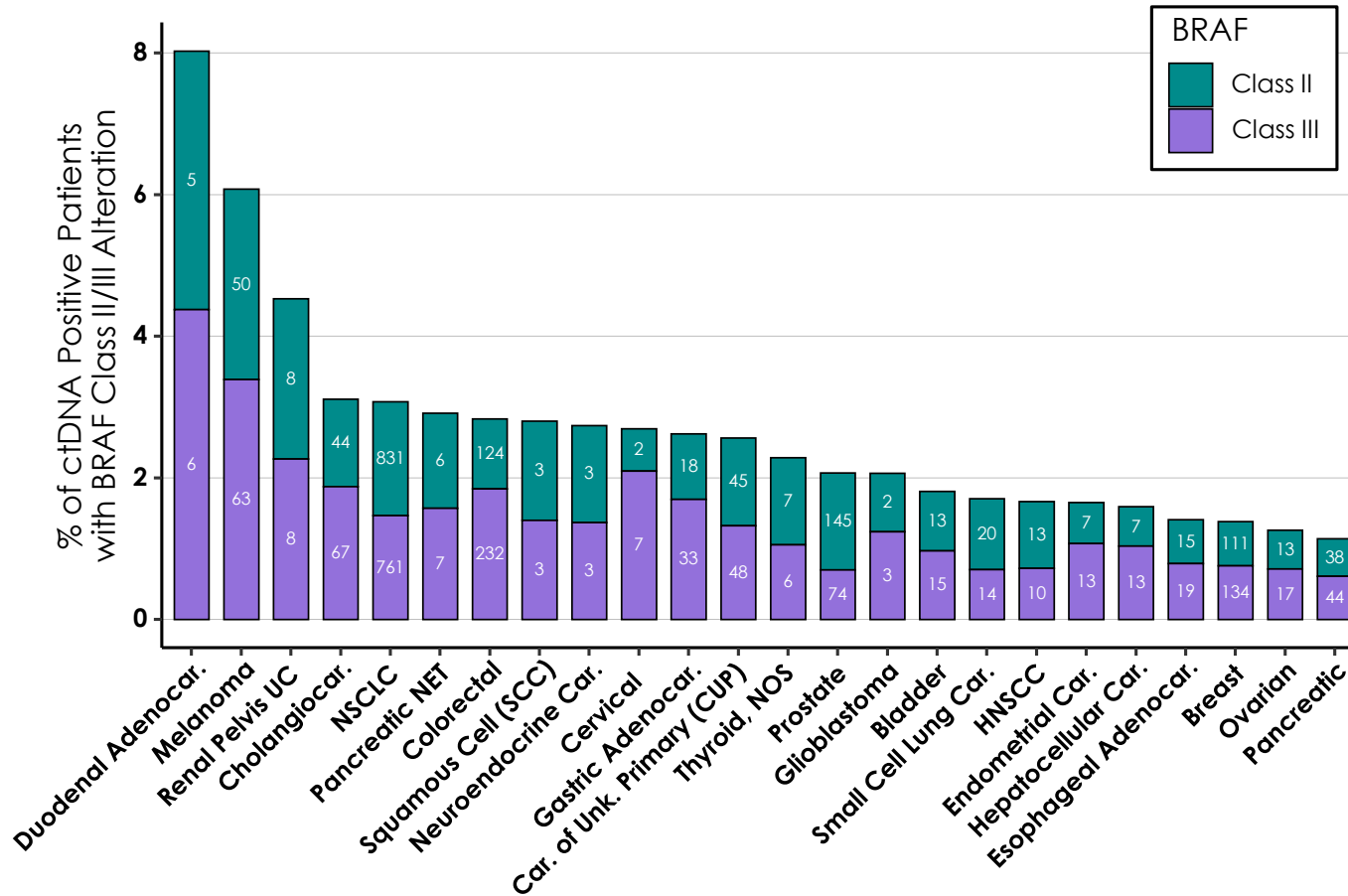
# BRAF Alteration Prevalence by Tumor Type based on GuardantINFORM™



- **Greater proportion** of patients with Class II or Class III alterations across NSCLC, Melanoma and Colorectal versus prior public databases
- **Majority** of patients with BRAF alterations with **NSCLC** are Class II or Class III
- Percent of oncogenic BRAF alterations that are Class II or III:
  - NSCLC: 65%
  - Melanoma: 21%
  - Colorectal: 31%



# BRAF Class II & III Alterations are Common Across Tumor Types



**white** labels indicate the # of patients

Figure includes tumor types with:

- $\geq 130$  tested patients &  $\geq 2\%$  BRAF Class II/III or
- $\geq 1,000$  tested patients &  $\geq 1\%$  BRAF Class II/III

A broad survey identified many tumor types with BRAF Class II & III occurrence rates  $> 1\%$

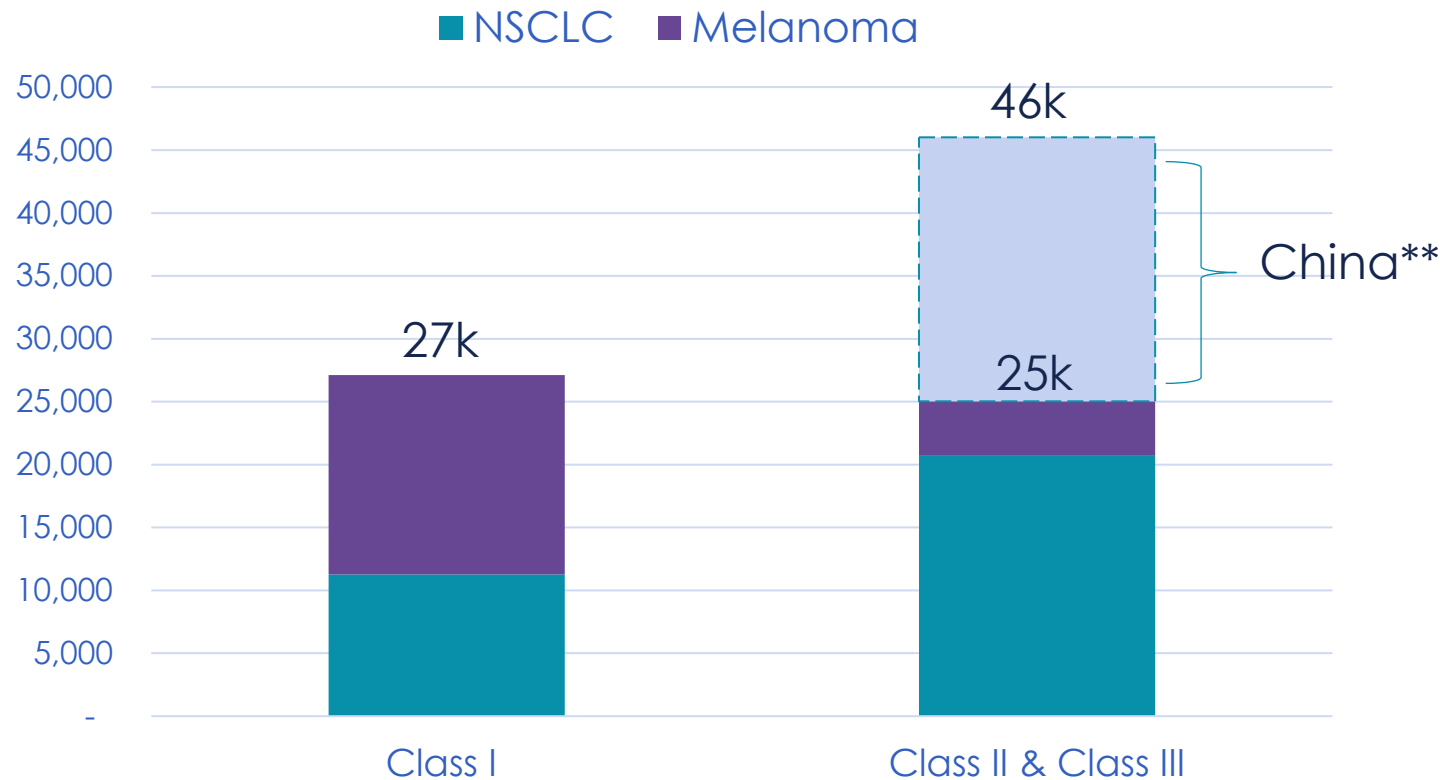
Tumor types with  $>100$  patients each with BRAF Class II & III alterations in GuardantINFORM™:

- NSCLC
- Colorectal
- Breast
- Prostate
- Melanoma
- Cholangiocarcinoma

BRAF Class II & III alterations represent a sizable unmet need across a variety of tumor types

# Class II & Class III Population Across Tumor Types is Greater than Class I But Without Any Approved Drugs

Patients with BRAF alterations for NSCLC & Melanoma\*



Approved Products: **3** (Class I) **0** (Class II & Class III)

\*US, EU5 and Japan; Stages IIIb and IV for NSCLC and Stage IV for Melanoma

\*\* Stage IIIb and IV NSCLC in Urban Markets only

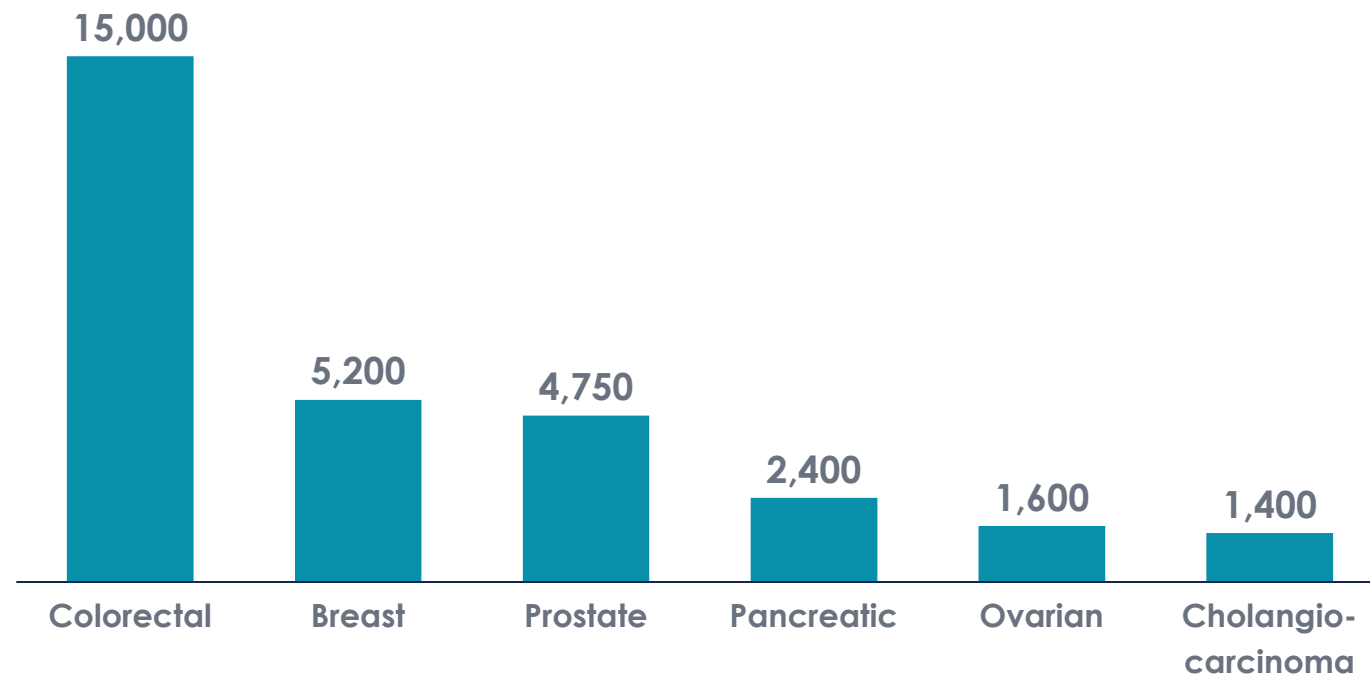
- 2020 sales of the 3 approved products for Class I BRAF alterations were \$1.8B
  - 20% growth from 2019 sales
- Substantial opportunities for growth
  - Class II & III may have higher pricing, in-line with newer drug launches
  - Class II & III drug may not require combination therapy and/or have better profile
  - Broader use of NGS identifying more Class II & III patients
  - Additional tumor types with significant prevalence



# BRAF Program Opportunities for Expansion

## Opportunities to Expand Beyond Current Target of ~46k patients

Additional Tumor Types with significant BRAF Class II or Class III alteration prevalence:



- Additional opportunities in various cancer types beyond NSCLC & Melanoma with Class II / Class III alterations
- Earlier treatment lines and less advanced disease settings
  - 2,700 patients have **Stage IIIa NSCLC** with Class II & Class III alterations
  - 3,200 patients have **Stage III Melanoma** with Class II & Class III alterations
- Class I BRAF alterations, including both first line and second line for intrinsic and acquired resistance
  - 27,000 patients have advanced NSCLC and Melanoma with Class I alterations + China
  - ~25% of acquired resistance may be dimer based
- Expanding into other geographies with high disease burden (e.g. South Korea, Australia, Canada)

