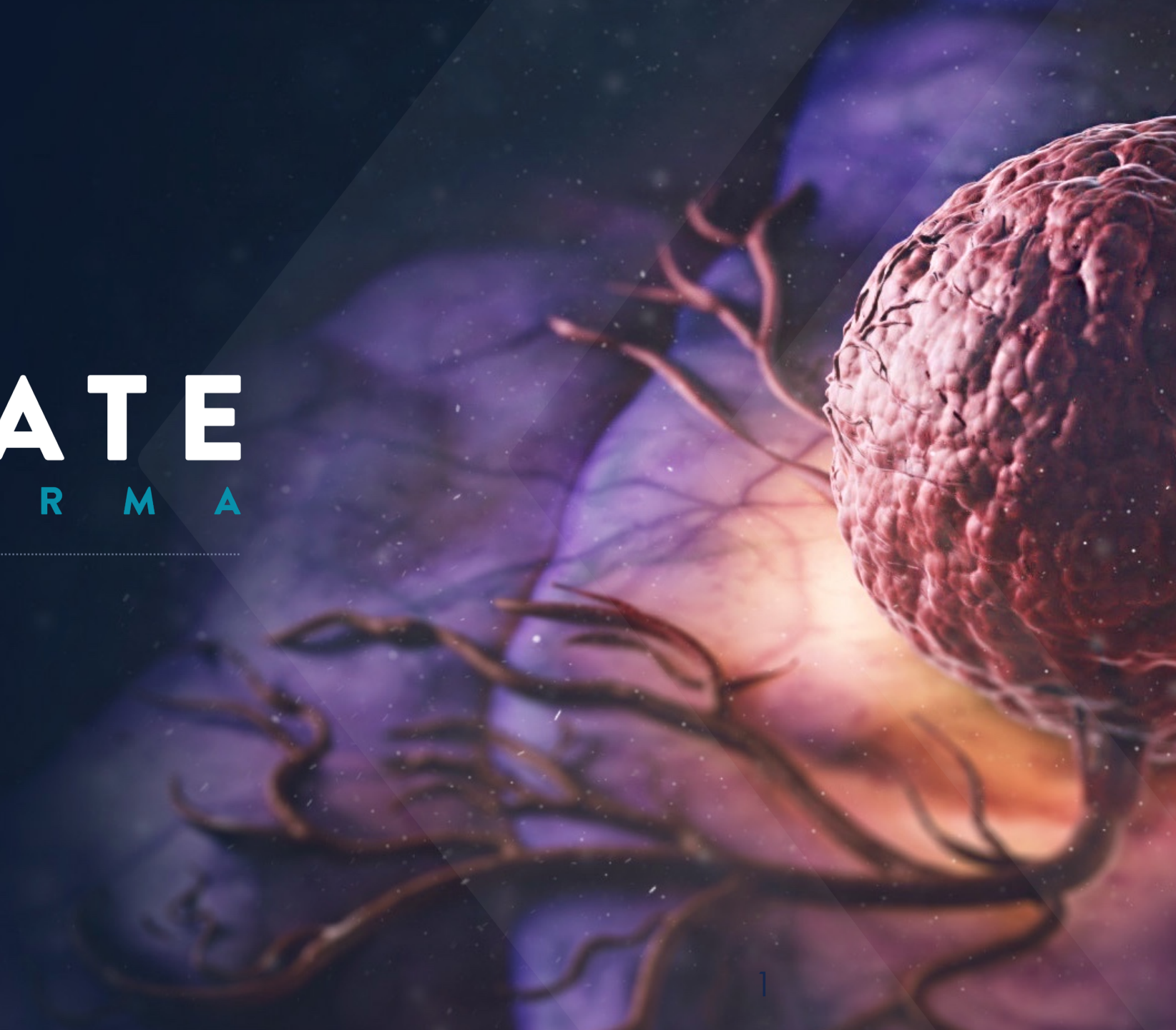
KINNATE BIOPHARMA

# Investor Presentation

February, 2020



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This presentation (including the accompanying oral presentation) contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding the future financial condition, results of operations, business strategy and plans, and objectives of management for future operations of Kinnate Biopharma Inc. ("we," "us" or "our"), as well as statements regarding industry trends, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potentially" "predict," "should," "will" or the negative of these terms or other similar expressions. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: the timing of the initiation, progress and potential results of our preclinical studies, clinical trials and our research programs; our ability to advance product candidates into, and successfully complete, preclinical studies and clinical trials; the timing or likelihood of regulatory filings and approvals; the negative impacts of the COVID-19 pandemic; our estimates of the number of patients who suffer from the diseases we are targeting and the number of patients that may enroll in our clinical trials; the commercializing of our product candidates, if approved; our ability and the potential to successfully manufacture and supply our product candidates for clinical trials and for commercial use, if approved; future strategic arrangements and/or collaborations and the potential benefits of such arrangements; our estimates regarding expenses, future revenue, capital requirements and needs for financing and our ability to obtain capital; the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements; our ability to retain the continued service of our key personnel and to identify, hire and retain additional qualified professionals; the implementation of our business model, strategic plans for our business and product candidates; the scope of protection we are able to establish and maintain for intellectual property rights, product candidates and our pipeline; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; the pricing, coverage and reimbursement of our product candidates, if approved; and developments relating to our competitors and our industry, including competing product candidates and therapies.

These and other risks, uncertainties, assumptions and other factors are described in greater detail under the heading "Risk Factors" in the registration statement (including a preliminary prospectus) that we have filed with the SEC. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward- looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information.

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We have filed a registration statement (including a preliminary prospectus) on Form S-1 (File No. 333-250086) with the SEC for the offering to which this presentation relates. Before you invest, you should read the preliminary prospectus in that registration statement and other documents we have filed with the SEC for more complete information about us and this offering. You may get these documents for free by visiting the SEC website at http://www.sec.gov. Alternatively, copies of the prospectus may be obtained from Goldman Sachs & Co. LLC, Attention: Prospectus Department, 200 West Street, New York, NY 10282, by telephone at (866) 471-2526, or by email at prospectus-ny@ny.email.gs.com; SVB Leerink LLC, Attention: Syndicate Department, One Federal Street, 37th Floor, Boston, MA 02110, by telephone at (800) 808-7525, ext. 6132, or by email at syndicate@svbleerink.com; or Piper Sandler & Co., 800 Nicollet Mall, J12S03, Minneapolis, MN 55402, Attn: Prospectus Department, by telephone at (800) 747-3924, or by email at prospectus@psc.com.

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# Kinnate: Kinase Inhibitors for Genomically Defined Cancers

## Striving to Expand the Promise of Precision Medicine in Oncology

**Programs**

Multiple compounds advancing to the clinic in next 12-18 months

- All developed in house with IP & commercial rights fully retained

Lead RAF program targets large population not served by current approved RAF inhibitors

- IND filing expected in H1 2021

FGFR program targets significant unmet need of resistance to current FGFR inhibitors

- IND filing expected in H1 2022

R&D pipeline of additional compounds, including CDK12 inhibitor with synthetic lethality mechanism

**Platform**

Productive Kinnate Drug Discovery Engine powered by structure-based drug discovery, translational research and patient-driven precision medicine

**People**

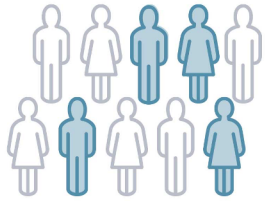
Experienced management team responsible for multiple approved precision oncology drugs

Strong scientific collaborations and KOL relationships with leading academic and medical centers

Funded by leading life science investors including Foresite, Orbimed and RA Capital

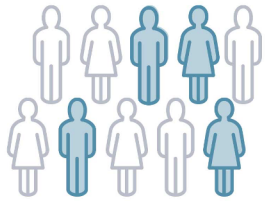
# Limitations of Current Targeted Therapies Drive Clinical Need

## Our Research and Development Programs Will Focus on Three Patient Populations



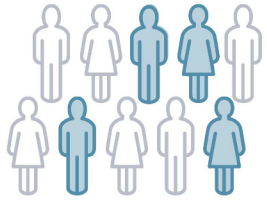
**Target known oncogenic drivers in cancers that are not addressed by approved therapies.**

- Example: KIN002787, our Class II and Class III BRAF-targeting small molecule kinase inhibitor



**Overcome acquired resistance mutations to existing targeted therapies, potentially improving the durability of response.**

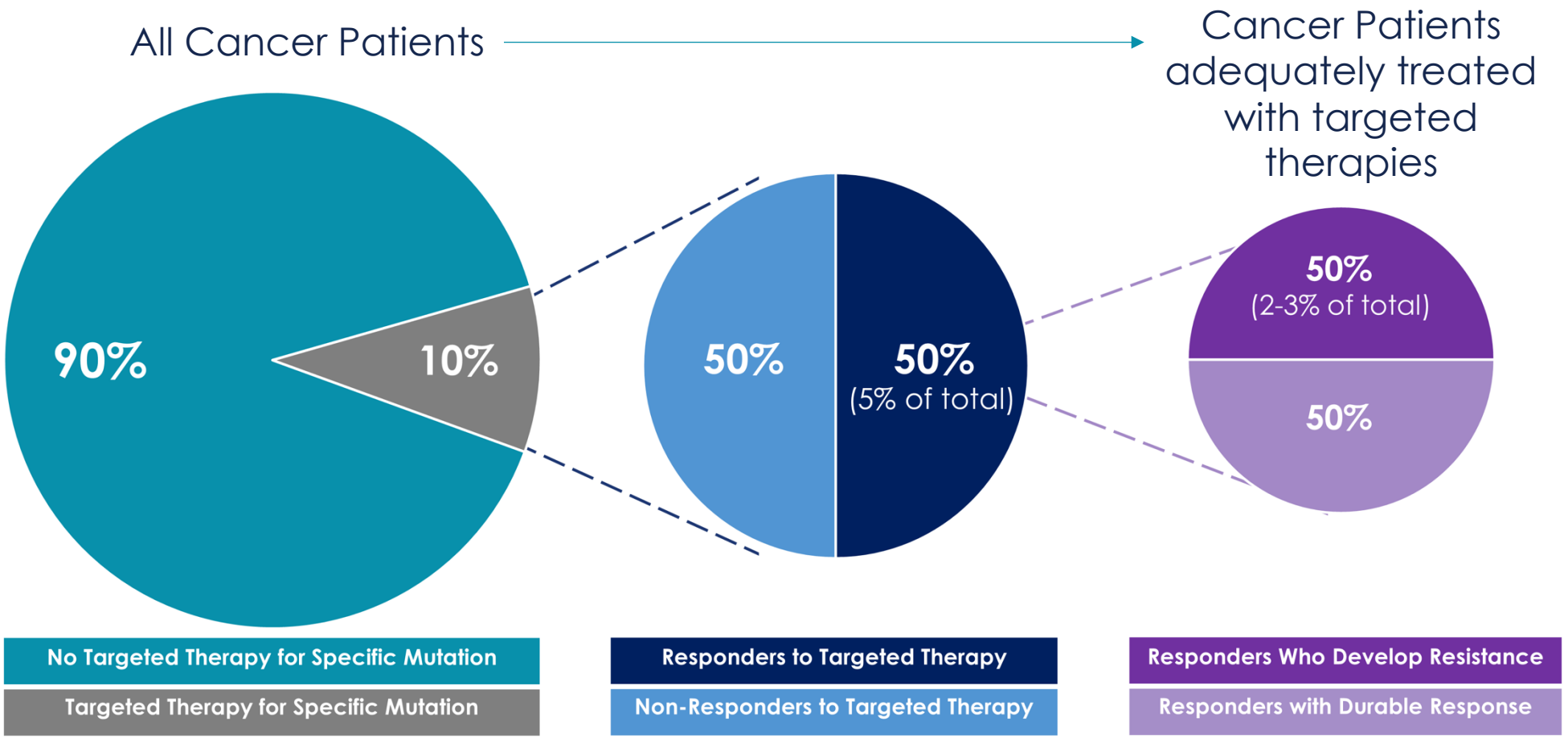
- Example: KIN003, our FGFR2/3-targeting small molecule kinase inhibitor



**Treat non-responders to approved therapies by identifying genomic drivers of intrinsic resistance through advanced technologies.**

- Example: KIN004, our selective CDK12 kinase inhibitor

# Substantial Opportunity in Targeted Therapies for Oncology

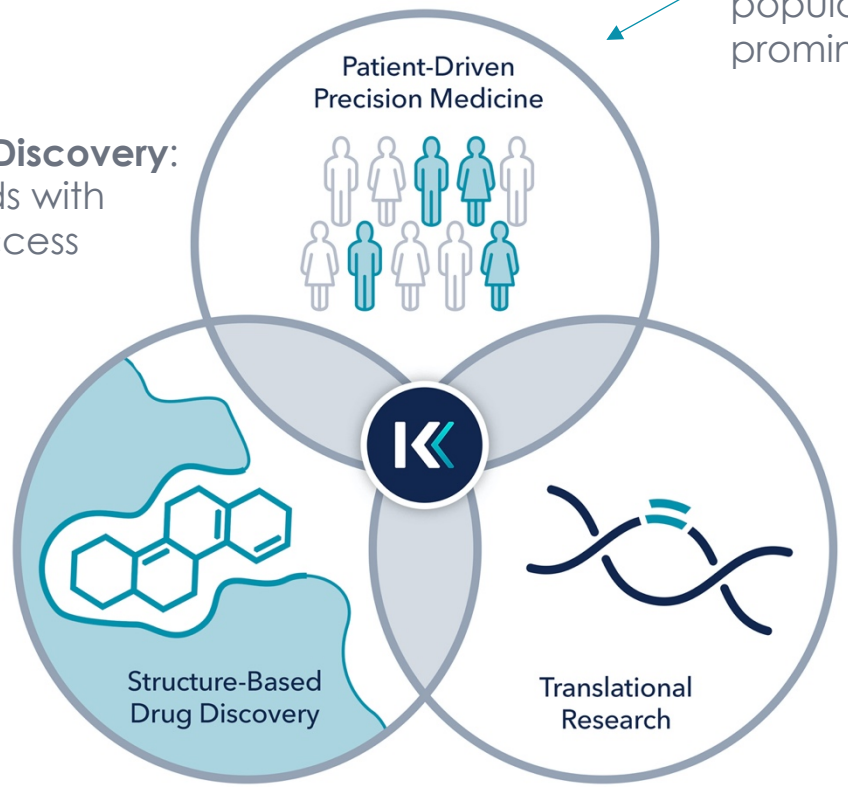



Source: Marquart JAMA ONOCLOGY 2018 https://pubmed.ncbi.nlm.nih.gov/29710180/; data available in USPIs for targeted cancer therapies approved in the US

# Kinnate Drug Discovery Engine

**Patient Driven Precision Medicine**: Defining emerging patient populations. Guided by premier cancer centers such as MGH and prominent KOLs

**Structure Based Drug Discovery**: Identifying compounds with high probability of success




Since company funded in March 2018

- >3300 NCEs generated
- >4000 DMPK studies
- >170 unique in vitro assays developed
- >80 animal studies across 17 xenograft models
- 30 compounds profiled for kinome selectivity
- 17 provisional patent applications filed across 14 families
- 3 Drug Candidates nominations in 2020
- **2 INDs expected by 2022**

**Translational Research**: Biomarker-driven approach to predict and increase the likelihood of therapeutic response

***Research & Development Team Experience:***
Crizotinib, Ceritinib, Axitinib, Cabozantanib, Capmatinib, Entrectinib, Encorafenib, Lorlatinib, Binimetinib, EGF816, LXH254, RXDX-105, PLX9486, PLX8394

# Kinnate Pipeline

| Target, Program | Discovery | Lead Optimization | IND-Enabling | Phase 1 | Phase 2 | Phase 3 | Next Anticipated Milestones |
|---|---|---|---|---|---|---|---|
| RAF KIN002787 |  | | | | | | IND H1 2021<br>Initiate Phase 1 in 2021 |
| FGFR2/3 KIN003 |  | | | | | | IND H1 2022<br>Initiate Phase 1 in H1 2022 |
| CDK12 KIN004 |  | | | | | | |

**Kinnate also working on other undisclosed targets in Research stage**

# Kinnate Team

## Creators of Multiple Marketed Drugs and High Value Exits

### Nima Farzan

*CEO*

- CEO PaxVax (BLA approval, M&A exit)
- Novartis – global & US commercial and development roles

### Eric Murphy, PhD

*CSO, Co-Founder*

- Novartis, CrownBio, Samumed, Moores UCSD Cancer Center
- Contributions: **Braftovi**, **Mektovi**, **LXH254**, Zykadia, Tabrecta, EGF816

### Steve Kaldor, PhD

*BOD, Co-Founder*

- >$2B M & A Value as CEO/Founder
- Inventor of Viracept, Nesina, Zafatek

### Richard Williams. MD

*CMO*

- Wuxi NextCode, GRAIL, Puma & Amgen
- Led Amgen's early oncology program

### Eric Martin, PhD

*SVP, Translational Medicine*

- Pfizer, Ignyta, Plexxikon
- Contributions: Palbociclib, Entrectinib, PLX9486, **PLX8394**

### Sanjeev Thohan, PhD

*VP, Non-Clinical Development*

- AZ, Exelixis, Novartis
- Over 35 INDs (20+ in Oncology)
- Contributions: Cabozantinib, Tafenoquine, Glucagon approvals

### Mark Meltz

*COO & GC*

- Led $3.5B Corporate Development Transactions
- Public company GC (Audentes)
- Novartis, Biogen, PaxVax, Audentes

### Rob Kania, PhD

*SVP Drug Discovery*

- Led Pfizer Cancer Chemistry group
- Co-inventor of 13 DCs
- Co- Inventor of Inlyta (axitinib), Xalkori (crizotinib), Lorbrena (lorlatinib)

Lilly · Pfizer · Takeda · Biogen · NOVARTIS · AstraZeneca · AMGEN

Plexxikon · Furiex Pharmaceuticals · ignyta · samumed · affymetrix · AUDENTES · GRAIL

Crinetics · CrownBio · WuXiNextCODE · syrrx · PaxVax · Puma Biotechnology · quanticel PHARMACEUTICALS

# Kinnate Board of Directors

## Kinnate Well-Funded $157M* on Hand +$276M Gross Proceeds from IPO

### Series A: March 2018-April 2019

- **Foresite Capital**
- Eshelman Ventures
- $19m raised

Jim Tananbaum
*Board Member*
*Foresite*

Michael Rome
*Board Member*
*Foresite*

Carl Gordon
*Board Member*
*Orbimed*

### Series B: December 2019

- **OrbiMed**
- Foresite Capital, Nextech Invest, Vida Ventures, Eshelman Ventures
- $74.5m raised

Keith Flaherty
*Board Member*
*Independent - MGH*

Dean Mitchell
*Board Chairman*
*Independent*

Laurie Smaldone
*Board Member*
*Independent*

### Series C: July-August 2020

- **RA Capital**
- Existing investors plus
- Viking, Fidelity, Venrock, Surveyor/Citadel, Boxer, Janus, Logos
- $98m raised

Melissa Epperly
*Board Member*
*Independent*

Steve Kaldor
*Board Member*
*Kinnate Co-founder*

Nima Farzan
*Board Member*
*Kinnate CEO*

*Cash and cash equivalents as of Sept 30th 2020

# Kinnate Scientific Collaborators

## Leaders in the Field of Precision Oncology

### Scientific Advisory Board

**Keith Flaherty**

- Professor, Harvard Medical School
- Director of Clinical Research, MGH Cancer Center
- Director, MGH Termeer Center for Targeted Therapy
- Loxo co-founder; RAF expert

Massachusetts General Hospital Cancer Center · Harvard Medical School

**Andy Lowy**

- Chief, Surgical Oncology
- PDAC expert

UC San Diego Moores Cancer Center

**Luis Diaz**

- Head of the Division of Solid Tumor Oncology Memorial Sloan Kettering Cancer Center

Memorial Sloan Kettering Cancer Center

**Ryan Corcoran**

- Associate Professor, Harvard Medical School
- Scientific Director, MGH Termeer Center for Targeted Therapy
- RAF & FGFR expert

Massachusetts General Hospital Cancer Center · Harvard Medical School

**Ezra Cohen**

- Co-Director San Diego Center for Precision Immunotherapy
- Assoc. Dir, Translational Science

UC San Diego Moores Cancer Center

**John Iafrate**

- Director of Center for Integrated Diagnostics at MGH
- Professor Pathology at Harvard Medical School

Massachusetts General Hospital Cancer Center · Harvard Medical School

*"I am a deeply invested advisor actively steering Kinnate's portfolio maturation and spending a large majority of my efforts advising Kinnate following the acquisition of Loxo by Eli Lilly ."* – Keith Flaherty

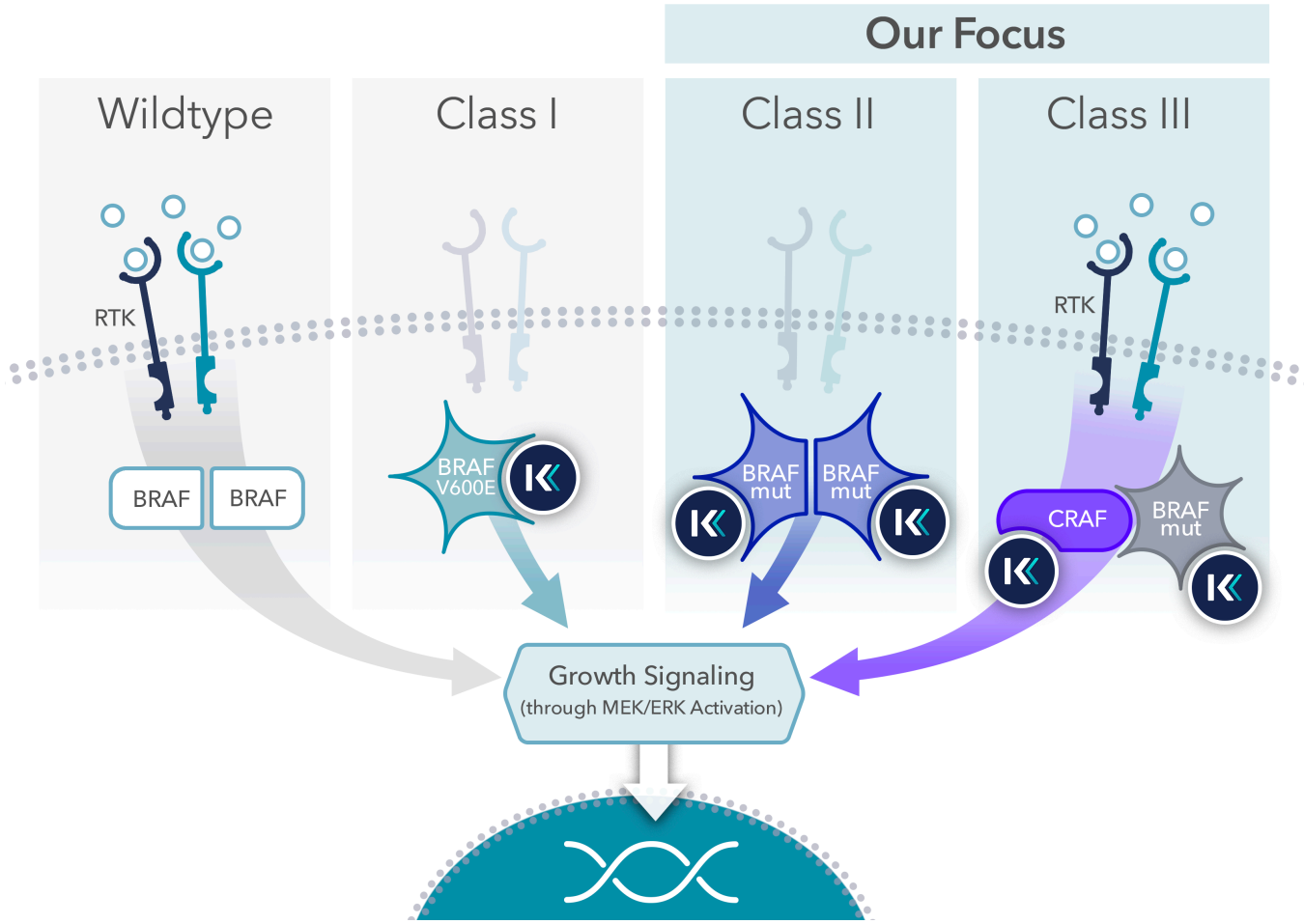
# RAF Program

KIN002787

# The RAF Opportunity

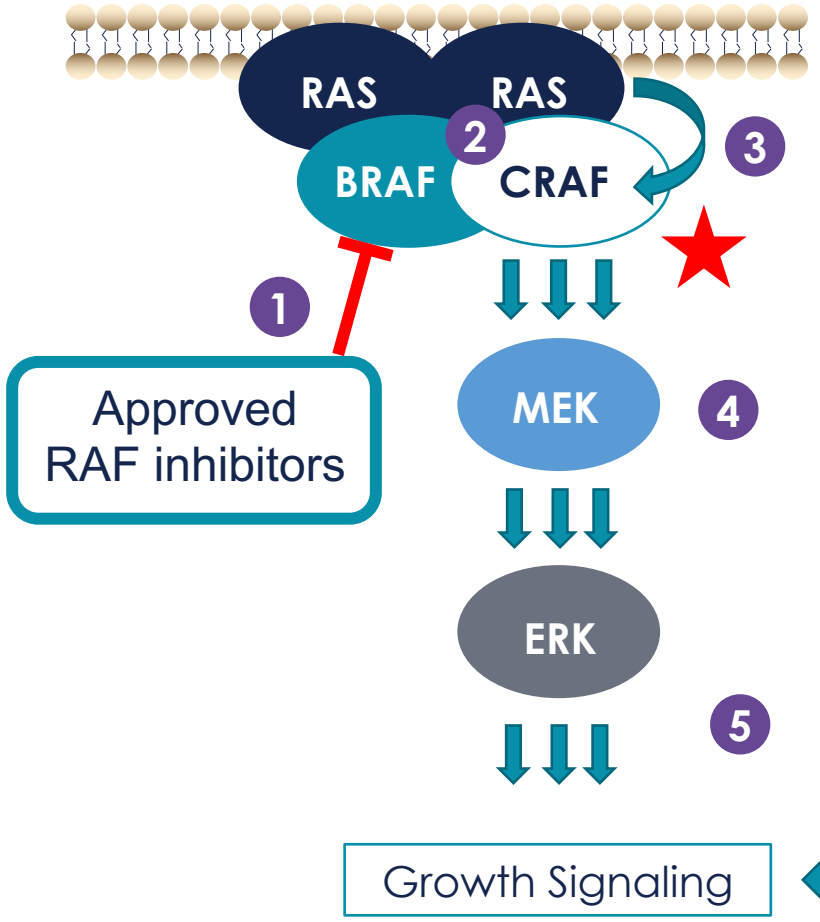
## Targeting BRAF Mutant Populations Without Approved Precision Therapies

- Approved Class I BRAF inhibitors include Vemurafenib, Dabrafenib, Encorafenib
- The Class II and Class III BRAF mutants represent a patient population with unmet need
- Kinnate's approach targets dimer signaling in these patient populations while minimizing MAPK pathway rebound in normal wild type signaling



# Inhibition of Both RAF Kinases in Dimer is Required

## Otherwise Transactivation drives MAPK signaling and Pathway Activation




1. BRAF Inhibitor binds to BRAF Target
2. BRAF + CRAF heterodimerize, recruited to RAS
3. Transactivation of CRAF via RAS binding
4. MEK and ERK activation
5. Elevated growth promoting signaling

★
- Paradoxical activation from BRAF with altered drug binding site due to asymmetric dimerization or CRAF in heterodimer
- Need molecule that can inhibit second kinase active site

- Why approved BRAF inhibitors can cause squamous cell carcinoma (SCC) in skin cells
- Why Class I BRAF inhibitors are often combined with a MEK inhibitor

Adapted from: S. Heidorn SJ et. al., **Kinase-Dead BRAF and Oncogenic RAS Cooperate to Drive Tumor Progression through CRAF**. Cell 140: 209-221, 2010

# Pathway Rebound & Target Coverage Present Challenges

## These Limitations Have Been Seen in Prior Attempts in Class II & Class III (LXH254 & PLX8394)

**Pathway Rebound:**

- Occurs when the non-inhibited BRAF molecule in the RAF dimer is activated
- Observed with both approved and In-development RAF inhibitors
- Occurs as drug concentrations approach & dip below effective levels

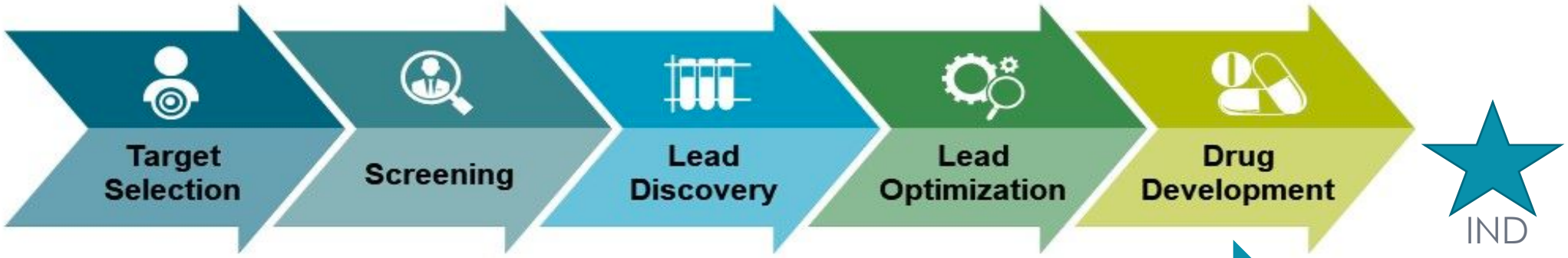

**Target Coverage:**

- Sub-optimal pharmaceutical properties (e.g. drug solubility, *in vivo* drug exposure) limit target coverage
- Dosing to high levels and drug combinations are compensatory strategies with limited or unproven benefit

Equivalent & Persistent Inhibition of Both RAF molecules in the Dimer Is Required to Avoid Pathway Rebound AND Target BRAF Dimer-driven cancers

# Kinnate RAF Franchise

## KIN002787 Has Demonstrated Dimer Inhibition & Target Coverage, Avoiding Pathway Rebound




1st Gen KIN002787

- Improved pharmaceutical properties and HED vs competitive efforts
- Solve pathway rebound & target coverage issues
- IND Enabling work ongoing with rat & cyno GLP tox complete – expect IND filing in H1 2021

Backup

- Back up in case of idiosyncratic issue in Ph1 – otherwise won't be developed

2rd Gen ongoing

- RAF isoform specificity (BRAF or CRAF selective)
- Possibility to target new populations – eg *RAF-1* fusion-driven CNS tumors
- Goal is to develop alongside and after 2787 in new populations

# Dimer Inhibition Demonstrated Across Several Cell Lines

## While Maintaining Selectivity Against Non BRAF Mutated Cells

| Mutant *BRAF* Class | Cell Line | BRAF / MAPK Pathway Alteration(s) | Roche cobimetinib $EC_{50}$ (nM) | Novartis LXH254 $EC_{50}$ (nM) | Kinnate KIN002787 $EC_{50}$ (nM) |
|---|---|---|---|---|---|
| **I** | A375 | *BRAF*$^{V600E}$ | 4 | 157 | **62** |
| **II** | BxPC3 | *BRAF* indel | 6 | 25 | **31** |
| **II** | OV90 | *BRAF* indel | 2 | 16 | **25** |
| **II** | H2405 | *BRAF* indel | 2 | 6 | **4** |
| **III** | WM3629 | *BRAF*$^{D594G}$ / *NRAS*$^{G12D}$ | 3 | 4 | **8** |
| **III** | CAL12T | *BRAF*$^{G466V}$ | 4 | 22 | **12** |
| **WT** | MiaPaCa-2 | *BRAF* WT / *KRAS*$^{G12C}$ | 9 | 357 | **517** |
| **WT** | CHL-1 | *BRAF* WT / *NRAS* WT | 5 | 368 | **579** |

**pERK Inhibition**

Note: More potent inhibition is reflected by a lower $EC_{50}$ number presented in nM concentration

- Clear differentiation from MEK inhibitors that do not differentiate against WT (wild type)
- NVS LXH254 has similar profile in cells, but suffers from sub-optimal exposure *in vivo*

# Improved Solubility Increases *In Vivo* Target Exposure

## Increased Target Exposure Prevents Pathway Rebound & Lowers Necessary Dose

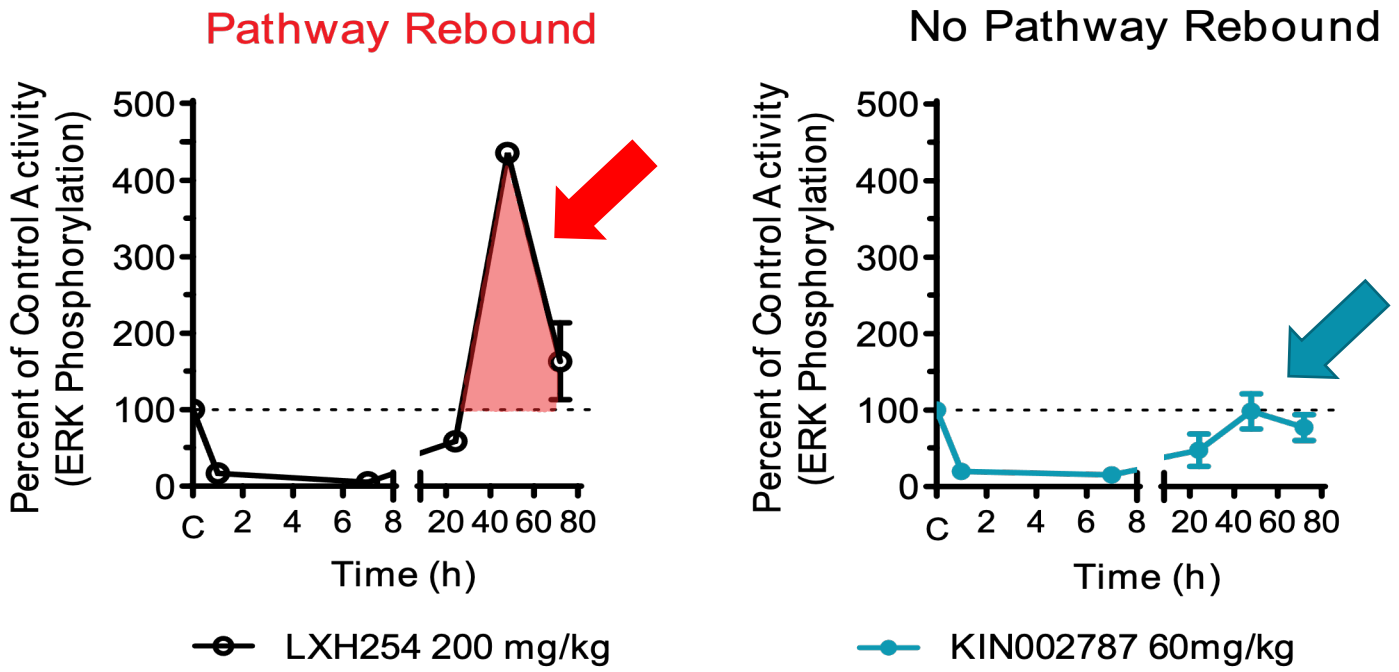
| Feature | Parameter | Novartis LXH254 | Kinnate KIN002787 |
|---|---|---|---|
| ***In vitro* drug solubility** | **Aqueous Solubility (μM)**<br>pH = 7.4<br>pH = 4.5<br>pH = 2.0 | <br>**8**<br>**7**<br>**50** | <br>**29**<br>**196**<br>**312** |
| ***In vivo* mouse pharmacology** | **100 mg/kg per oral dose**<br>Clearance (mL/min/kg)<br>AUC / dose (ng*h/mL) | <br>**10**<br>**1123** | <br>**8**<br>**3335** |

} **Relevant physiological pH**

Improved aqueous solubility, lower clearance in vivo, and increased drug exposure all enhance the likelihood that KIN002787 may achieve greater target coverage in the clinical setting

# Unlike LXH254, KIN002787 Did Not Show Pathway Rebound

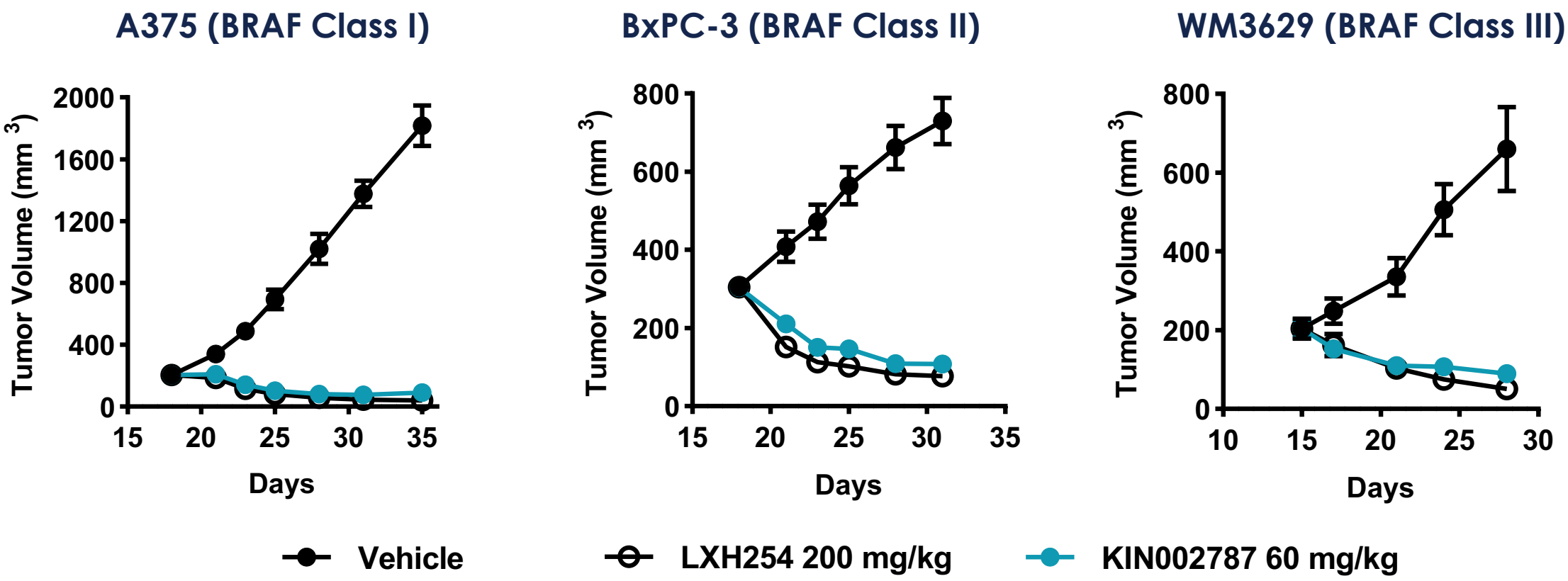
## Due to Potent Dimer Inhibition & Improved Target Exposure




- No pathway rebound was observed with KIN002787 in WM3629 (Class III, *BRAF*$^{D594G}$/*NRAS*$^{G12D}$) xenografts compared to >400% pERK levels observed with LXH254 at 48 hours post-dose

# Tumor Regressions Achieved Across All Classes of Mutation

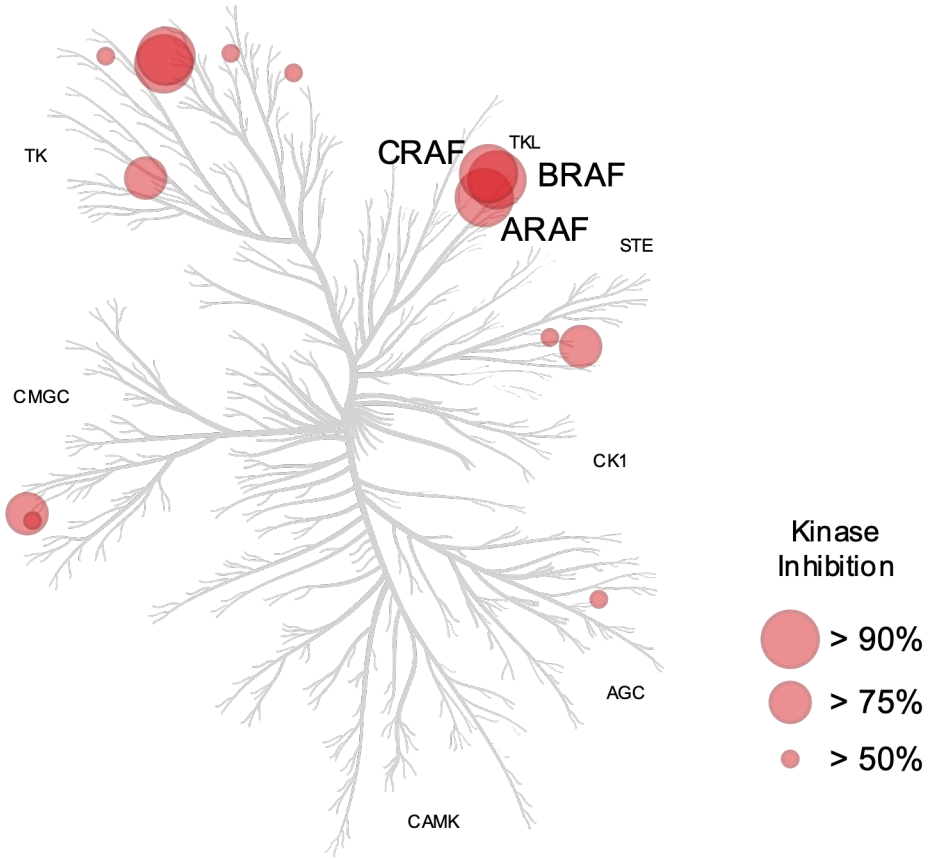
## Head to Head Data Shows Benefit from Target Exposure & Limited Pathway Activation & Rebound




- KINN02787 (60 mg/kg QD) and LXH254 (200 mg/kg QD) both demonstrated tumor regressions
- 200 mg/kg LXH254 is **>4-fold** increased free drug exposure relative to the highest clinical dose (600 mg BID)

# KIN002787 Displays a Highly Selective RAF Kinase Profile

## Kinome Profiling



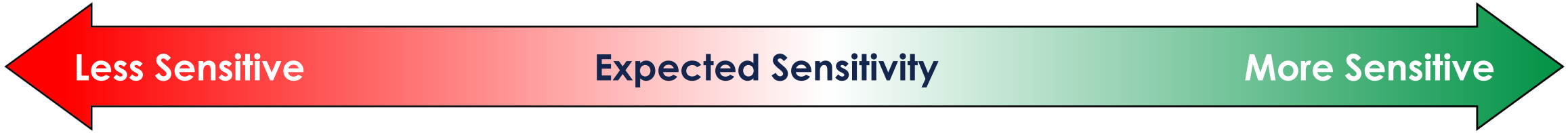

## 10-point Dose Response

| Kinase | KIN002787 $IC_{50}$ (nM) |
|---|---|
| **CRAF** | **0.573** |
| **BRAF $^{V600E}$** | **1.53** |
| **ARAF** | **2.41** |
| **BRAF** | **3.46** |
| DDR1 | 108 |
| PDGFRB | 445 |
| p38alpha | 1230 |
| EPHA2 | >3000 |
| KDR | >3000 |
| LCK | >3000 |
| SRC | >3000 |

- Kinome profiling @ 1µM across >600 enzymatic assays at Reaction Biology Corp (*372 WT, 23 atypical, 258 MT)*
- Follow-up 10 pt dose response enzymatic assays (right table) for known BRAF inhibitor off-targets

# Sensitivity to BRAF Inhibition in BRAF Mutation-Driven Cancers

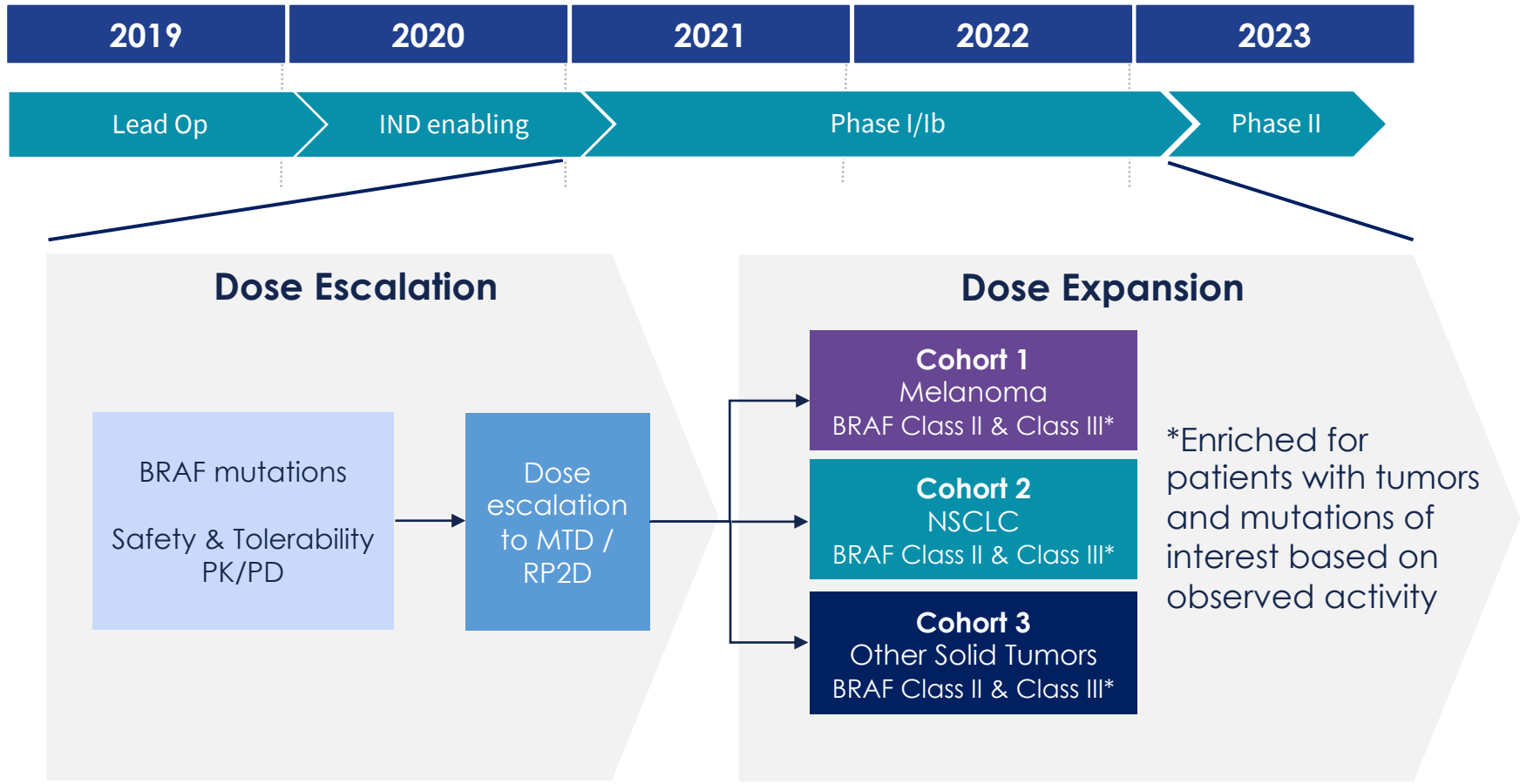
## Spectrum of Sensitivity Will be Directly Evaluated in our FIH Trial




| **BRAF Class I:** Refractory to prior RAFi therapy | **BRAF Class I:** BRAFi-Naive patients | **BRAF Class III:** SNVs | **BRAF Class II:** Indels + SNVs | **BRAF Class II:** Gene Fusions |
|---|---|---|---|---|
| ▪ Diverse resistance mechanisms raise uncertainty for substantial human clinical efficacy of KIN002787 monotherapy | ▪ KIN002787 demonstrated substantial *in vitro* activity & *in vivo* tumor regressions | ▪ KIN002787 sensitivity likely depends upon identity of co-occurring upstream RAS activation (e.g. EGFR amplification, KRAS mutation, NF1 loss) | ▪ KIN002787 demonstrated very substantial *in vitro* activity & *in vivo* tumor regressions | ▪ KIN002787 demonstrates very substantial *in vitro* activity & *in vivo* tumor regressions<br>▪ Complete regressions reported in limited BRAF gene fusion-driven cancers treated with PLX8394 |

# KIN002787 Expected Development Plan: Phase 1 Trial

## Well Positioned for Expedited POC

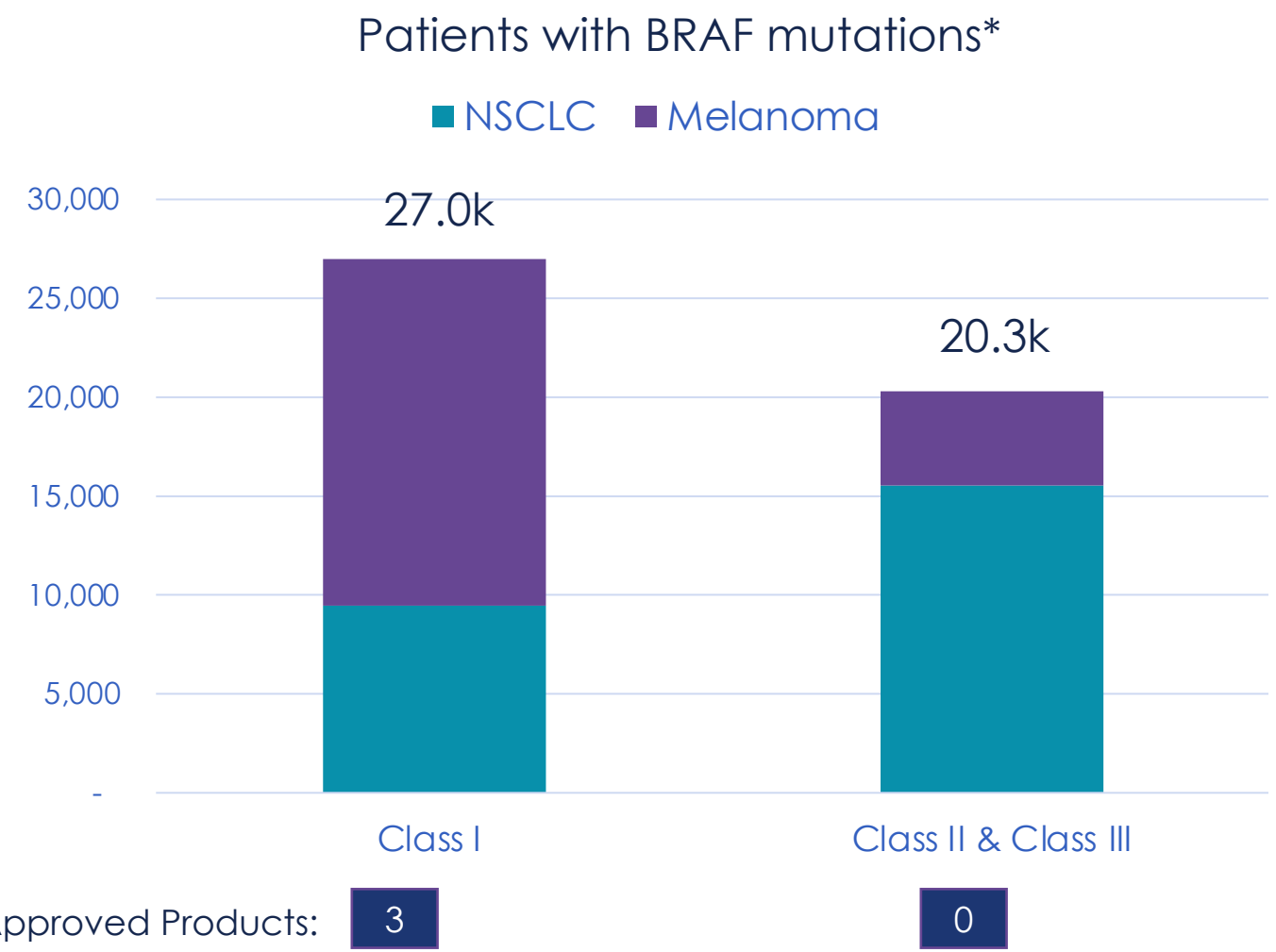


# FIH Study: Inclusion Criteria

## Phase 1 Trial Patient Inclusion Criteria for Dose Escalation and Dose Expansion

| Study Part | Population (Advanced or Metastatic cancers) |
|---|---|
| **A. Dose Escalation** (n=25) | Patients with any of the following:<br>• Class I ($BRAF^{V600}$) mutant positive cancer, or<br>• Class II BRAF mutant positive cancer, or<br>• Class III BRAF mutant positive cancer |
| **B. Dose Expansion** (3 cohorts, n=25 each) | #1 Melanoma (*BRAF* Class II or Class III mutations) |
| | #2 NSCLC (*BRAF* Class II or Class III mutations) |
| | #3 Other solid tumors (*BRAF* Class II or Class III mutations) |

# Class II & Class III Population is Similar to Class I But Without Approved Drugs




- 2019 sales of the 3 approved products for Class I BRAF mutations were $1.4B
  - 18% growth from 2018 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

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

Kinnate calculations based on Kantar data and data available at Genie v8.0 (https://genie.cbioportal.org/) and the AACR Project GENIE (Cancer Discov; 7(8); 818–31, 2017).

# BRAF Program Opportunities for Expansion

## Opportunities to Expand Beyond Initial Target of ~20k patients

- Additional cancers (e.g., CRC, ovarian & thyroid) including potential tumor agnostic indication
  - 8,900 patients have advanced CRC with Class II & Class III mutations
  - Additional patients with ovarian and thyroid cancers - to be determined
- Earlier treatment lines and less advanced disease settings
  - 2,000 patients have Stage IIIa NSCLC with Class II & Class III mutations
  - 3,500 patients have Stage III Melanoma with Class II & Class III mutations
- Class I BRAF mutations, including both first line and second line for intrinsic and acquired resistance
  - 27,000 patients have advanced NSCLC and Melanoma with Class I mutations
- Expanding into other geographies (e.g., China) with high disease burden
  - 15,000 patients with advanced NSCLC and Class II & Class III mutations in urban markets of China

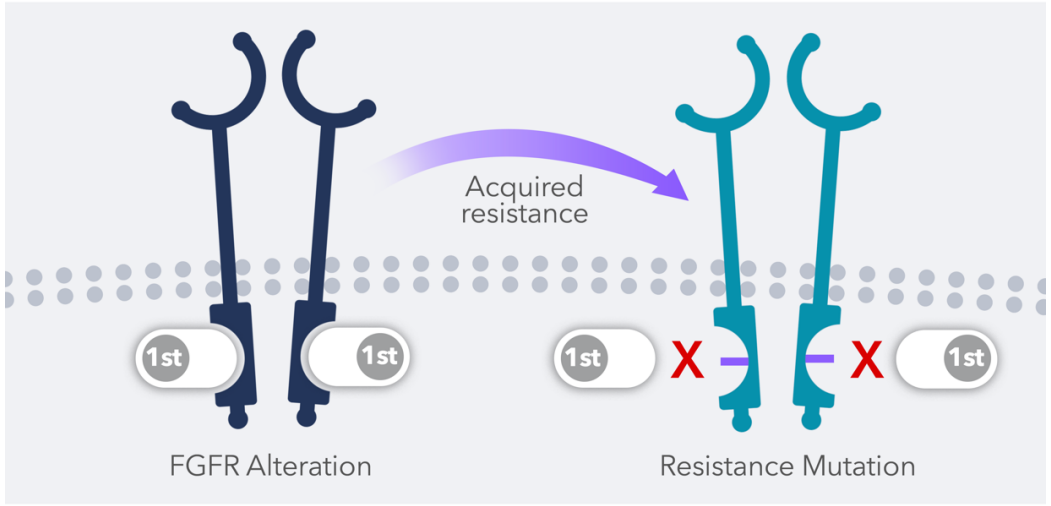
# FGFR2/3 Program

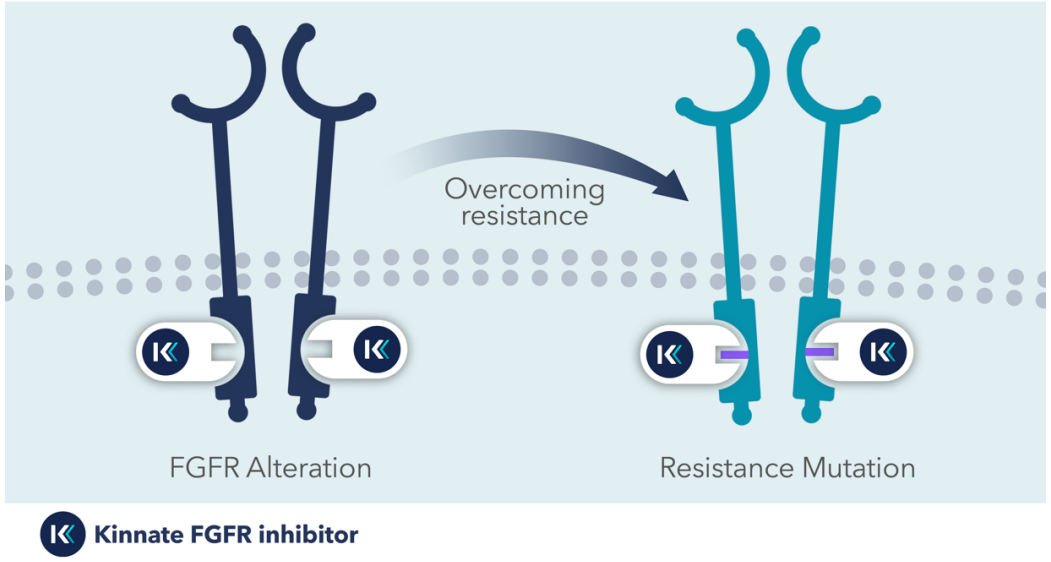
KIN003

# Kinnate FGFR 2/3 Inhibitor Program

## Targeting Acquired Resistance Mechanisms

- Current marketed (erdafitinib, pemigatinib) and clinical (futibatinib) FGFR inhibitors provide benefit, but duration of response limited by acquired resistance mutations
- Kinnate next generation FGFR inhibitor designed to cover fusions, insertion/deletions & SNVs in FGFR2 altered ICC & FGFR3 altered UC
- To improve duration of response, our program also targets acquired resistance mutations to existing therapies (e.g. gatekeeper & molecular brake)
- Analogous to development of EGFR inhibitors – erlotinib followed by osimertinib
- Also, broadly covering FGFR1, 2 & 3 isoforms may prevent bypass mechanisms improving response rates and duration of response

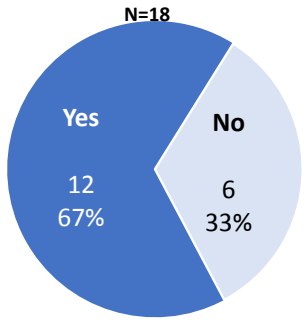


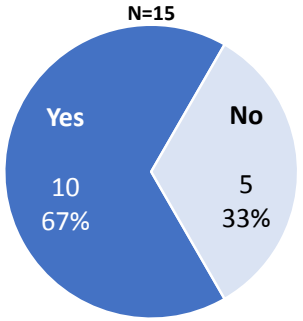
# Acquired Resistance to First Generation FGFR Inhibitors

**FGFR2 Kinase Domain Mutation**

**Reversible FGFRi (Erdafitinib, Pemigatinib, etc)**




**Irreversible FGFRi (Futibatinib)**



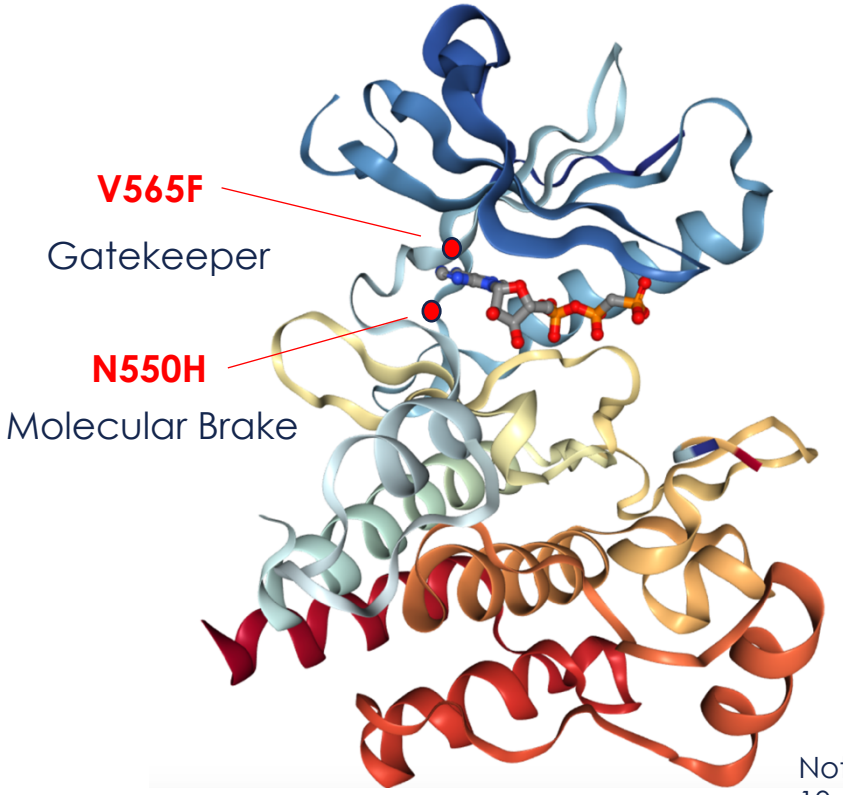

| | Erdafitinib, Pemigatinib, etc | | Futibatinib | | |
|---|---|---|---|---|---|
| | Reversible (n=13) | | Irreversible (n=10) | | |
| FGFR2 KDmuts Detected* | N | Frequency of Alteration | N | Frequency of Alteration | |
| N550D | 3/13 | 23% | 3/10 | 30% | Molecular Brake |
| N550H | 3/13 | 23% | 3/10 | 30% | |
| N550K | 2/13 | 15% | 7/10 | 70% | |
| N550T | 1/13 | 8% | 0/10 | 0% | |
| V565F | 4/13 | 31% | 3/10 | 30% | Gatekeeper |
| V565I | 2/13 | 15% | 1/10 | 10% | |
| V565L | 0/13 | 0% | 3/10 | 30% | |
| E566A | 1/13 | 8% | 3/10 | 30% | Molecular Brake |
| L618V | 2/13 | 15% | 0/10 | 0% | |
| L618F | 1/13 | 8% | 0/10 | 0% | |
| C492F | 0/13 | 0% | 1/10 | 10% | |

- Majority (67%) of patients treated with FGFR inhibitors developed secondary FGFR2 kinase domain mutations

Goyal (Uboha) et al; Presented at the 32nd EORTC-NCI-AACR Symposium (October 2020)

# KIN003 is Differentiated in Enzymatic Assays

## Overcomes FGFR2 and FGFR3 Gatekeeper and Molecular Brake Resistance Mutations



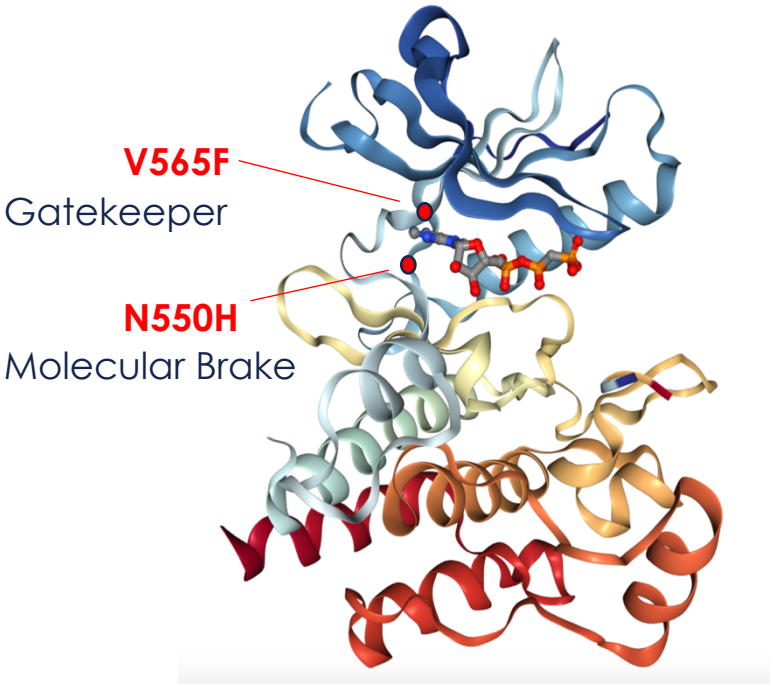

| Kinase Domain | Alteration | Janssen erdafitinib $IC_{50}$ (nM) | Incyte pemigatinib $IC_{50}$ (nM) | Taiho futibatinib $IC_{50}$ (nM) | Kinnate KIN003 $IC_{50}$ (nM) |
|---|---|---|---|---|---|
| FGFR1 WT | N/A | 0.22 | 0.4 | 2.1 | **4.2** |
| FGFR2 WT<br>FGFR2 V565F<br>FGFR2 N550H | N/A<br>Gatekeeper<br>Mol. Brake | 0.15<br>330<br>4.1 | 0.4<br>>500<br>19.8 | 1.4<br>>500<br>36.4 | **3.8**<br>**22.5**<br>**22.5** |
| FGFR3 WT<br>FGFR3 V555M<br>FGFR3 K650M | N/A<br>Gatekeeper<br>Mol. Brake | 0.73<br>137<br>3.5 | 1.5<br>>500<br>20 | 5.3<br>324<br>8.3 | **6.0**<br>**23.5**<br>**4.2** |
| **Ratios of Resistance Mutations Compared to Unmutated (WT) (Fold Difference in $IC_{50}$)** | | | | | |
| R2 V565F / R2 WT<br>R2 N550H / R2 WT<br>R3 V555M / R3 WT<br>R3 K650M / R3 WT | Gatekeeper<br>Mol. Brake<br>Gatekeeper<br>Mol. Brake | 2200X<br>27X<br>188X<br>5X | >1250X<br>50X<br>>333X<br>13X | >385X<br>31X<br>61X<br>1.6X | **6X**<br>**6X**<br>**4X**<br>**0.7X** |

Note: Ratios <10x = equivalent kinase inhibition of either the resistance mutations or corresponding WT kinase. Ratios > 10x = substantial loss of activity against the indicated resistance mutations compared to the corresponding WT kinase

- KIN003 showed inhibition of the gatekeeper and molecular brake mutations when compared to the FDA approved and clinical candidate FGFR inhibitors

# Cellular Data on FGFR2 Also Supports Differentiation

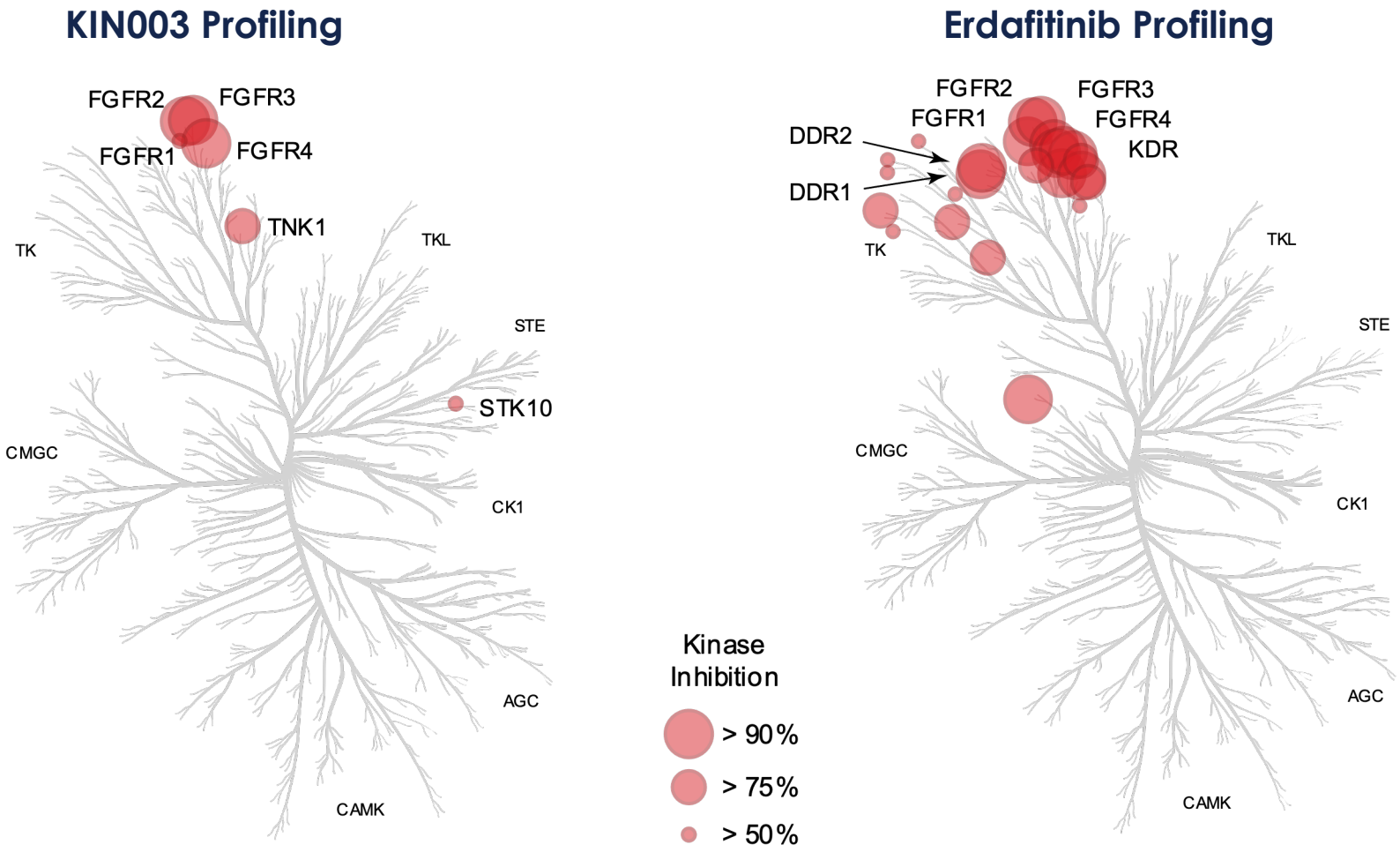
## Equivalent Inhibition of Multiple Mutations Critical to Overcoming Resistance




| Kinase Domain | Alteration | Janssen erdafitinib $EC_{50}$ (nM) | Incyte pemigatinib $EC_{50}$ (nM) | Taiho futibatinib $EC_{50}$ (nM) | Kinnate KIN003 $EC_{50}$ (nM) |
|---|---|---|---|---|---|
| FGFR2 WT | Fusion | 1.3 | 10.2 | 0.42 | **3.7** |
| M538I | Fusion + Activating Mut. | 2.8 | 27.3 | 0.98 | **7.3** |
| N550H | Fusion + Mol. Brake | 6.5 | 68.9 | 2.1 | **6.7** |
| N550K | Fusion + Mol. Brake | 19.6 | 1579 | 5.9 | **7.6** |
| V565F | Fusion + Gatekeeper | 2423 | >10000 | 170 | **5.9** |
| V565L | Fusion + Gatekeeper | 23.9 | -- | -- | **6.7** |
| V565I | Fusion + Gatekeeper | 6.5 | -- | -- | **7.0** |
| **Ratios of Resistance Mutations to Unmutated WT FGFR2 Alleles (Fold Difference in $EC_{50}$)** | | | | | |
| M538I / WT | Activating Mutation | 2.1x | 2.7x | 2.1x | **2.0x** |
| N550H / WT | Molecular Brake | 4.9x | 6.8x | 5x | **1.8x** |
| N550K / WT | Molecular Brake | 14.7x | 155x | 14x | **2.1x** |
| V565F / WT | Gatekeeper | 1823x | >1000x | 405x | **1.6x** |
| V565L / WT | Gatekeeper | 18x | -- | -- | **1.8x** |
| V565I / WT | Gatekeeper | 4.9x | -- | -- | **1.9x** |

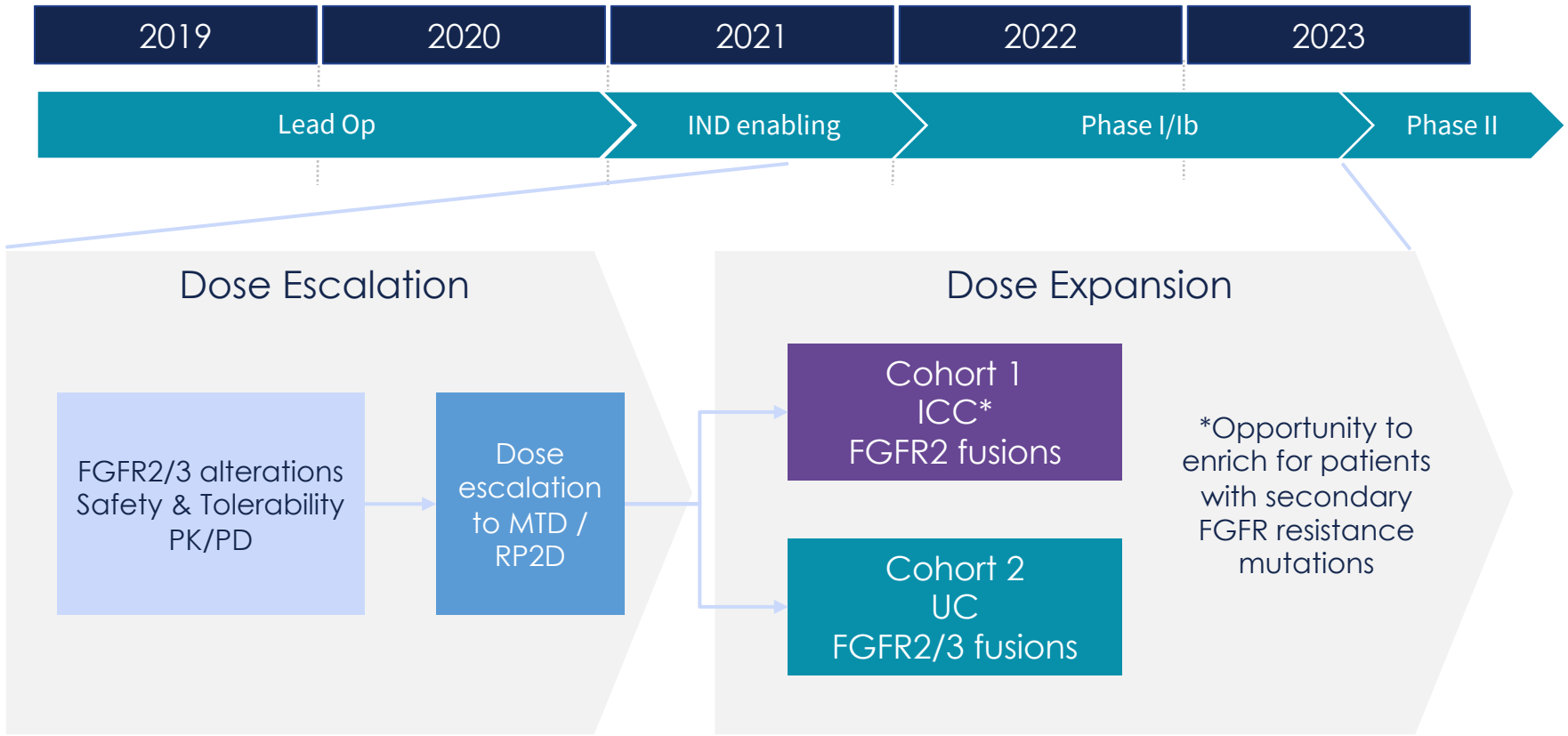
Note: Ratios <10x = equivalent inhibition of CCLP-1 cells expressing either the indicated resistance mutation or the WT FGFR fusion. Ratios >10x = a significant loss of inhibition against the indicated resistance mutation compared to the WT FGFR fusion. Ratios > 100x = a substantial loss of inhibition against the indicated resistance mutation compared to the WT FGFR fusion.

# KIN003 Displays a Selective & Differentiated Kinase Profile



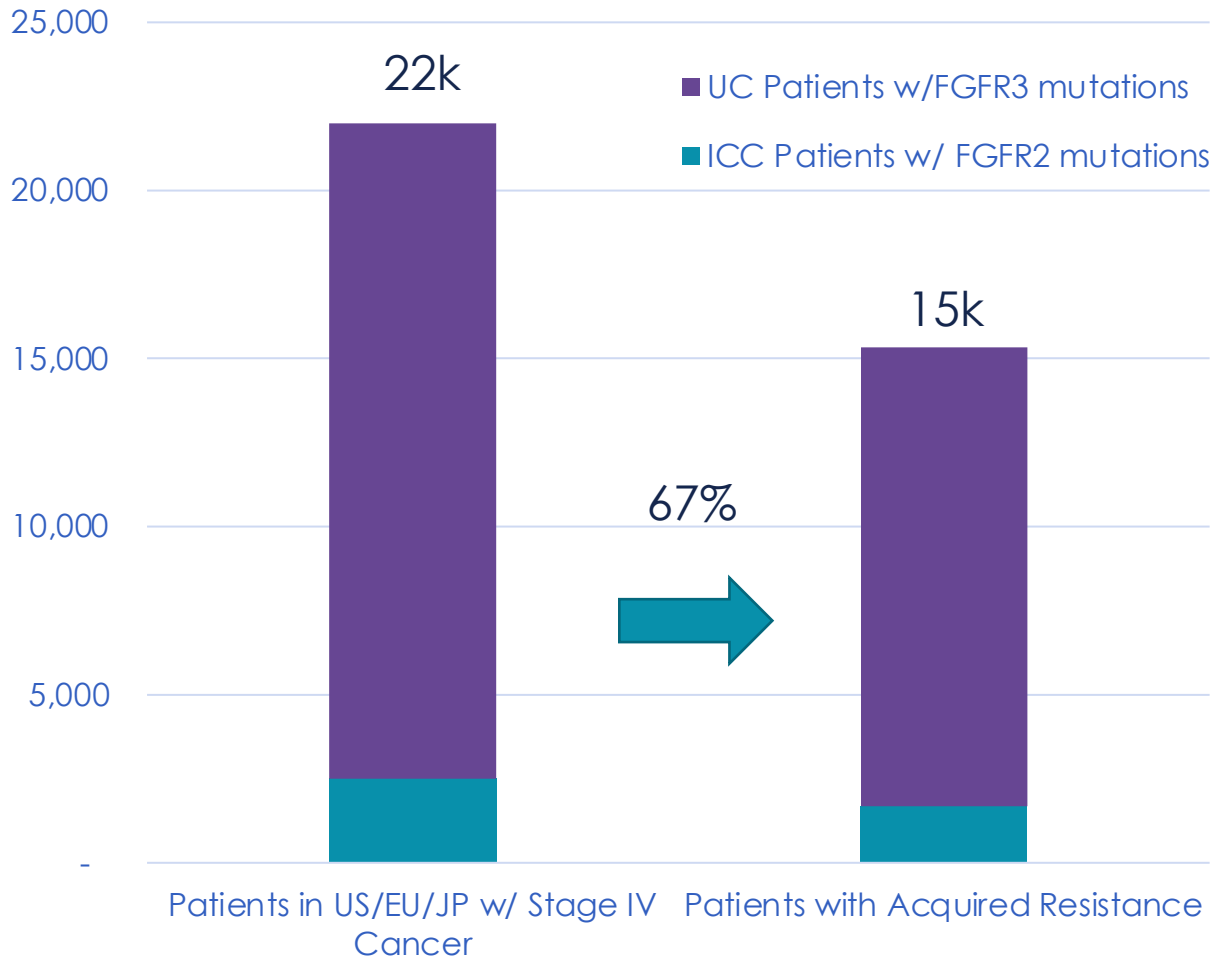

- Kinome profiling @ 1µM across 322 kinases at Carna Biosciences Corp
- Erdafitinib is approved for treatment of FGFR2 and FGFR3 alteration-driven urothelial cancer

# FGFR2/3 Expected Clinical Development Plan



# FGFR Market Opportunity – UC & ICC Patients in US, EU & Japan

## Patients with Active Disease




<u>Opportunities for Growth</u>

- FGFR alterations have been found in other tumors (e.g. breast)
- NGS technologies identifying additional patients with FGFR fusions
- Expansion beyond fusions into indels and SNVs in FGFR
- Geographic expansion (e.g. China)

# Kinnate Discovery Engine

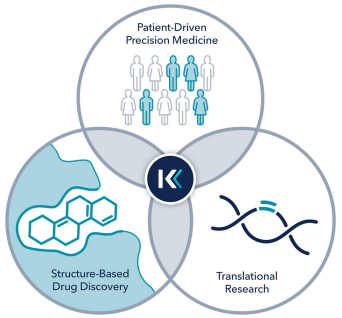
## Research Capabilities

## KIN004 – CDK12 Program

# Cancer Biology & Genomics Drives Drug Discovery Opportunities

## Continued Advancements of our Understanding of Disease Reveal our Next Generation Drug Targets

**Our Focus:** We remain focused on validated oncogenic drivers that directly inform patient selection strategies and are associated with enhanced probabilities of technical, clinical & regulatory success

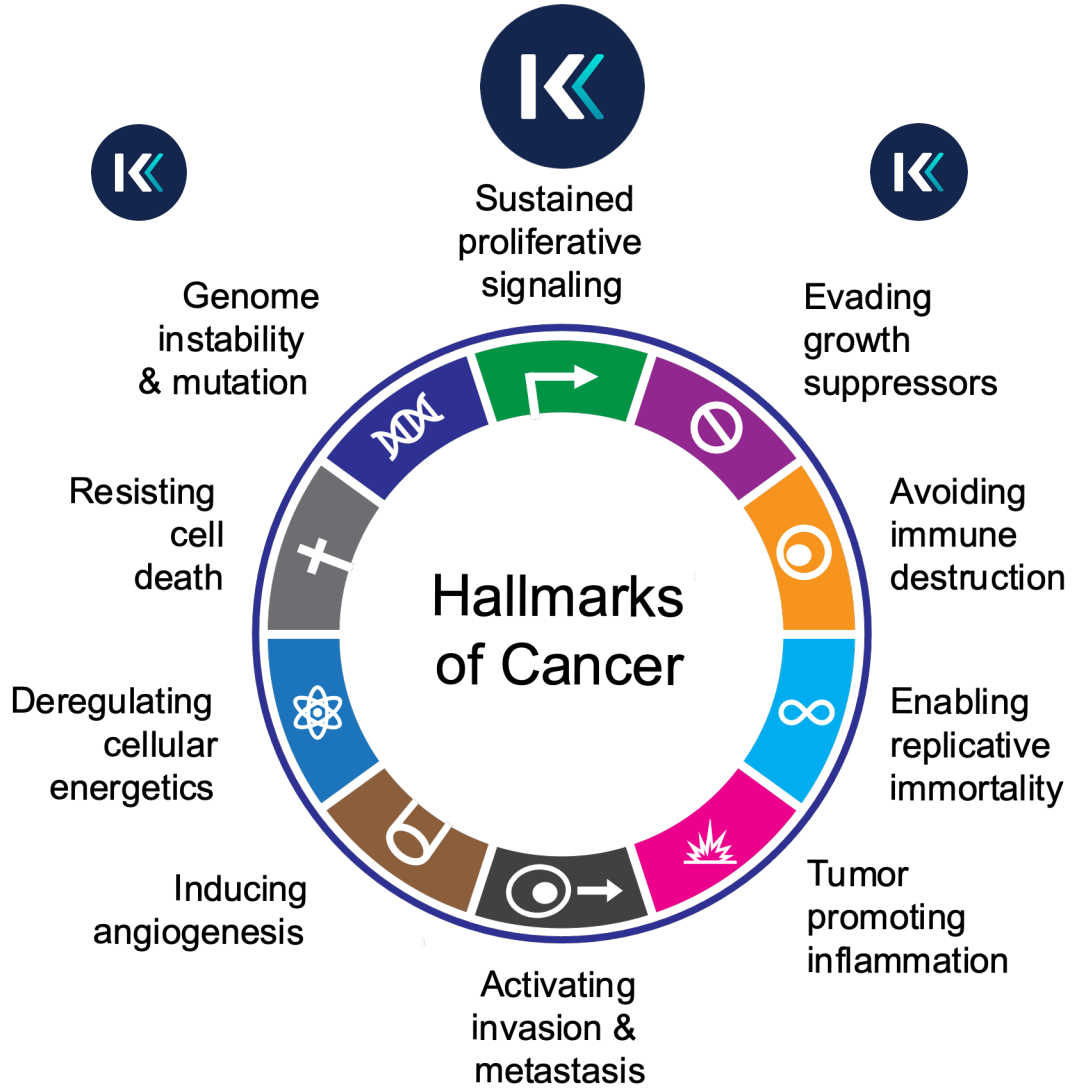



**Our Approach:** Our Kinnate Discovery Engine, fueled by our small molecule structure-based drug design capabilities and translational research strategies, will serve as the foundation for continued success

**Not Kinnate's Focus:** 'Pure-play' Immuno-oncology approaches, tumor micro-environment directed strategies, microbiome-based therapies, cellular therapies & cancer vaccines, and biology that is non-tractable with current technology

# Therapeutic Targeting of the Hallmarks of Cancer

## Focus on Validated Signaling Drivers, Growth Suppressors and Regulators of Genome Stability




**Modified from Hanahan and Weinberg, Cell 2011.**

# Kinnate Discovery Engine Resources

**Internal Preclinical Development:**
- DMPK/ADME
- Nonclinical Pharm
- Nonclinical Toxicology
- CMC Manufacturing

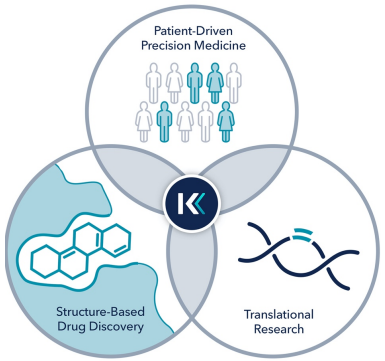
**7 FTEs + 9 Contractors**

**External Preclinical Development:**
- DMPK/ADME
- Nonclinical Pharm
- Nonclinical Toxicology
- CMC Manufacturing

**17 CROs**

**Internal Drug Discovery:**
- MedChem
- Comp Chem
- Cheminformatics
- Screening Team

**10 FTEs + 2 Contractors**




**Internal Translational Research:**
- *In Vitro* Pharm
- *In Vivo* Pharm
- Biomarkers
- Bioinformatics

**9 FTEs + 4 Contractors**

**External Drug Discovery:**
- Chemistry
- ARD/PRD Chemistry
- Structural Biology
- Biochemical & Biophysical

**64 FTE Chemists + 13 CROs**

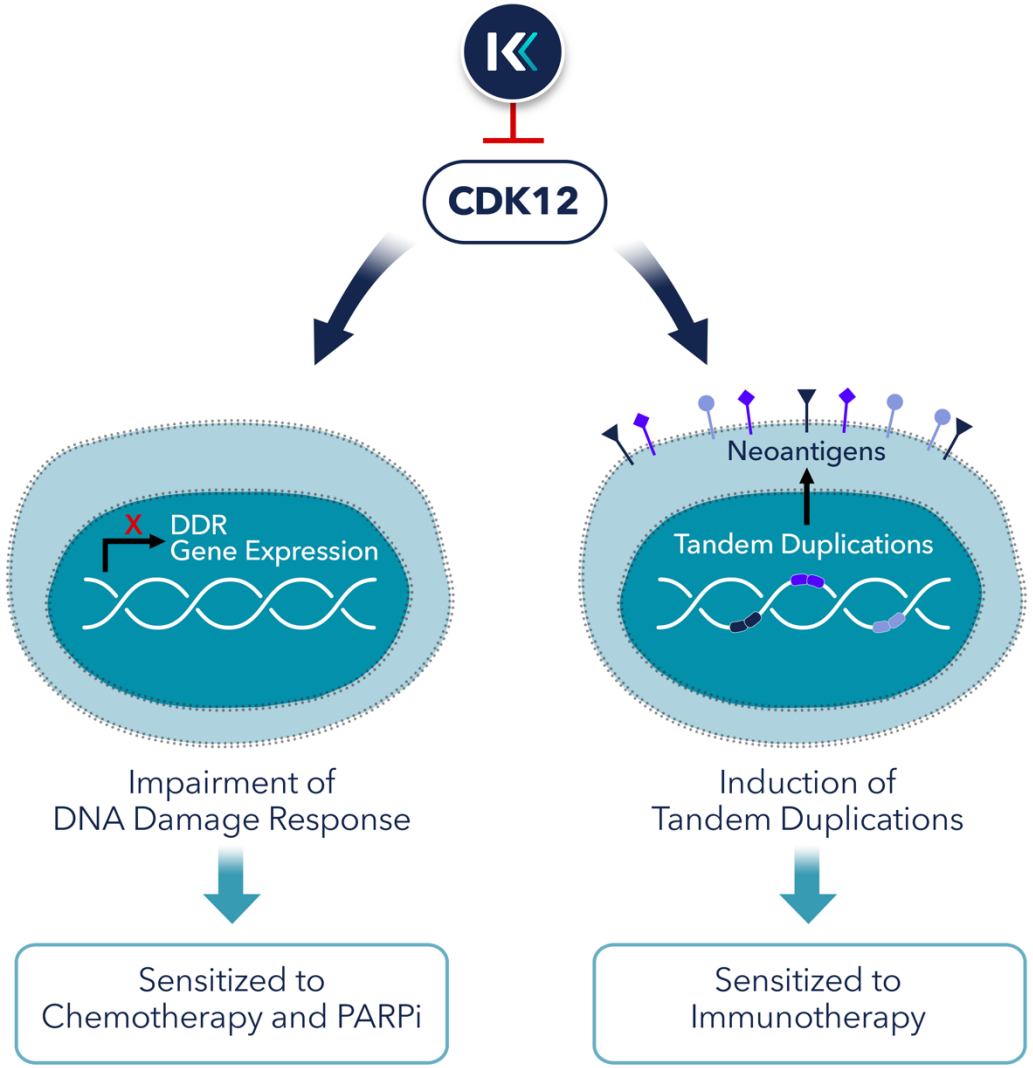
>150 FTEs Across Core CROs

**External Translational Research:**
- *In Vitro* Pharm
- *In Vivo* Pharm
- Biomarkers
- Bioinformatics

**21 CROs**

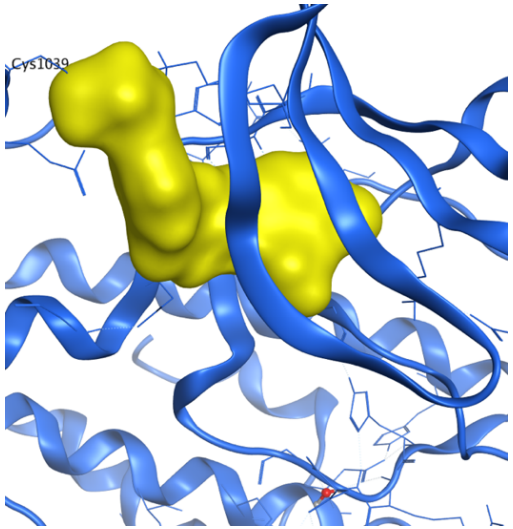
# CDK12 Inactivation Impairs DNA Damage Response and Induces Tandem Duplications

- CDK12, a RNA polymerase II C-Terminal Domain (CTD) kinase, is an essential regulator of various DNA damage response (DDR) genes
- Inhibition of CDK12 sensitizes tumors to DNA damaging agents and induces synthetic lethality in both DDR-deficient and the greater unmet need in DDR-proficient tumors
- CDK12-mutant ovarian and prostate cancers demonstrate an accumulation of large Tandem Duplications (TDs) resulting in accumulation of fusion-induced neoantigens (FINAs) in cancer cells

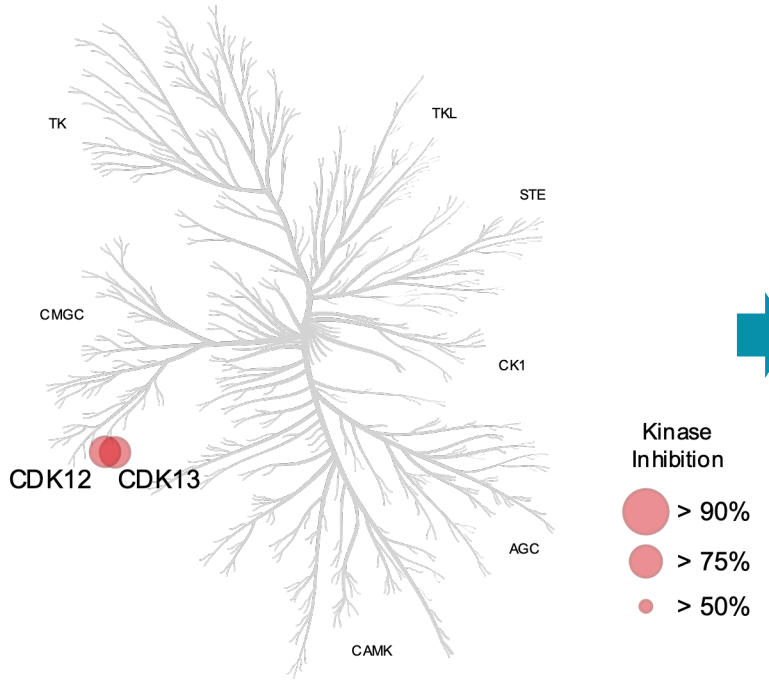


# Program Has Demonstrated Selective CDK12 Inhibition

**KIN004**
**Co-Crystal Structure**




**Kinome Profile – KIN004**



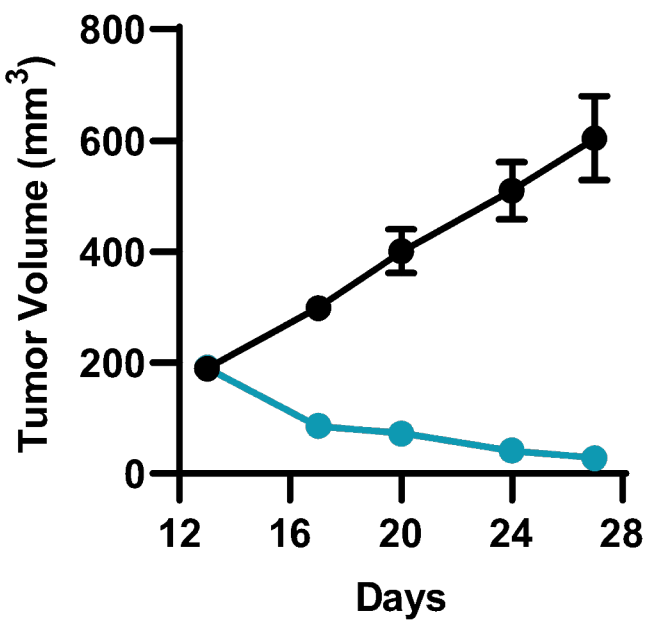

**CDK Family Selectivity – KIN004**

| Kinase | KIN004 $IC_{50}$ (nM) |
|---|---|
| **CDK12** | **97** |
| **CDK2** | **5104** |
| **CDK7** | **3913** |
| **CDK9** | **3952** |
| **Ratios (Fold Difference in $IC_{50}$)** | |
| CDK12/CDK2 | >50X |
| CDK12/CDK7 | >40X |
| CDK12/CDK9 | >40X |

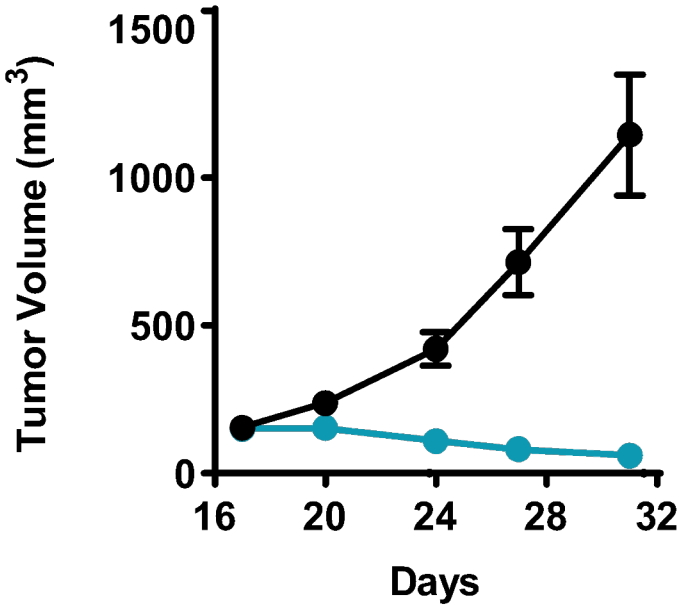
- KIN004 demonstrated selective CDK12 inhibition compared to highly homologous CDK2, CDK7 and CDK9 family members
- Structure-based design enabled by Kinnate proprietary co-crystal structure

# Tumor Regressions Demonstrated with Selective Inhibition of CDK12

***In Vivo* Efficacy – HCC70 (BRCA$^{WT}$)**




***In Vivo* Efficacy – OVCAR3 (BRCA$^{WT}$)**





Note: HCC70 breast tumors (left) and OVCAR-3 ovarian tumors (right) represent BRCA 1/2 WT cancers that were DDR-proficient and were not sensitized to PARP inhibitor treatment

# Kinnate: Kinase Inhibitors for Genomically Defined Cancers

## Striving to Expand the Promise of Precision Medicine in Oncology

### Programs

- Multiple compounds advancing to the clinic
- Lead RAF program in unserved population
- FGFR program targeting  resistance
- R&D pipeline of additional compounds

### Platform

- Productive Kinnate Drug Discovery Engine

### People

- Experienced management team
- Strong scientific collaborations
- Funded by leading life science investors