# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, D.C. 20549**

# FORM 8-K
## CURRENT REPORT

**Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

Date of report (Date of earliest event reported): **January 7, 2020**

# Verastem, Inc.

(Exact Name of Registrant as Specified in Charter)

| **Delaware** | **001-35403** | **27-3269467** |
|---|---|---|
| (State or Other Jurisdiction of Incorporation) | (Commission File Number) | (IRS Employer Identification No.) |

| **117 Kendrick Street, Suite 500, Needham, MA** | **02494** |
|---|---|
| (Address of Principal Executive Offices) | (Zip Code) |

Registrant's telephone number, including area code: **(781) 292-4200**
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| **Title of each class** | **Trading Symbol(s)** | **Name of each exchange on which registered** |
|---|---|---|
| Common stock, $0.0001 par value per share | VSTM | The Nasdaq Global Market |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 1.01 Entry into a Material Definitive Agreement**

On January 7, 2020 (the "Effective Date"), Verastem, Inc. (the "Company") entered into a license agreement (the "Agreement") with Chugai Pharmaceutical Co., Ltd. ("Chugai"), whereby Chugai granted an exclusive, worldwide license to the Company for the development, commercialization and manufacture of products containing CH5126766 (CKI27), a dual RAF/MEK inhibitor (the "Chugai Compound").

Under the terms of the Agreement, the Company receives an exclusive right to develop and commercialize products containing the Chugai Compound at its own cost and expense. The Company is required to pay Chugai a non-refundable payment of $3,000,000 by February 21, 2020. The Company is obligated to pay Chugai double-digit royalties on net sales of products containing the Chugai Compound, subject to reduction in certain circumstances. Chugai also obtained opt back rights to develop and commercialize the Chugai Compound (a) in the European Union, which option may be exercised through the date that the Company submits a New Drug Application to the U.S. Food and Drug Administration (the "FDA") for a product which contains the Chugai Compound as the sole active pharmaceutical ingredient, and (b) in Japan and Taiwan, which option may be exercised through the date the Company receives marketing authorization from the FDA for a product which contains the Chugai Compound as the sole active pharmaceutical ingredient. As consideration for executing either option, Chugai would be obligated to make a payment to the Company to be calculated on the Company's development costs to-date. The Company and Chugai have made customary representations and warranties and have agreed to certain customary covenants, including confidentiality and indemnification.

Unless earlier terminated, the Agreement will expire upon the fulfillment of the Company's royalty obligations to Chugai for the sale of any products containing the Chugai Compound, which royalty obligations expire, on a product-by-product and country-by-country basis, upon the last to occur, in each specific country, of (a) expiration of valid patent claims covering such product or (b) 12 years from the first commercial sale of such product in such country.

The Company may terminate the Agreement upon 180 days' written notice. Subject to certain limitations, Chugai may terminate the Agreement upon written notice if the Company challenges any patent licensed by Chugai to the Company under the Agreement. Either party may terminate the Agreement in its entirety with 120 days' written notice for the other party's material breach if such party fails to cure the breach. Either party may also terminate the Agreement in its entirety upon certain insolvency events involving the other party.

The foregoing description of the Agreement does not purport to be complete and is qualified in its entirety by reference to the text of the Agreement, which will be filed as an exhibit to a subsequent periodic report to be filed under the Securities Exchange Act of 1934, as amended (the "Exchange Act").

**Item 7.01 Regulation FD Disclosure**

The Company will be conducting meetings with investors attending the 38th Annual J.P. Morgan Healthcare Conference in San Francisco, California beginning on January 13, 2020. As part of these meetings, the Company will deliver the slide presentation attached to this report as Exhibit 99.1, which is incorporated herein by reference.

The information in this report (including Exhibit 99.1) is being furnished pursuant to Item 7.01 and shall not be deemed filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor will it be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific referencing in such filing.

**Item 9.01 Financial Statements and Exhibits**

(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Verastem, Inc. presentation for 38th Annual J.P. Morgan Healthcare Conference |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**Verastem, Inc.**

Dated: January 13, 2020

By: /s/ Brian M. Stuglik
Brian M. Stuglik
*Chief Executive Officer*

Exhibit 99.1


Verastem
Oncology
Verastem Oncology
Corporate Overview | J.P. Morgan Healthcare Conference | January 13, 2020

# Safe Harbor Statement



This presentation includes forward-looking statements about, among other things, Verastem Oncology's products and product candidates, including anticipated regulatory submissions, approvals, performance and potential benefits of Verastem Oncology products and product candidates, that are subject to substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements.

Additional information regarding these factors can be found in Verastem's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and in any subsequent filings with the SEC, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors that May Affect Future Results", as well as in our subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission (SEC) and available at www.sec.gov and www.verastem.com.

The forward-looking statements in this presentation speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements.

## Corporate Overview

Novel small molecule kinase inhibitors targeting malignant cells both directly and through modulation of the tumor microenvironment

- **NASDAQ:** VSTM
- **Headquarters:** Needham, MA
- **Incorporated:** 2010

Verastem Oncology



## Products

Copiktra® (duvelisib) 15mg | 25mg capsules

- The first-approved oral inhibitor of PI3K-δ and PI3K-γ
- Exclusively marketed in the US by Verastem Oncology
- Partnered in Japan, China, Russia/CIS, Turkey, Middle East, & Africa

**Full prescribing information, including BOXED WARNING and Medication Guide, is available at www.COPIKTRA.com**

## Investigational Research & Pipeline

### Duvelisib Program

- Ongoing registration study in PTCL (FDA Fast Track Designation)
- Ongoing clinical investigation as monotherapy and in combination in multiple hematologic malignancies
- Phase 2 I-O Combination in Solid Tumors
- Pre-Clinical data completed and planned clinical study in combo with CAR-T

### Defactinib Program

- First in Class Investigational FAK inhibitor
- Activity in KRAS Mutant Tumors
- Phase 2 I-O Combinations
- Orphan Designation: Ovarian & mesothelioma in the US & EU

### CH5126766 Program

- First in Class Investigational RAF/MEK inhibitor
- Acquired WW Rights from Chugai in Jan-20
- Activity in KRAS Mutant Tumors
- Novel Dosing Schedule

- Oral Combination study in KRAS Mutant Tumors
- Phase 2 Dose defined, ongoing basket trial
- Initiate Regulatory Discussions, present Clinical Data in 1H 2020

# The Verastem Corporate Plan



**6 MONTHS** — Dec 2019

- Refocused commercial efforts on large accounts
- Right-sized organization
- Completed debt restructuring
- Advanced new indications for COPIKTRA®

**2 YEARS** — June 2021

- Achieve cash flow break even for both the commercial and clinical COPIKTRA® program

**5 YEARS** — June 2024

- Broaden indications for COPIKTRA®
- Additional marketed products
- Robust pipeline of assets in development

# 2019 Recap



## Corporate and Financial

- ✓ FY19 Revenue Guidance in the range of $12-$14M
- ✓ Refinanced Hercules Loan Facility
- ✓ Appointed Brian Stuglik as CEO
- ✓ Signed Exclusive License Agreement with Sanofi for the Development and Commercialization of Duvelisib in Russia and CIS, Turkey, the Middle East, and Africa, for a total of 78 countries
- ✓ Announced a plan to right-size operations that is expected to yield $25M of annualized costs savings beginning in 2020
- ✓ FY20 Operating Expense guidance in the range of $110-$115M
- ✓ Refinanced $121M of Convertible Notes due 2048
- ✓ Signed License Agreement with Chugai for the worldwide development and commercialization rights to the RAF/MEK inhibitor CH5126766

## COPIKTRA® & Development Pipeline

- ✓ US Launch of COPIKTRA® in Follicular Lymphoma (FL)
- ✓ Duvelisib received orphan drug designation from FDA for the treatment of T-Cell Lymphoma
- ✓ Yakult dosed first patient in Japanese bridging study evaluating COPIKTRA in relapsed or refractory CLL/SLL
- ✓ Submitted MAA for COPIKTRA® in Europe
- ✓ ASH 2019 – Presented Duvelisib & Venetoclax Phase 1 Data, and Dose Optimization Data for R/R PTCL from the Phase 2 PRIMO Trial
- ✓ Expansion of IST Program with focus on combination, earlier lines of therapy, and aggressive cancers

**Initiation of key company sponsored trials:**

- ✓ **TEMPO Study** – Phase 2, open-label, intermittent dosing study for patients with R/R iNHL. Expected to enroll ~100 patients.
- ✓ **Duvelisib + PD-1 Inhibitor** (Pembrolizumab) – Phase 1b/2 combination study for patients with head and neck squamous cell carcinoma.
- ✓ **DUETTO Study** – FL Confirmatory Phase 3 Study

# 2020 Milestones



## Commercial

### COPIKTRA®

- ❑ EU Regulatory Opinion
- ❑ EU Partnership
- ❑ CSPC First Patient In (FL)
- ❑ Sanofi Regulatory Filings

## Development

### Duvelisib

- ❑ NCCN Guidelines – PTCL
- ❑ Complete Accrual on PRIMO
- ❑ Japan First Patient In – PRIMO
- ❑ DUV + I/O – First Patient In, Safety Data
- ❑ Updates on multiple ISTs

### FAK & RAF/MEK

- ❑ Clinical Data on FAK + MEK in 1H 2020
- ❑ Clinical Data on FAK + I/O in 1H 2020
- ❑ Regulatory Discussions on FAK + MEK in 1H 2020

# Key Financial Statistics



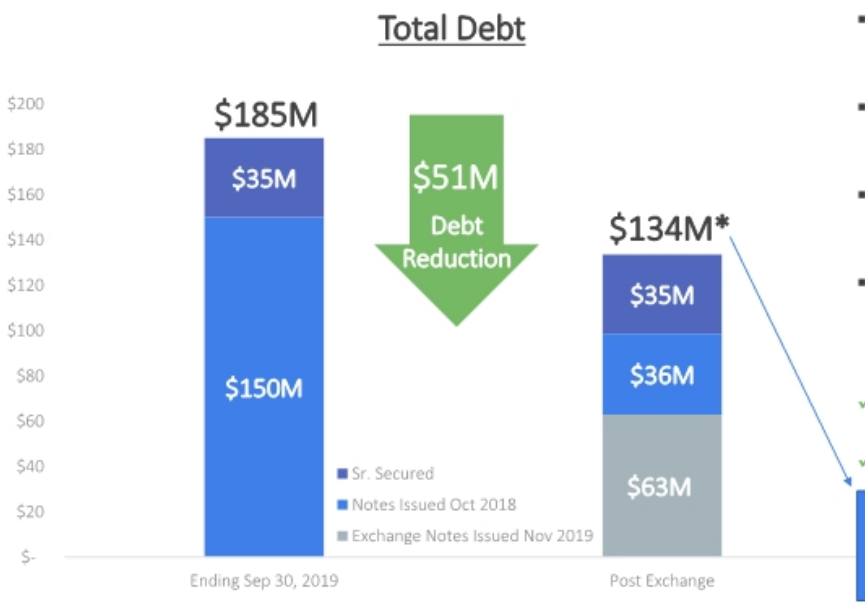
| | |
|---|---|
| QTD Net Revenue as of 9/30/2019 | $9.0M |
| Cash, cash equivalents & investments as of 9/30/2019 | $160.2M |
| Shares outstanding as of 9/30/2019 | 74.3M |
| Shares fully diluted as of 9/30/2019 | 112.6M |
| Hercules Term Loan Facility | $35.0M* |
| 5.00% Convertible Senior Notes Due 2048 | $74.6M** |
| QTD Non-GAAP net loss as of 9/30/2019 | $26.2M |
| Full-time employees as of 9/30/2019 | 168 |
| Insider ownership (outstanding / vested) as of 9/30/2019 | 19.2% / 9.6% |

*On April 23, 2019, we entered into a 4th Amendment to our existing Agreement with Hercules Capital, Inc. whereas we may borrow up to an aggregate amount of $75.0 million, of which $35.0 million was outstanding as of the date of amendment and 6/30/2019.

**The Senior Convertible Notes consist of $28.3M of notes originating from the October 2018 Issuance and $46.4M of notes exchanged under the new notes issued in November 2019.

# Refinancing of Convertible Senior Notes due 2048






- Exchanged $114M of 5.00% Notes due in 2048 for ~$63M in newly issued notes and ~$12M in Cash
- Lowered the initial conversion price to $1.65 per share.
- Lowered the trigger for the company to exercise its conversion option to $2.00 per share
- Coupon (5.00%) and Maturity (2048) are unchanged

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- ✓ Lowered Total Debt by $51M
- ✓ Improved Verastem's Debt to Equity Ratio

**Since the transaction ~$21M of Bonds have converted and an additional $7M has been exchanged– Proforma Debt Balance of ~$110M*

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# Senior Management Team



**Brian Stuglik**
Chief Executive Officer
Global VP & Chief Marketing Officer – Lilly Oncology
Founding Member – Proventus Health Solutions

**Cathy Carew**
Chief People & Organizational Strategy Officer
Principal - HR Collaborative
Ironwood, ActiveBiotics, Dynogen, Tufts Health Plan

**Hagop Youssoufian, MSc, M.D.**
Head of Medical Strategy
CMO, BIND Therapeutics, EVP, Progenics,
CMO & EVP, Ziopharm Oncology, SVP, Imclone

**Daniel Paterson**
President and Chief Operating Officer
CEO - The DNA Repair Co. (now On-Q-ity)
PharMetrics (now IMS), Axion

**Jonathan Pachter, Ph.D.**
Chief Scientific Officer
Head of Cancer Biology - OSI (now Astellas)

**Amy C. Cavers**
Chief of Engagement and Innovation
VP Scientific Affairs – TG Therapeutics, Inc.
Sr.Dir Scientific Strategy and Communications – Onyx Therapeutics, VP Marketing – Celgene Corp.

**Rob Gagnon**
Chief Business and Financial Officer
CFO – Harvard Bioscience, Clean Harbors
VP of Finance – Biogen Idec


Verastem
Oncology
COPIKTRA® / Duvelisib

Copiktra® (duvelisib) 15mg | 25mg capsules

# Building a Global Brand

## COPIKTRA® Global Expansion Strategy


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# Changes in Execution to Shift the Launch Trajectory



**Optimize**

- Moving to Account Based Selling
- Upgrading and flattened Field Organization for improved account access and experience
- Shifting focus to efficacy based messaging

**Accelerate**

- Improving Thought Leader support
- Secure PI3K of choice within several accounts and EMR systems
- Executing volume based contracting with GPOs and IDNs

**Expand**

- Increasing focus on 'Reach' and 'Breadth' of prescribing base
- Host In-Practice Educational Programs to support field teams across the US
- Deploy Nurse Educator roles

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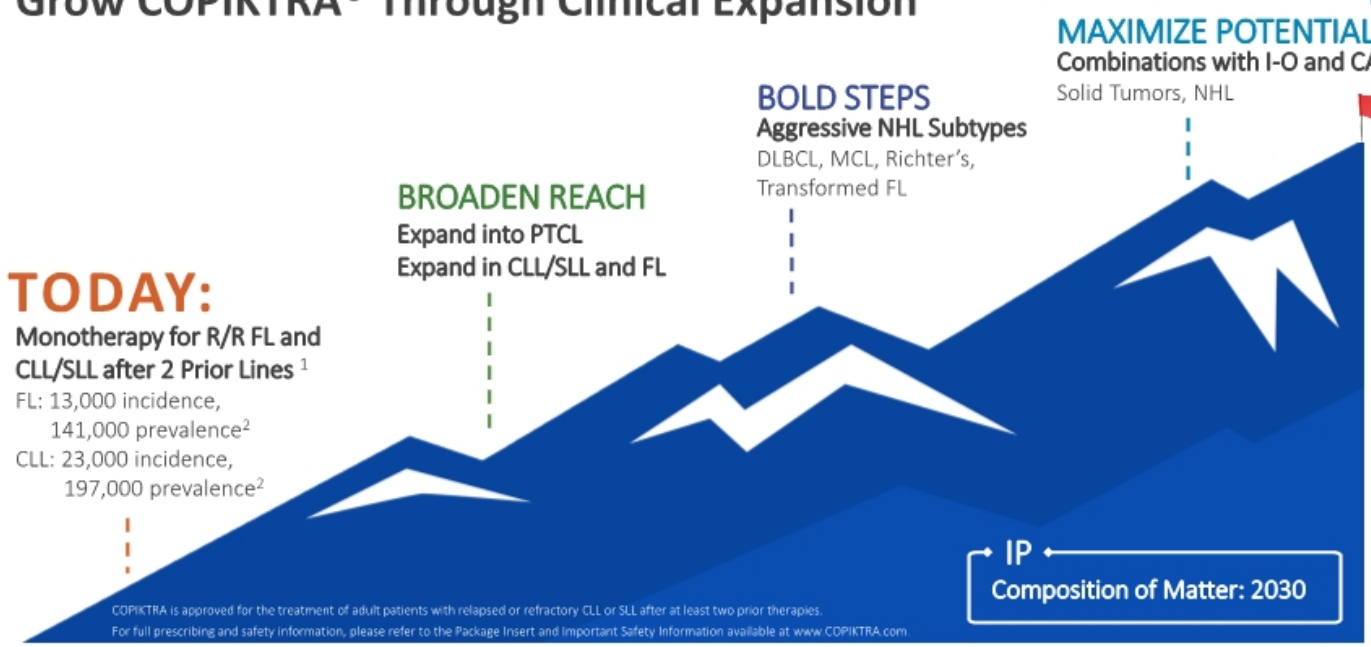
# Grow COPIKTRA® Through Clinical Expansion




COPIKTRA is approved for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.
For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

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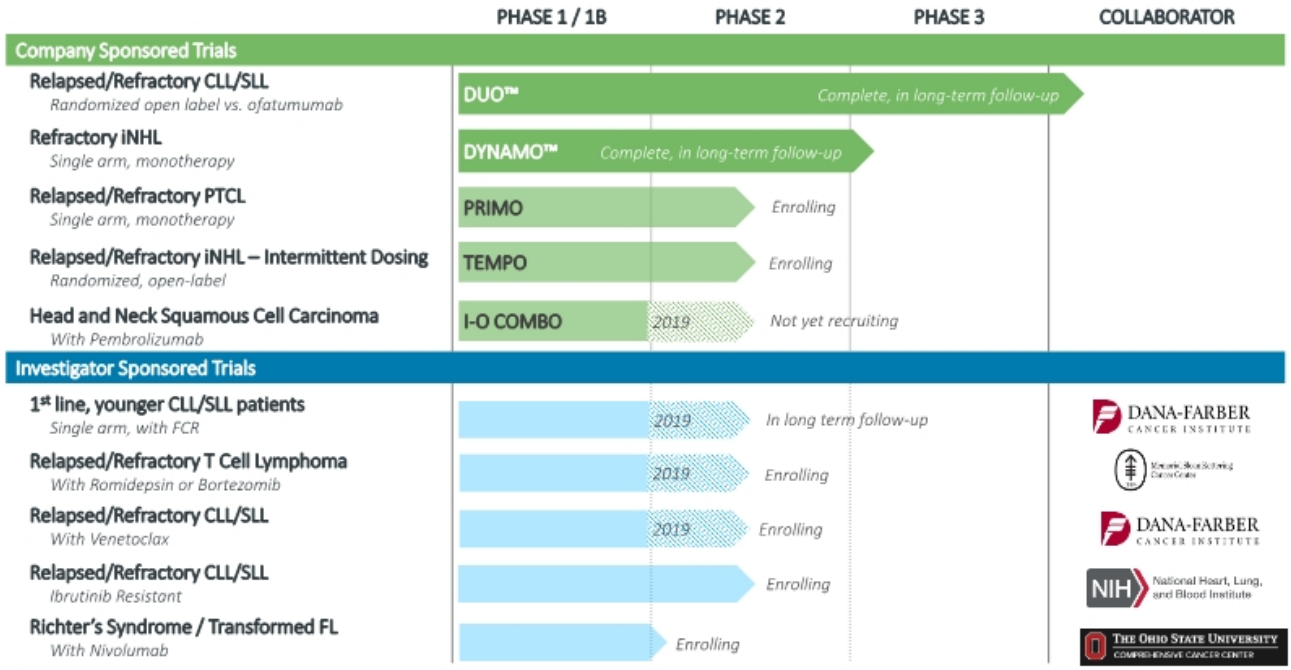
**Sources:**
1. Copiktra USPI, 2018 – Accelerated Approval in FL, Full approval in CLL/SLL;
2. Decision Resources, US 2018

# Duvelisib Pipeline – PI3K DELTA / PI3K GAMMA INHIBITOR



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# Relapsed/Refractory Peripheral T-Cell Lymphoma (PTCL)



## US PREVALENCE[3]

- 1st Line Treatable: **4,000**
- R/R Treatable: **2,800**

## UNMET NEED

- Median OS is < 6 months[1]
- NCCN guidelines still recommend clinical trials for relapsed patients[2]
- KOLs are unsatisfied with the available treatment options

## EARLY CLINICAL SIGNALS

| | Drug / Trial | ORR | CR | FDA decision |
|---|---|---|---|---|
| INVESTIGATIONAL | **duvelisib** (oral monotherapy)<br>Ph 2 Dose Optimization, n = 33<br>(Horwitz et al., ASH 2019) | **54%**<br>**(62% IRR)** | **31%** | **Fast Track Designation** |
| INVESTIGATIONAL | **duvelisib + romidepsin**<br>Ph 1 IST, n = 27<br>(Horwitz et al., ASH 2018) | **59%** | **36%** | - |
| APPROVED[3] | **Folotyn** (pralatrexate IV)<br>Single arm, n = 109 | 27% | 8% | AA 2009 |
| APPROVED[3] | **Istodax** (romidepsin IV)<br>Single arm, n = 130 | 25.4% | 14.6% | AA 2011 |
| APPROVED[3] | **Beleodaq** (belinostat IV)<br>Single arm, n = 120 | 25.8% | 10.8% | AA 2014 |

AA = accelerated approval; CR = complete response; ORR = overall response rate

## ONGOING DEVELOPMENT

1 PRIMO **Enrolling**
(~22 sites in US; ~28 sites in Germany, Italy, UK, and Japan)

2 **IST expansion**
(total enrollment ~50)

LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

COPIKTRA is not indicated for use in the treatment of PTCL, and the safety and efficacy of COPIKTRA in PTCL has not been established. Any such use is investigational only. No head-to-head studies have been conducted comparing Duvelisib to these approved products.

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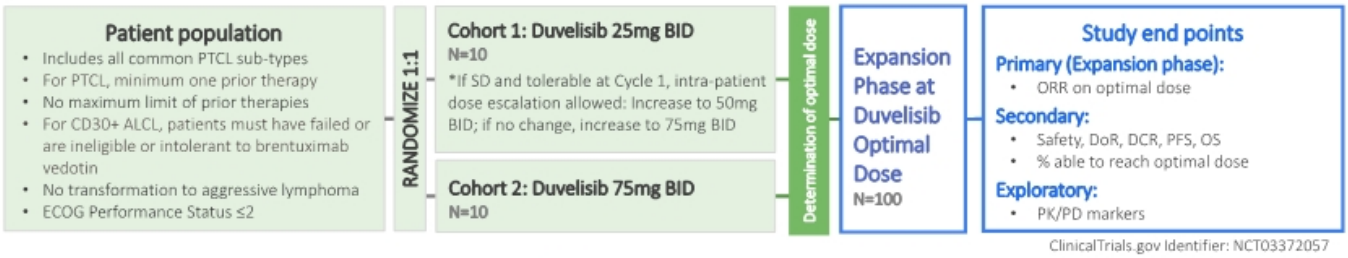
**Sources**
1. Mak et al., Blood 2011 – mOS for relapsed patients ineligible for HDC/SCT; 2. NCCN Guidelines, T-cell Lymphoma Version 2.2017; 3. FDA PTCL approval packages 3. Teras et. Aa. 2016 US Lymphoid malignancy statistics by World Health Organization subtypes. CA Cancer J Clin Nov 2016; R/R PTCL 70% 1L PTCL Bellei et. al., The outcome of Peripheral T-Cell Lymphoma patients failing first line therapy: A report from the prospective, international T-Cell project, Haematologica Jul 2018

# PRIMO Overview: Optimal Dose Decision






ClinicalTrials.gov Identifier: NCT03372057

## Dose Optimization Phase Insights

- ✓ ORR = 50% in evaluable population for each cohort
- ✓ Responses across PTCL subtypes
- ✓ No new safety signals
- Data suggests need for rapid disease control:
  - All early dropouts were on 25 mg BID (n = 7)
  - Increased near-term Gr3+ AEs and SAE on 25 mg cohort
- **PK:** Correlation between dose and higher exposure
- **PD:** Greater baseline immunosuppression in early dropouts as assessed by CD4/CD8 counts

## Optimal Dose Decision

- **Start with 75 mg BID for the first 2 cycles then reduce to 25 mg BID**
  - **Rationale:** Debulk, then proactively reduce dose to potentially reduce longer-term toxicities
  - May re-escalate to 75 mg BID if progression at 25 mg BID
- Include all PTCL subtypes and add central pathology review
- Exclude patients with CD4 lymphocytes <50/mm3
- Add an interim data review after 40 patients for safety and futility
- Add ex-US sites (Italy, Germany, UK, Japan)

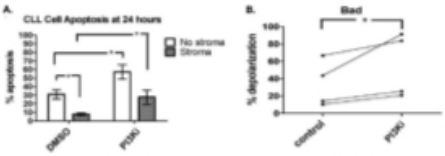
**Expansion phase activated immediately**

# Phase 1/2 Study of Duvelisib and Venetoclax in Patients with Relapsed or Refractory CLL/SLL



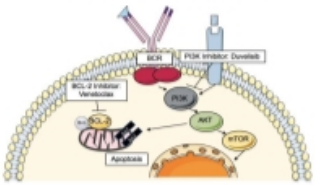
## RATIONALE

- Duration of response to monotherapy is limited, especially for patients who have failed BTK inhibitors or have TP53 dysfunction
- PI3K inhibitors kill *ex vivo* CLL cells even in the presence of stroma and enhance cell dependence on the anti-apoptotic protein, BCL-2, for survival (Fig. A/B).




(A) Treatment with a PI3K inhibitor demonstrates an ability to kill *ex vivo* CLL cells from peripheral blood even in the presence of stroma. (B) PI3K inhibition restores higher levels of apoptotic priming in stroma-exposed CLL cells (Davids et al., *Blood*, 2012

**Mechanism of action of DUV and VEN.**

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## EFFICACY

**Best Response to Date:**

- ORR: 92% (11/12)
- CR/CRi: 33% (4/12)
- uMRD Blood: 33% (4/12)
- uMRD Marrow: 33% (4/12)
- To date, 3/12 pts completed 4 cycles, 7/12 completed 7 cycles and 2/12 completed 12 cycles

## SAFETY

- No DLTs observed
- SAEs (all grade 3): Asymptomatic elevation in amylase and/or lipase (n=2), febrile neutropenia (n=1), pneumonia (n=1)
- No laboratory or clinical TLS
- Poster Reference:

## OVERVIEW

- 1-year, time-limited, all oral regimen are encouraging, with CRs and uMRD already observed despite short follow-up
- RP2D of VEN is 400 mg QD in combination with DUV 25 mg BID
- A phase 2 portion of the trial is now accruing for R/R CLL/SLL and includes a separate cohort for Richter's syndrome

Participating Institutions:

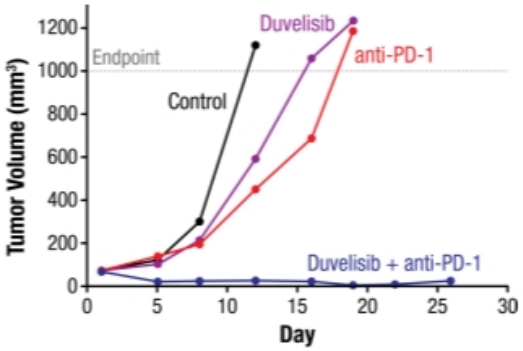
- Dana Farber Cancer Institute
- University of Miami - Sylvester
- University of Iowa - Holden
- Northern Light Eastern Maine Medical Center
- Massachusetts General Hospital
- Boston Medical Center
- Berkshire Medical Center



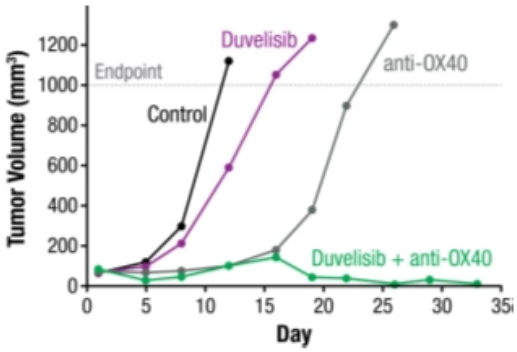
COPIKTRA is not indicated for use in combination with Venetoclax. Any such use is investigational only.

# Duvelisib is synergistic with PD-1 and OX40 antibodies in B-cell lymphoma (A20) preclinical model






- Duvelisib @ 50 mg/kg po, BID
- Anti-PD-1 @ 100 mg/mouse ip, biweekly x 2




- Duvelisib @ 50 mg/kg po, BID
- Anti-OX40 @ 100 µg/mouse ip, biweekly x 2

- PI3K-delta inhibition is known to reduce immunosuppressive Tregs & enrich memory T cells
- PI3K-gamma inhibition is known to reduce immunosuppressive myeloid cells

***COPIKTRA is not indicated for use in the treatment of B-cell lymphoma or in combination with PD-1. The safety and efficacy of COPIKTRA in this setting has not been established. Any such use is investigational only.***

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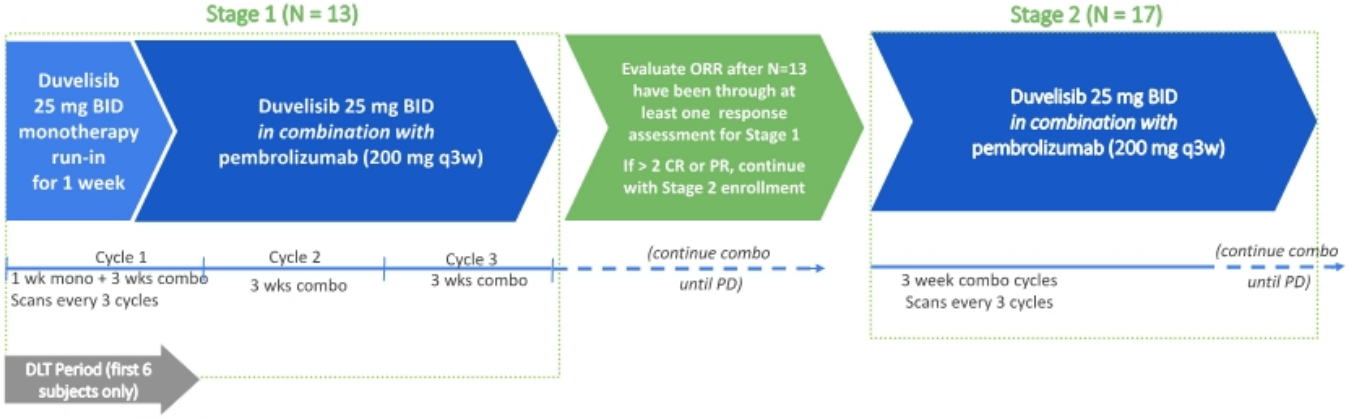
COPIKTRA is not indicated for use in combination with PD-1 and OX40 antibodies in B-cell lymphoma. Any such use is investigational only.

**Source:** 1. Ali, Nature 2014; Abu Eid, Cancer Res 2017; 2. Kaneda, Nature 2016; De Henau, Nature 2016

# Ph 1b/2 I-O combination trial in HNSCC



- **Stage 1 Primary Objective:** Determine safety & tolerability of duvelisib in combination with pembrolizumab (Keytruda®[1], anti-PD-1) in recurrent/ metastatic head and neck squamous cell carcinoma (R/M HNSCC)
- **Stage 2 Primary Objective:** Characterize the overall response rate of duvelisib in combination with pembrolizumab
- **Phase 1b/2 trial design:** Simon 2-stage, R/M HNSCC 1st or 2nd line, IO naïve (*trial design updated following review with CRO and investigators)*

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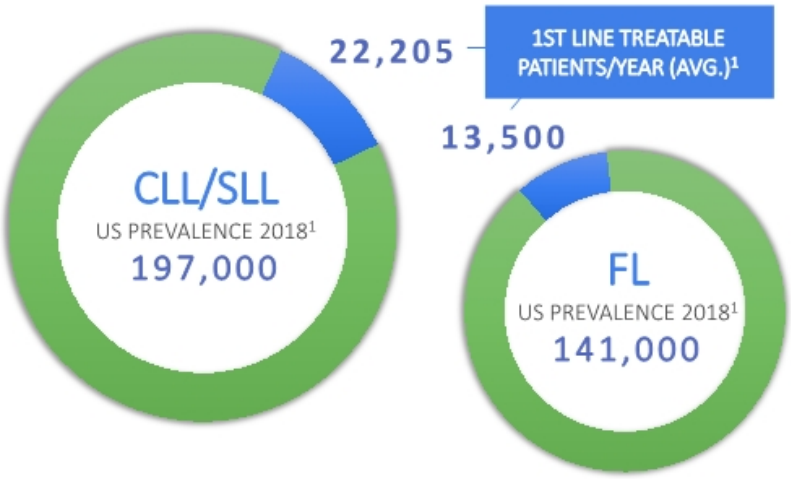
1. KEYTRUDA® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.

# Opportunity: Additional Therapy Options are Needed for Chronic iNHL Patients






**Increasing Elderly At-Risk Patient Population**

65-75
AGE AT DIAGNOSIS[2]

AGING BABY BOOMER POPULATION

INCREASED DIAGNOSES

**Additional Therapy Options Needed for Chronic Disease Control**

MEDIAN OS
10+ YEARS[3]

NEED FOR MORE LINES OF THERAPY

INCREASED DEMAND FOR ORAL TARGETED THERAPIES

**Sources**
1. Decision Resources, 2016-2018 annual estimates; 2018 annual estimates;
2. SEER, FL and CLL statistics; 3. NHI, NHL and CLL PDQ

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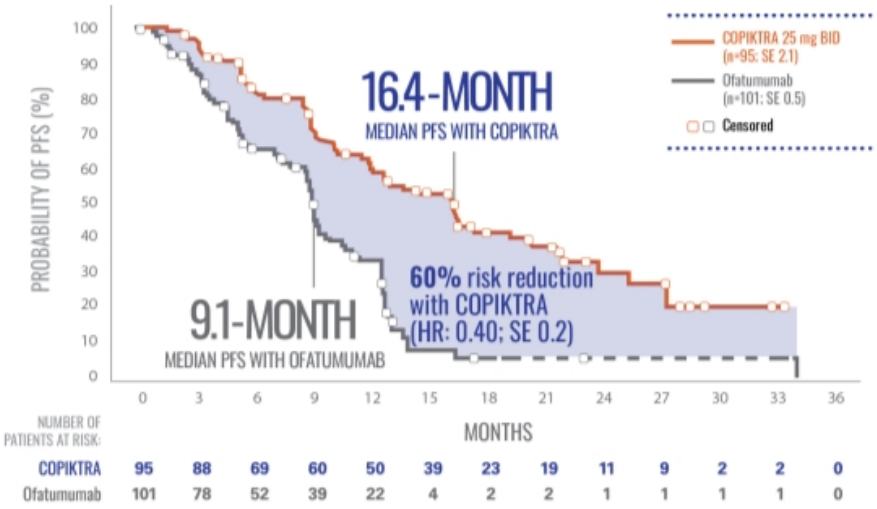
Copiktra® (duvelisib) 15mg | 25mg capsules

## COPIKTRA® for CLL/SLL Patients with at Least 2 Prior Therapies

# Progression-free Survival (COPIKTRA vs. Ofatumumab)

PFS per IRC in Patients with at Least 2 Prior Therapies (N = 196)




| NUMBER OF PATIENTS AT RISK: | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| COPIKTRA | 95 | 88 | 69 | 60 | 50 | 39 | 23 | 19 | 11 | 9 | 2 | 2 | 0 |
| Ofatumumab | 101 | 78 | 52 | 39 | 22 | 4 | 2 | 2 | 1 | 1 | 1 | 1 | 0 |

COPIKTRA is approved for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.
For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

Verastem Oncology



**Sources**
Copiktra USPI, 2018
Kaplan-Meier estimate. CI, confidence interval; HR, hazard ratio; ITT, intention to treat; SE, standard error

# PFS Analysis by Selected Variables



## PFS Analysis in High-Risk Patient Subgroups (N = 196)*

| Variable | PFS analysis (COPIKTRA / Ofatumumab) | N | HR |
|---|---|---|---|
| Overall | | 196 | 0.40 |
| High-risk cytogenetics | | 43 | 0.32 |
| No high-risk cytogenetics | | 133 | 0.38 |
| Refractory/early relapse | | 49 | 0.50 |
| No refractory/early relapse | | 147 | 0.34 |
| Grade 4 cytopenia(s) at baseline | | 13 | 0.19 |
| No grade 4 cytopenia(s) at baseline | | 183 | 0.39 |
| Male | | 115 | 0.47 |
| Female | | 81 | 0.28 |
| Age <65 years | | 59 | 0.42 |
| Age ≥65 years | | 137 | 0.38 |
| Prior anticancer therapy <12 months | | 82 | 0.34 |
| Prior anticancer therapy ≥12 months | | 114 | 0.42 |
| Not previously treated with ofatumumab | | 190 | 0.40 |
| del[17p] or TP53 | | 59 | 0.36 |
| No del[17p] or TP53 | | 103 | 0.45 |

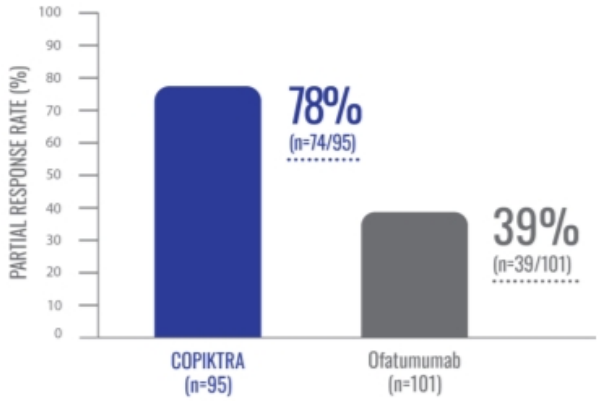

COPIKTRA is approved for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.
For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

**Sources**
Data on file
* Pre-specified patient subgroups; Analysis not powered to show statistical significance in PFS

# ORR and LNRR

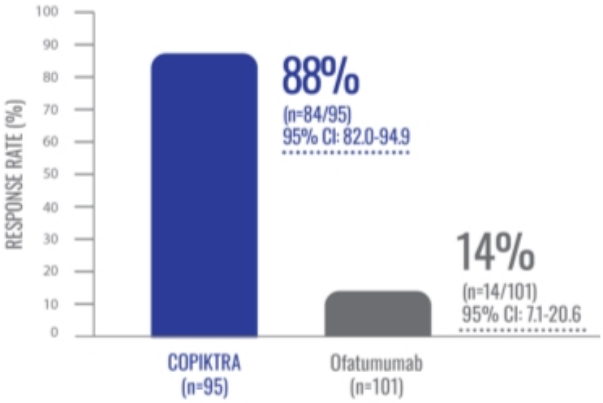


## Overall Response Rate (ORR) per IRC[1]




Data were evaluated based on the International Workshop on CLL or revised International Working Group response criteria, with modification for treatment-related lymphocytosis

## Lymph Node Response Rate (LNRR) per IRC[2]




LNRR was not ranked or formally tested in the hierarchy of key secondary endpoints
Lymph node response was defined as ≥50% reduction in target lesion size



**Sources**
1. Copiktra USPI, 2018;
2. Data on file

# FL: Data Supporting Accelerated Approval

## Efficacy in Patients with Relapsed or Refractory FL

| Outcome per IRC | FL N = 83 |
|---|---|
| **ORR, n (%) [a]** | **35 (42%)** |
| 95% CI | (31, 54) |
| CR, n (%) | 1 (1%) |
| PR, n (%) | 34 (41%) |
| **Duration of response** | |
| Range, months | 0.0* to 41.9+ |
| Patients maintaining response at 6 months, n/N (%) | 15/35 (43%) |
| Patients maintaining response at 12 months, n/N (%) | 6/35 (17%) |

Abbreviations: CI = confidence interval; CR = complete response; IRC = Independent Review Committee; ORR = overall response rate; PR = partial response
[a] Per IRC according to Revised International Working Group criteria
[+] Denotes censored observation

- Primary data supporting accelerated approval is from the DYNAMO™ Phase 2 trial of duvelisib in patients with refractory indolent NHL
- Heavily pre-treated double refractory patient population, with median of 3 prior lines of therapy

*Inclusion criteria required that patients be refractory to both rituximab and a chemotherapy regimen or RT.*

*Refractory is defined as no response while on therapy, or progressive disease within 6 months of the last dose.*



**Sources**
Copiktra USPI, 2018

# Pooled Analysis of Safety Supporting Approval

## 442 Patients with Previously Treated Hematologic Malignancies

**Most Common Adverse Reactions (≥ 10% Grade ≥ 3 or ≥ 20% Any Grade) in Patients with B-cell Malignancies Receiving COPIKTRA®**

| Adverse Reactions | COPIKTRA 25 mg BID (N = 442) | |
|---|---|---|
| | Grade ≥ 3 n (%) | Any Grade n (%) |
| Neutropenia † | 132 (30%) | 151 (34%) |
| Diarrhea or colitis †[a] | 101 (23%) | 222 (50%) |
| Pneumonia †[b] | 67 (15%) | 91 (21%) |
| Anemia † | 48 (11%) | 90 (20%) |
| Rash †[c] | 41 (9%) | 136 (31%) |
| Fatigue † | 22 (5%) | 126 (29%) |
| Pyrexia | 7 (2%) | 115 (26%) |
| Musculoskeletal pain † | 6 (1%) | 90 (20%) |
| Nausea † | 4 (<1%) | 104 (24%) |
| Cough † | 2 (<1%) | 111 (25%) |
| Upper respiratory tract infection † | 2 (<1%) | 94 (21%) |

Serious adverse reactions were reported in 289 patients (65%). The most frequent serious adverse reactions that occurred were:

- infection (31%) †
- diarrhea or colitis (18%) †
- pneumonia (17%) †
- rash (5%) †
- pneumonitis (5%) †

† Grouped term for reactions with multiple preferred terms

[a] Diarrhea or colitis includes the preferred terms: colitis, enterocolitis, colitis microscopic, colitis ulcerative, diarrhea, diarrhea hemorrhagic

[b] Pneumonia includes the preferred terms: All preferred terms containing "pneumonia" except for "pneumonia aspiration"; bronchopneumonia, bronchopulmonary aspergillosis

[c] Rash includes the preferred terms: dermatitis (including allergic, exfoliative, perivascular), erythema (including multiforme), rash (including exfoliative, erythematous, follicular, generalized, macular & papular, pruritic, pustular), toxic epidermal necrolysis and toxic skin eruption, drug reaction with eosinophilia and systemic symptoms, drug eruption, Stevens-Johnson syndrome

COPIKTRA is approved for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.

For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

**Sources**

Copiktra USPI, 2018


Verastem
Oncology
FAK and RAF/MEK Program
Targeting KRAS Mutant Cancers

# Defactinib + CH5126766: Potential Best-in-Class Combination for RAS/RAF-Mutant Cancers



- Defactinib and CH5126766 have each shown independent clinical activity in RAS mutant cancers
- MEK blockade activates pFAK as a potential escape mechanism
- Multiple preclinical studies provide rationale for why FAK and MEK inhibitors are synergistic
- Defactinib is generally well tolerated, and has a non-overlapping safety profile relative to CH5126766. A manageable all-oral combination regimen has been defined.
- Initial clinical data with the combination are promising including both objective response rate and durability
- We are exploring the breadth of this activity against KRAS mutant cancers and the clinical results will be presented at an upcoming scientific meeting (1H 2020)

# This licensing transaction and combination of defactinib + CH5126766 are potentially transformative for Verastem Oncology



- This transaction is aligned with and supports our 6-2-5 strategy to build a company with multiple products as we continue to make progress with our lead agent Copiktra®
- The RAS/RAF/MEK pathway represents a large market with high unmet need
- Given the potential of this opportunity, the company will be evaluating various partnering strategies
- Based on the promising objective response rate and manageable safety profile of this combination in patients with KRAS mutant tumors:
  - Verastem Oncology has in-licensed world-wide rights to CH5126766
  - Verastem Oncology to initiate regulatory discussions in 1H 2020 to further define the initial registration-directed study for the defactinib + CH5126766 combination

# Ongoing Investigator-Sponsored Basket Study of CH5126766 + Defactinib in KRAS-mutant Cancers



**Dr. Udai Banerji**
Royal Marsden Hospital

## Phase I

Advanced Solid Cancers

- CH5126766 oral twice wkly x 3 every 4 wks
- Defactinib oral BID daily x 3 wks q 4 wks
- 3 cohorts increasing doses to full single agent doses (CH5126766 4mg & Defactinib 400 mg)

**Recommended Phase 2 Dose has been determined and expansion cohorts are underway**

- **Advanced NSCLC KRAS-Mut*** (20 patients)
- **LGSOC*** (20 patients)
- **Advanced CRC RAS-Mut*** (10 patients)
- **Advanced Solid Tumors Enriched for RAS-Mut*** (Biopsy Amenable)

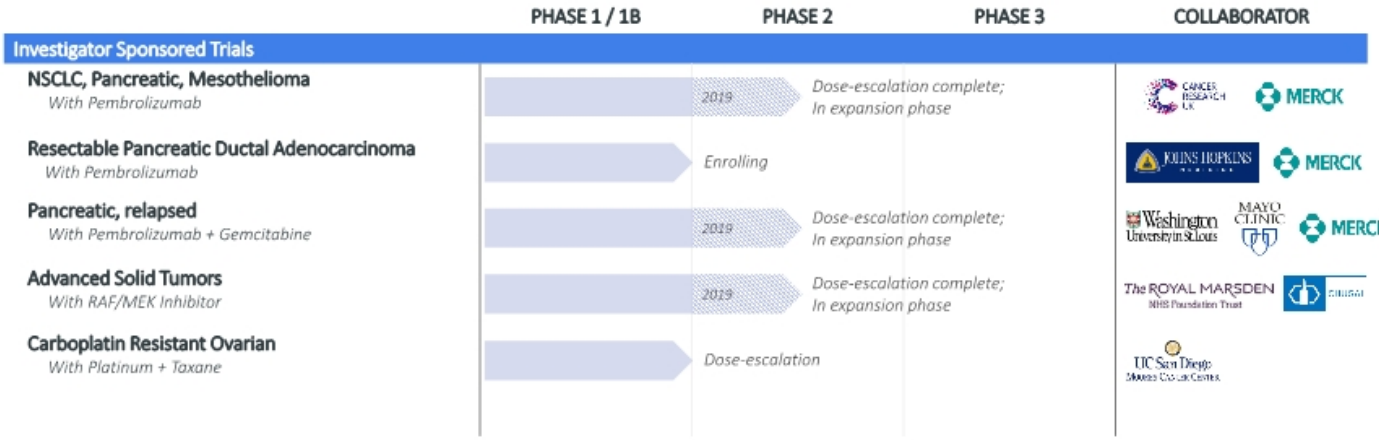
***"Refractory to conventional treatment or for which no conventional treatment exists"**

***Results to be presented at a scientific conference in 1H-2020***

Verastem Oncology

# Defactinib Pipeline – FAK Inhibitor






These studies are investigating treatments or outcomes that have not received approval from a Health Authority. The information presented is not intended to convey conclusions of safety or efficacy. There is no guarantee that the outcome of these studies will result in approval by a Health Authority.

# High Unmet Need in RAS/RAF/MEK/ERK-Driven Cancers



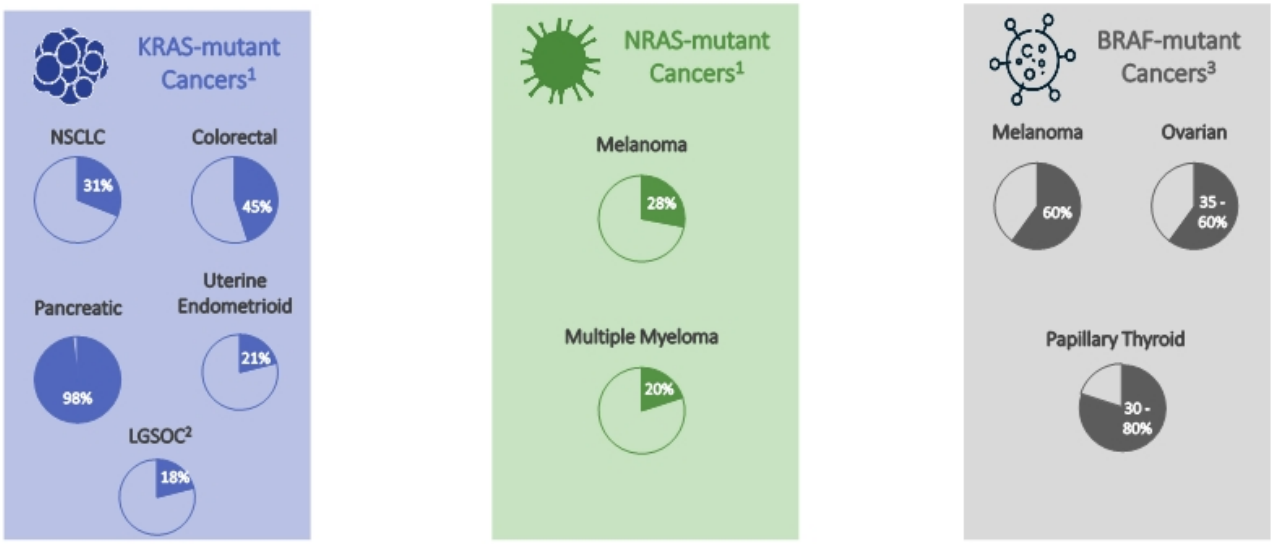
- 30 percent of all human cancers are driven by mutations of the RAS family of genes
- Patients with mutations of the RAS family have an overall worse prognosis
- Multiple approaches (direct targeting, blocking downstream signal processing, identify new targets that oncogenic RAS proteins depend on for their survival) have resulted in modest progress with a limited number of approved therapies
- Single agent therapies (e.g. MEK inhibitors) associated with the development of resistance
- Tolerable combination regimens with MEK inhibitors have been challenging

**References:**
McCormick F Clin Cancer Res 15April2015
Adderley H et al. EBioMedicine 01Mar2019
Papke B et al. Science 17Mar2017
Ryan M et al. Nature Reviews Clinical Oncology 01Oct2018
NIH cancer.gov/research/key-initiatives/ras

# The Importance of RAS Pathway in Human Cancers

***Common Mutations in Many Large Cancer Types***





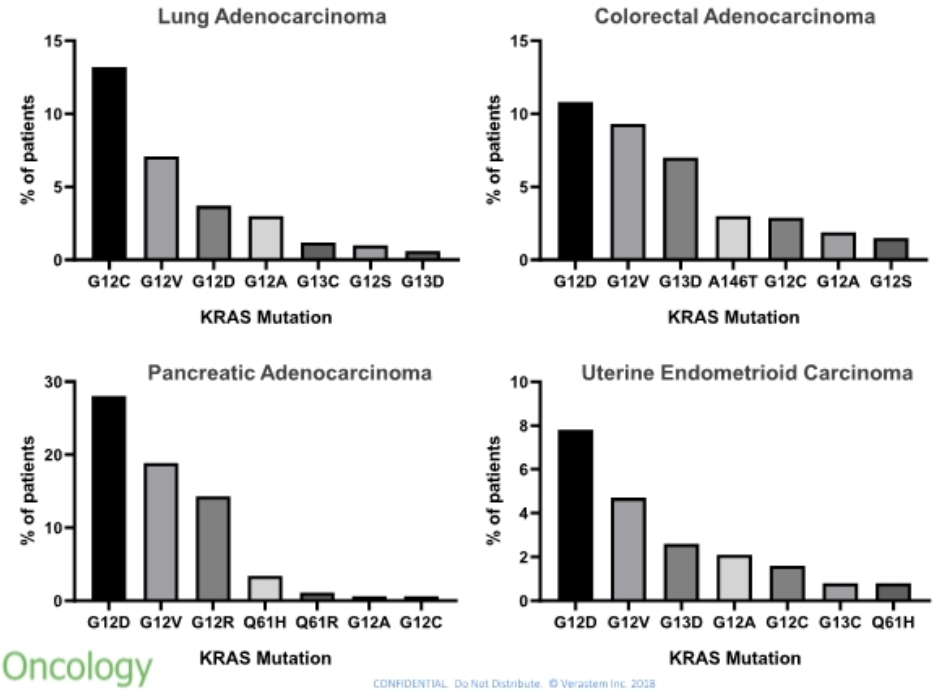

Other cancers driven by MEK-ERK pathway activation

**References:**

1. Reference for RAS mt frequencies – Cox et al. Nature Reviews 13: 828, 2014
2. Reference for KRAS mt in LGSOC – Grisham ASCO 2012
3. Reference for BRAF mt frequencies – Turski et al. Mol Cancer Ther 15: 533, 2016

# KRAS mutation status: % frequency by tumor type



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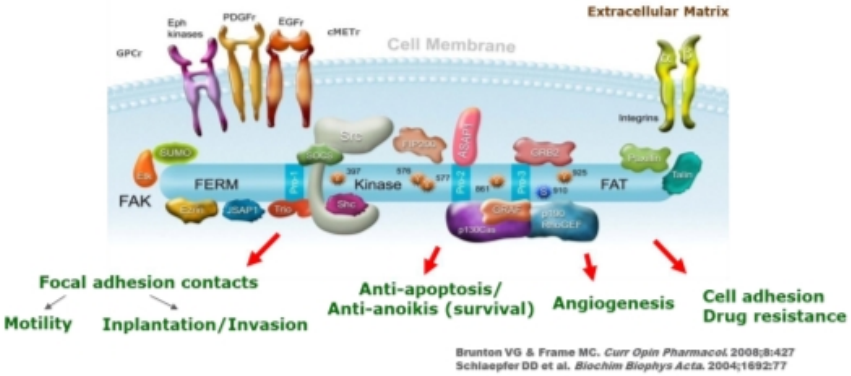
**Source:** TCGA Database

# FAK is critical for multiple aspects of tumor progression



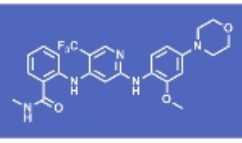


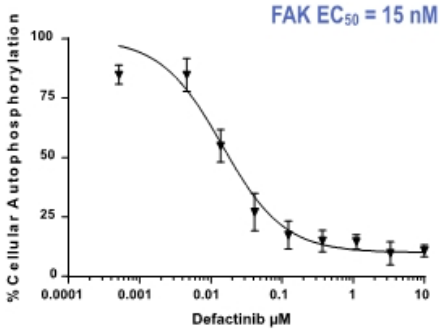

Brunton VG & Frame MC. *Curr Opin Pharmacol.* 2008;8:427
Schlaepfer DD et al. *Biochim Biophys Acta.* 2004;1692:77

- Focal Adhesion Kinase (FAK) is a non-receptor tyrosine kinase that mediates signaling downstream of integrins & growth factor receptors
- Plays key roles in metastasis and drug resistance
- Immuno-Oncology/Tumor Microenvironment
  - FAK inhibition reduces immune suppressive cell populations in the tumor microenvironment: Tregs, M2 tumor-associated macrophages, MDSCs
  - FAK inhibition reduces stromal density: Facilitates entry of cytotoxic T cells into tumor

# Defactinib (VS-6063) – Selective FAK Inhibitor

**Defactinib**

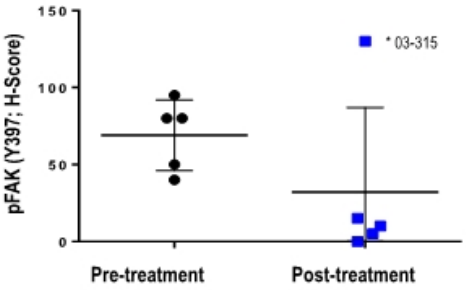




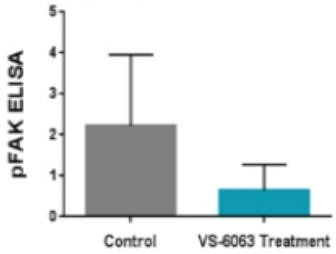

**Dosage**: Oral, 400mg BID

- **Studied in 300+ patients with good safety profile observed to date**
- DLT not reached
- Early signs of clinical efficacy
- Well established safety profile as a single agent and in combination:
  - MEK/RAF, PD-1, Chemotherapy

## OVARIAN CANCER: TUMOR BIOPSIES




## MESOTHELIOMA: TUMOR BIOPSIES

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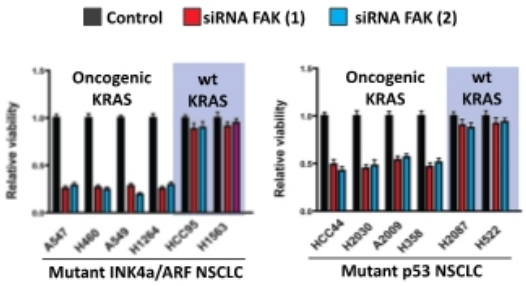
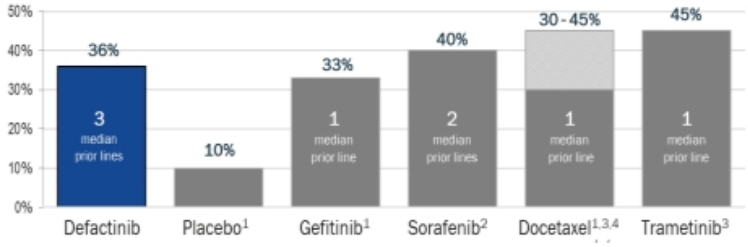
# Clinical Activity of Defactinib Monotherapy in KRAS mutant NSCLC



## KRAS mt is necessary for sensitivity to FAK inhibition in NSCLC cell lines




## 12-week PFS rate of experimental agents for KRAS mt NSCLC



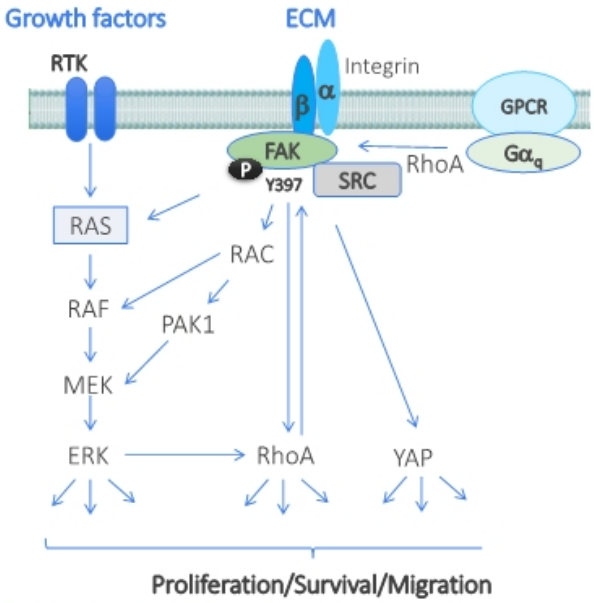

*"VS-6063 was generally well tolerated and suitable for long-term dosing. In this cohort of heavily pretreated patients, there were signs of single-agent activity comparable to other targeted agents and docetaxel.* ***Future directions include possible combination studies with existing standard and emerging therapies, including checkpoint inhibitors."***
—Dr. David Gerber, IASLC 2015; Lung Cancer 2020

**Reference:**
Konstantinidou G et al. Cancer Discovery 2013;3:444-57

**References:**
1. Phase 3 INTEREST, Douillard et al., JCO 2010
2. Phase 3 MISSION, Mok et al., ESMO 2012
3. Phase 2, Blumenschein et al., Ann Oncol 2015
4. Phase 2, Janne et al., Lancet 2013

# Targeting FAK Overcomes Key Resistance Mechanisms to BRAF & MEK Inhibitors



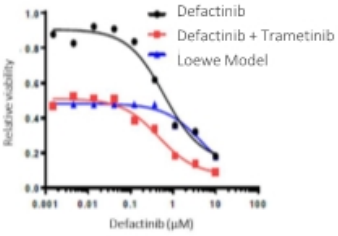



- **MEK inhibition induces compensatory activation of pFAK preclinically and clinically (Banerji, BTOG 2019)**
- BRAF & MEK inhibitors can block Growth Factor-stimulated ERK signaling, but Cell Attachment can also stimulate ERK signaling through a FAK-dependent pathway (Slack-Davis, JCB 162:281, 2003)
- GPCR-mediated activation of RhoA and YAP pathways through FAK (Feng, Cancer Cell, 2019) may also confer cancer cell proliferation and survival bypassing the ERK pathway
- Signaling through a RhoA-FAK axis is required for maintenance of KRAS-dependent lung adenocarcinomas (Konstantinou, Cancer Discovery 3:444, 2013)
- BRAF inhibition generates a drug-tolerant microenvironment for melanoma cells which can be abolished by FAK inhibition (Hirata, Cancer Cell 27:574, 2015)

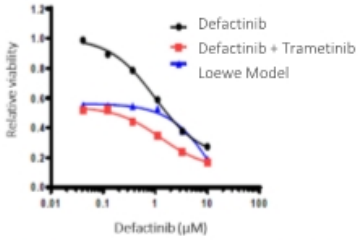
# Screen for Synergy with Defactinib Identified MEK Inhibitors (& CH5126766) as Top Hit



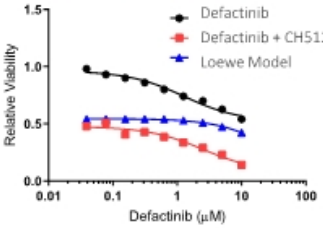
TOV-21G CELLS KRAS-MUTANT OVARIAN CANCER



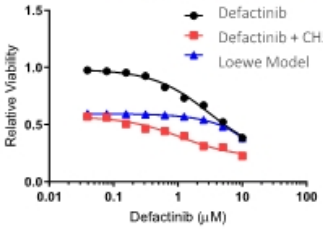

H441 CELLS KRAS-MUTANT NON-SMALL-CELL LUNG CANCER



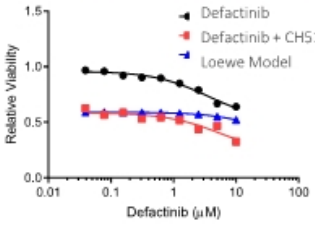

SW982 CELLS SARCOMA BRAF:pV600E




MERO-14 CELLS MESOTHELIOMA




CAL-51 CELLS TRIPLE NEGATIVE BREAST CANCER

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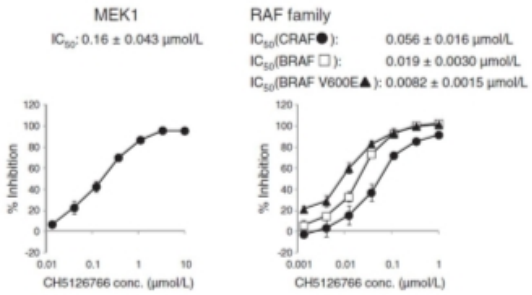
*Verastem issued patent on FAK/MEK inhibitor combinations*

# CH5126766 is a Unique Small Molecule RAF/MEK Inhibitor

- CH5126766 uniquely inhibits both MEK kinase and RAF kinase activities

RAS → RAF → MEK → ERK → Proliferation & Survival

- Standard MEK inhibitors (e.g. PD0325901) paradoxically induce MEK phosphorylation (pMEK) by relieving ERK-dependent feedback inhibition of RAF which may limit their efficacy
- By inhibiting RAF phosphorylation of MEK, CH5126766 has the advantage of not inducing pMEK
- This unique mechanism of CH5126766 enables more effective inhibition of ERK signaling, and may confer enhanced therapeutic activity against ERK-dependent, RAS or BRAF mutant tumors





**Reference:**
Ishii et al., Cancer Research, 2013

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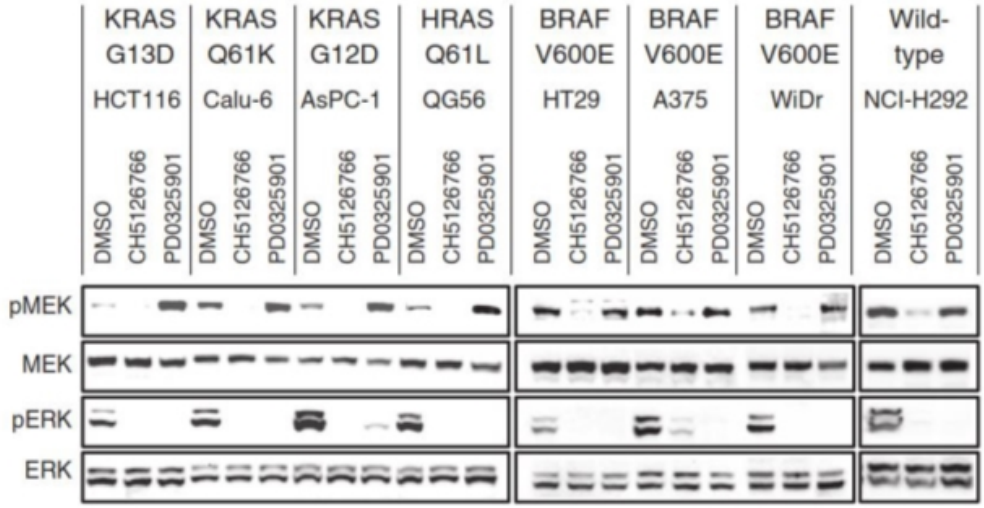
# CH5126766 is effective against multiple RAS & RAF mutations: Potential to act more broadly or be combined with agents targeting specific mutations only






**Reference:**
Ishii et al., Cancer Research, 2013

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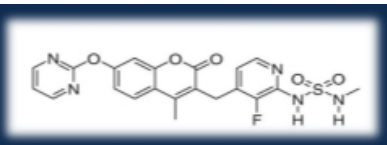
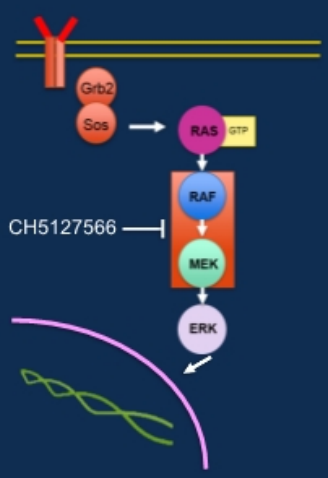
*PD0325901 (mirdametinib) is a conventional MEK inhibitor*

# Background








- CH5126766: MEK inhibitor with functional pan-RAF inhibition, first-in-class agent
- Dose escalation by Martinez-Garcia et al. 2012
  - MTD 2.25 mg, once daily
  - MTD 4.0 mg, 4 days on/3 days off
  - MTD 2.7 mg, 7 days on/7 days off
- Promising activity: tumor shrinkage in 40 % of pts
- Development of these schedules challenging

*Ishii et al. Cancer Res; 2013 Jul 1;73(13):4050-60*
*Martinez-Garcia et al. Clin Cancer Res. 2012 Sep 1;18(17):4806-19*

# Background



- In view of promising activity, a different trial design was investigated to mitigate toxicity
- Mean terminal $t_{1/2}$ of ≈ 60 hours
  - 2x-weekly and 3x-weekly scheduling, in 4 week cycles
- Led by the Drug Development Unit at RMH/ICR

# Adverse Events



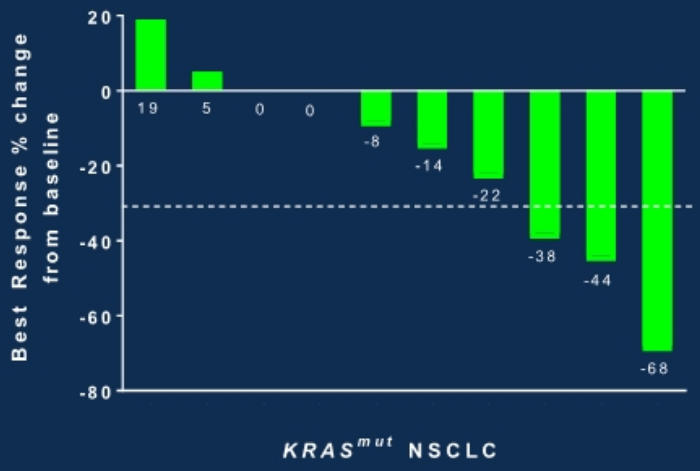
| Adverse event details | Expansion: 4mg 2x weekly n=26 | | Martinez-Garcia *et al.* CCR 2012 Patient treated at OD MTD n=6 |
|---|---|---|---|
| | All grades | ≥ Gr. 3 | ≥ Gr. 3 |
| Rash-related | 22 (84.6 %) | 5 (**19.2 %**) | 3 (**50.0 %**) |
| CK elevation | 15 (57.7 %) | 2 (**7.6%**) | 1 (**16.7 %**) |
| Blurred vision | 13 (50 %) | 0 | 0 |
| Peripheral oedema | 10 (38.5 %) | 0 | 0 |
| Diarrhoea | 9 (34.1 %) | 1 (3.8 %) | 0 |
| Mucositis/Mouth ulcer | 8 (30.8 %) | 1 (3.8 %) | 0 |
| Fatigue | 6 (23.1 %) | 1 (3.8 %) | 0 |
| Nausea | 5 (19.2 %) | 0 | 0 |

Martinez-Garcia et al. Clin Cancer Res. 2012 Sep 1;18(17):4806-19

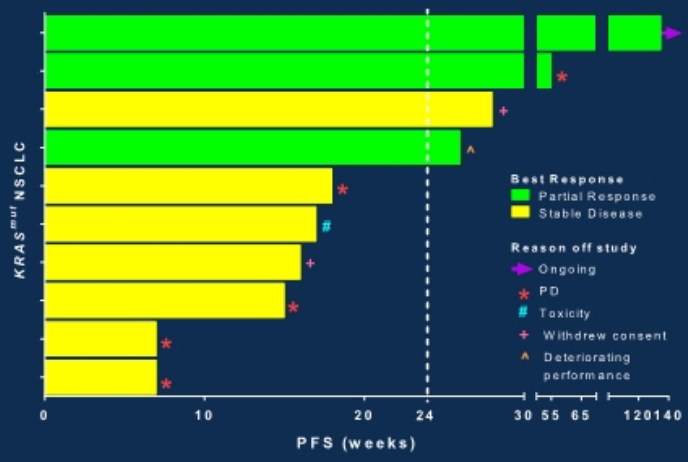
# Results: *KRAS*$^{mut}$ NSCLC - Adenocarcinoma



## Best response by RECIST v1.1



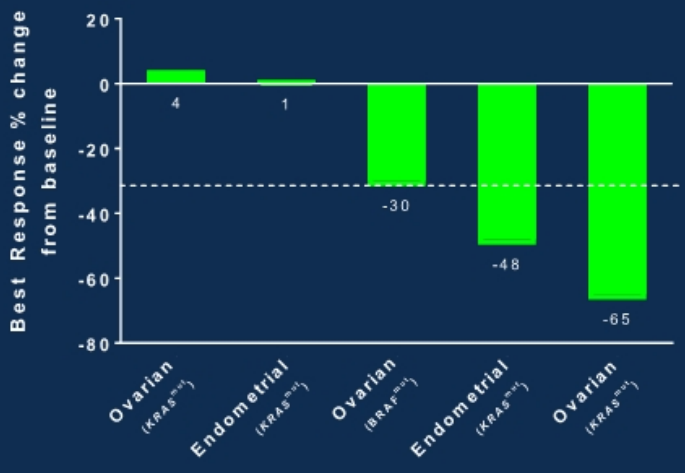

## Progression Free Survival



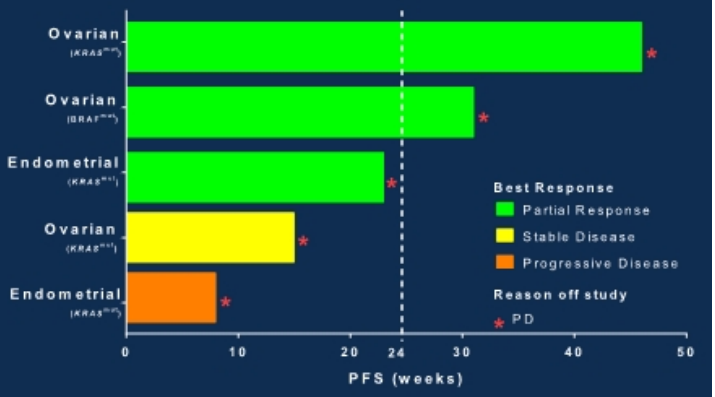
# Results: Gynaecological cancers



## Best response by RECIST v1.1




## Progression Free Survival



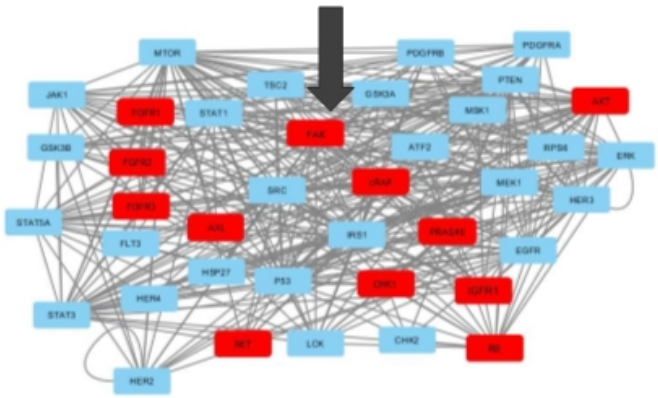
# Conclusion



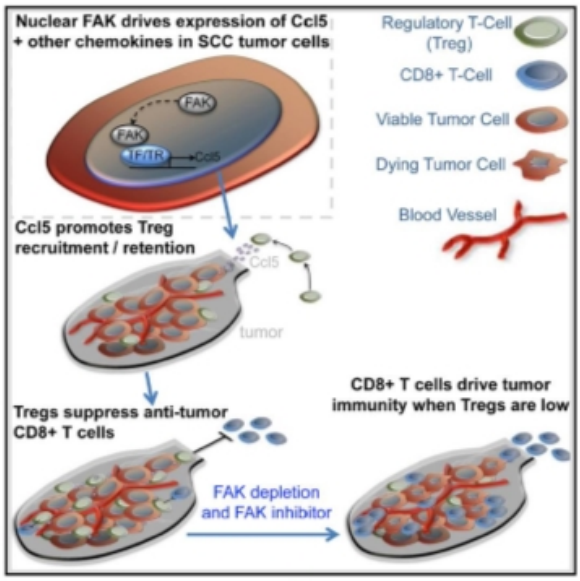
- CH5127566 (RO5126766) is a potent and well-tolerated RAF-MEK inhibitor
- Twice-weekly scheduling improved therapeutic index
- Multiples responses in *KRAS*- and *BRAF*-mutated malignancies, with impressive results in NSCLC and gynaecological cancers
- Preliminary results suggesting single-agent activity in relapsed/refractory multiple myeloma
  - Ongoing cohort

# *KRAS*$^{M}$ MEK + FAK inhibitor combinations






Phosphoproteomic signature of *KRAS*$^{M}$ A549 NSCLC cell line exposed to Trametinib for 1hr shows feedback loops involving FAK

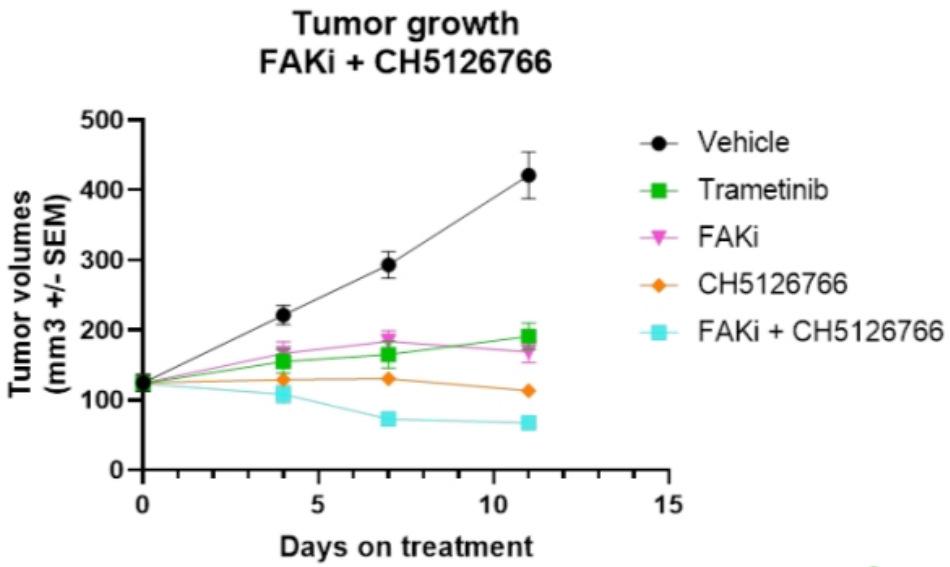



*Serrels A Cell 2015, 163:160-173*

Verastem Oncology

# Tumor regression achieved with FAK + RAF/MEK Combination in KRAS-mutant Ovarian Xenograft Model (TOV21G)





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# Supporting Materials

Copiktra®
(duvelisib) 15mg | 25mg capsules

## Indication

COPIKTRA is a kinase inhibitor indicated for the treatment of adult patients with:

- **Relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies.**
- **Relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies.**

**This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.**

## Dosing & Administration

25 mg orally, twice daily. Modify dosage for toxicity.

## Selected Important Safety Information

**WARNING: FATAL AND SERIOUS TOXICITIES: INFECTIONS, DIARRHEA OR COLITIS, CUTANEOUS REACTIONS, and PNEUMONITIS**

- **Fatal and/or serious infections occurred in 31% of COPIKTRA-treated patients. Monitor for signs and symptoms of infection. Withhold COPIKTRA if infection is suspected.**
- **Fatal and/or serious diarrhea or colitis occurred in 18% of COPIKTRA-treated patients. Monitor for the development of severe diarrhea or colitis. Withhold COPIKTRA.**
- **Fatal and/or serious cutaneous reactions occurred in 5% of COPIKTRA-treated patients. Withhold COPIKTRA.**
- **Fatal and/or serious pneumonitis occurred in 5% of COPIKTRA-treated patients. Monitor for pulmonary symptoms and interstitial infiltrates. Withhold COPIKTRA.**

**Warnings and Precautions**

- Hepatotoxicity: Monitor hepatic function.
- Neutropenia: Monitor blood counts.
- Embryo-Fetal toxicity: COPIKTRA can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.

**Contraindications:** None.

**Most common adverse reactions (≥ 20%):** Diarrhea or colitis, neutropenia, rash, fatigue, pyrexia, cough, nausea, upper respiratory infection, pneumonia, musculoskeletal pain, and anemia.

**Source**
Copiktra USPI, 2018



*For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.*

**Verastem, Inc.**
**Reconciliation of GAAP to Non-GAAP Financial Information**
(in thousands, except per share amounts)
(unaudited)

| | Three months ended September 30, | | Nine months ended September 30, | |
|---|---|---|---|---|
| | 2019 | 2018 | 2019 | 2018 |
| **Net Loss Reconciliation** | | | | |
| Net Loss (GAAP basis) | $ (30,139) | $ (21,668) | $ (110,435) | $ (61,085) |
| **Adjust:** | | | | |
| Amortization of acquired intangible asset | 392 | 31 | 1,177 | 31 |
| Stock-based compensation expense | 1,915 | 2,040 | 7,228 | 4,908 |
| Non-cash interest, net | 1,611 | 156 | 4,426 | 335 |
| Severance and Other | 40 | — | 1,820 | — |
| **Adjusted Net Loss (non-GAAP basis)** | $ (26,181) | $ (19,441) | $ (95,784) | $ (55,811) |