KURA ONCOLOGY

Developing Precision Medicines
for the Treatment of Cancer

Corporate Presentation

May 2019

Forward-Looking Statements

This presentation contains forward-looking statements. Such statements include, but are not limited to, statements regarding our research, preclinical and clinical development activities, plans and projected timelines for tipifarnib, KO-947 and KO-539, plans regarding regulatory filings, our expectations regarding the relative benefits of our product candidates versus competitive therapies, and our expectations regarding the therapeutic and commercial potential of our product candidates. The words “believe,” “may,” “will,” “estimate,” “promise,” “plan”, “continue,” “anticipate,” “intend,” “expect,” “potential” and similar expressions (including the negative thereof), are intended to identify forward-looking statements. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include: our preclinical studies and clinical trials may not be successful; the U.S. Food and Drug Administration (FDA) may not agree with our interpretation of the data from clinical trials of our product candidates; we may decide, or the FDA may require us, to conduct additional clinical trials or to modify our ongoing clinical trials; we may experience delays in the commencement, enrollment, completion or analysis of clinical testing for our product candidates, or significant issues regarding the adequacy of our clinical trial designs or the execution of our clinical trials may arise, which could result in increased costs and delays, or limit our ability to obtain regulatory approval; our product candidates may not receive regulatory approval or be successfully commercialized; unexpected adverse side effects or inadequate therapeutic efficacy of our product candidates could delay or prevent regulatory approval or commercialization; and we may not be able to obtain additional financing. Additional risks and uncertainties may emerge from time to time, and it is not possible for Kura’s management to predict all risk factors and uncertainties.

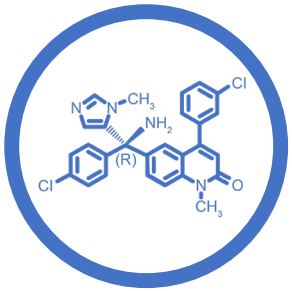
All forward-looking statements contained in this presentation speak only as of the date on which they were made. Other risks and uncertainties affecting us are described more fully in our filings with the Securities and Exchange Commission. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Investment Highlights

Targeted Oncology	Advance pipeline of targeted drug candidates for selected solid tumors and hematologic malignancies Utilize precision medicine approaches; Fast-to-market potential
Proprietary Pipeline	**Tipifarnib:** Potent farnesyl transferase inhibitor; Registration-directed and multiple Phase 2 trials ongoing; Biomarker-guided development; Issued patents and potential for regulatory exclusivity **KO-947:** ERK inhibitor; Phase 1 dose-escalation trial ongoing **KO-539:** Inhibitor of menin-MLL interaction; IND cleared March 2019
Near-Term Milestones	Additional Phase 2 data in CXCL12+ PTCL in June and HRAS mutant SCCs in 2nd half 2019
Team	Proven oncology drug development experience
Financials	$165.5M in cash as of March 31, 2019*

* Includes cash, cash equivalents and short-term investments

Advancing Pipeline of Targeted Drug Candidates



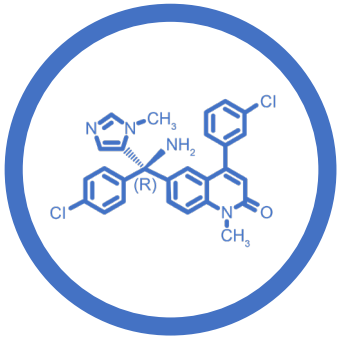
	Tipifarnib	KO-947	KO-539
Therapeutic Target	• Farnesyl transferase	• ERK kinase	• Menin-MLL interaction
Biomarker Strategies	• HRAS mutant solid tumors • CXCL12-expressing hematologic malignancies and solid tumors	• MAPK-pathway dysregulated tumors • 11q13 amplified solid tumors	• MLL-rearranged (MLL-r) leukemias • NPM1 and DNMT3A mutant liquid tumors
Development Status	• Registration-directed study and multiple Phase 2 trials ongoing* • Two biomarkers identified with issued patents	• Ongoing Phase 1 dose-escalation trial	• Phase 1 trial expected to initiate in mid-2019

* Tipifarnib previously studied in > 5,000 patients in > 70 studies with a manageable safety profile as a single agent

Note: Chemical structures of KO-947 and KO-539 not published

Biomarker Strategies May Unlock Clinical Activity and Commercial Value

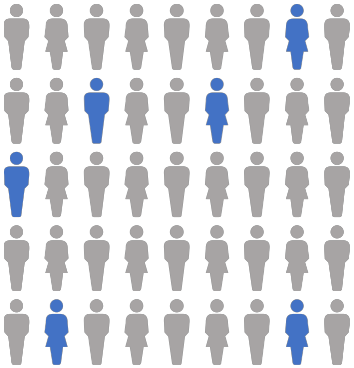
Targeted Therapy



Analytical Technologies

(next-generation sequencing, expression profiling, etc.)

Selected Patient Population



Potential Value

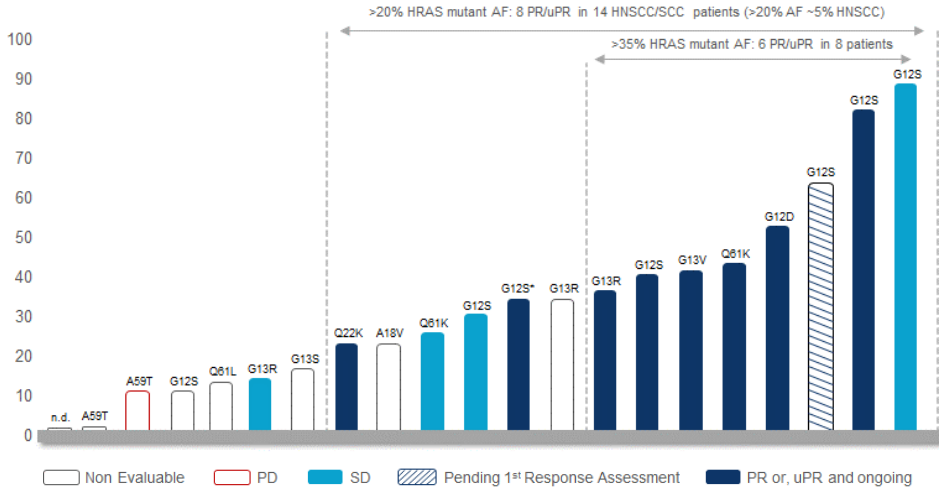
- Enrichment of clinical activity
- Higher probability of success
- Expedited development and regulatory path
- Strong commercial case

Multiple Clinical Proof-of-Concepts Reinforce Precision Medicine Approach

HRAS Mutant
HNSCC

HRAS Mutant Allele Frequency

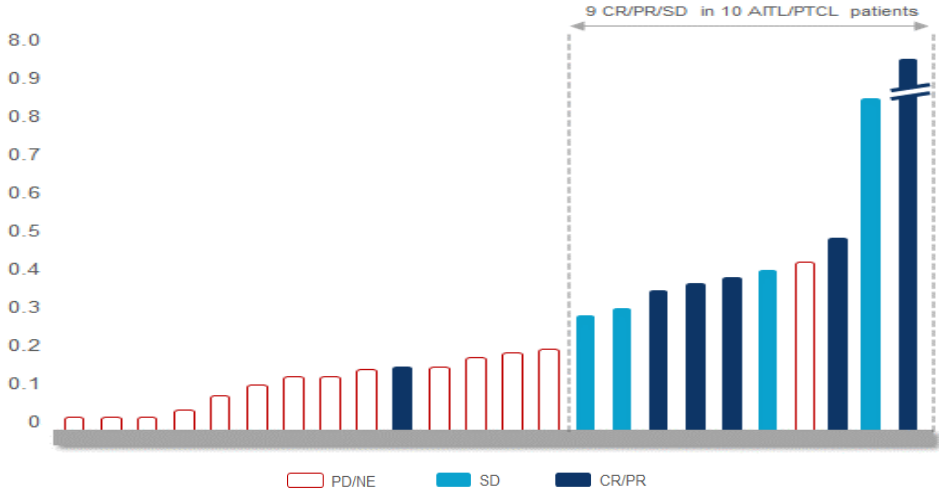
Clinical benefit observed in **high frequency HRAS mutant** population



CXCL12+
AITL/PTCL

High CXCL12 Levels

Clinical benefit observed in **high CXCL12 AITL / PTCL** population



Product Candidate Pipeline

Program		Preclinical	Phase 1	Phase 2	Pivotal
Tipifarnib Farnesyl Transferase Inhibitor	HRAS Mutant Indications	HNSCC			
		Other SCCs			
	CXCL12 Pathway Indications	AITL / PTCL			
		CMML / AML			
		Pancreatic			
KO-947 ERK Inhibitor — **MAPK Pathway Tumors**		Solid Tumors			
KO-539 Menin-MLL Inhibitor — **Acute Leukemia**		Acute Leukemias			

Investigator-Sponsored Trials | HRAS Mutant Urothelial Carcinomas, Samsung Medical Center | HRAS Mutant Lung Squamous Cell Carcinomas, Spanish Lung Cancer Group

01 • *Tipifarnib in HRAS Mutant Solid Tumors*

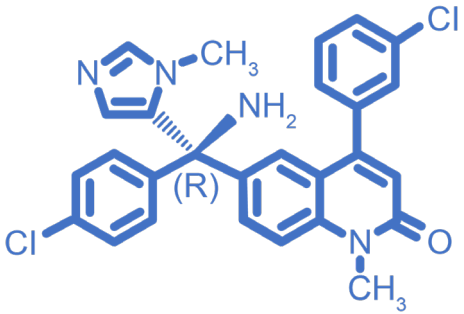
02 • *Tipifarnib Using CXCL12 Pathway Biomarkers*

03 • *KO-947 (ERK Inhibitor)*

04 • *KO-539 (Menin-MLL Inhibitor)*

Tipifarnib: Selective Farnesyl Transferase Inhibitor with Substantial Prior Clinical Experience

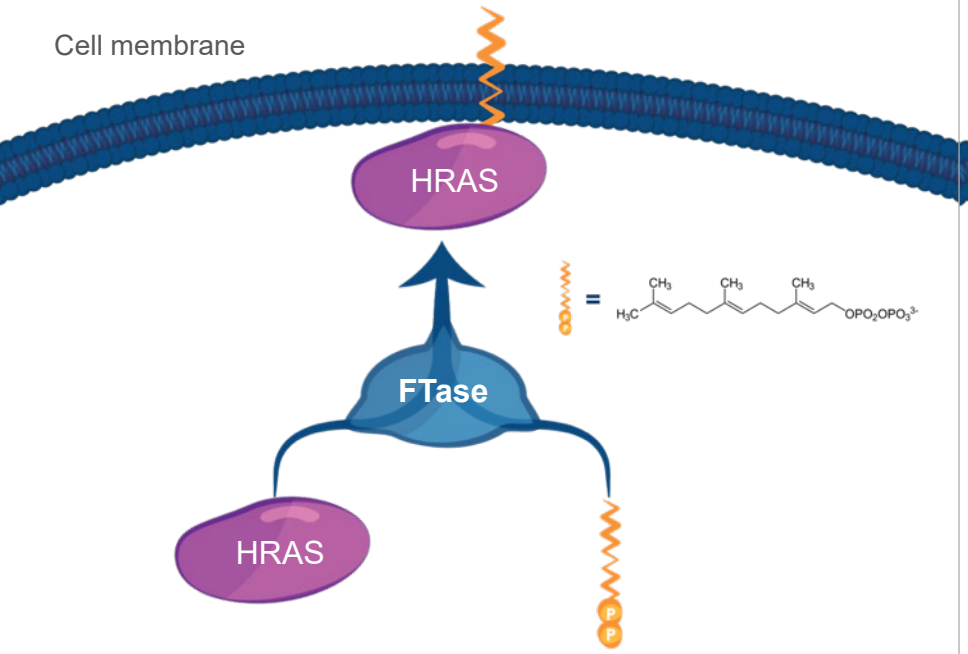
- Extremely potent and selective inhibitor of farnesyl transferase[1] licensed from Janssen
- Well characterized > 5,000 patients treated in > 70 prior studies
- Anecdotal activity of durable responses but developed before advent of personalized medicine approaches, including genetic selection
- Manageable safety profile as single agent therapy (< 25% treatment discontinuation)
- Tipifarnib adverse events (reported from 472 solid tumor patients):
  - Myelosuppression (neutropenia 25%, anemia 31%, thrombocytopenia 19%)
  - Non-heme > 25%: fatigue (41%) and GI unspecific (nausea 47%, anorexia 33%, diarrhea 32%, vomiting 32%)



[1] *End et al*. 2001. *Cancer Res*. 61:131-37

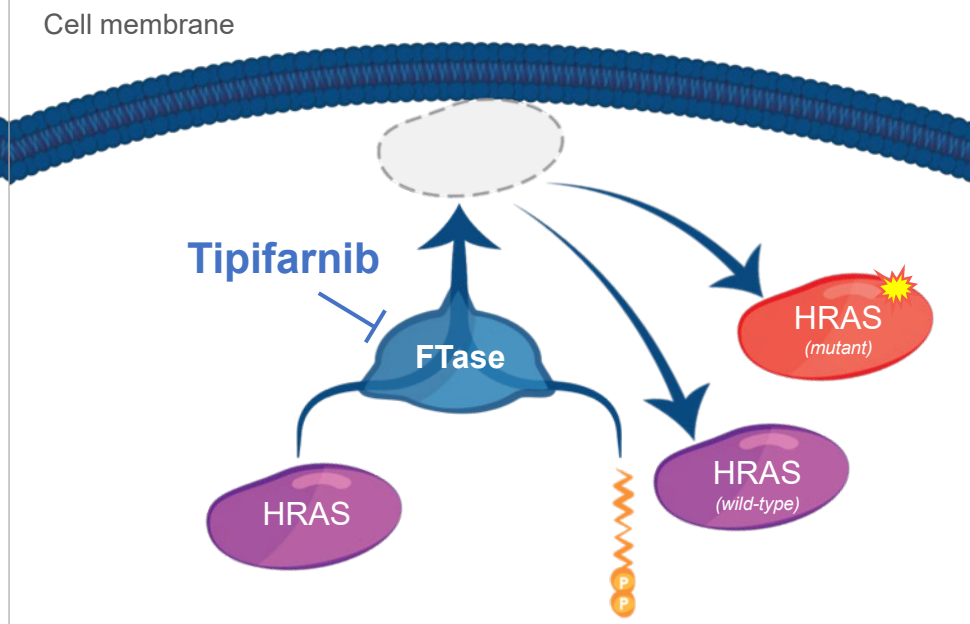
Farnesylation is Required for HRAS Activity

Normal FTase



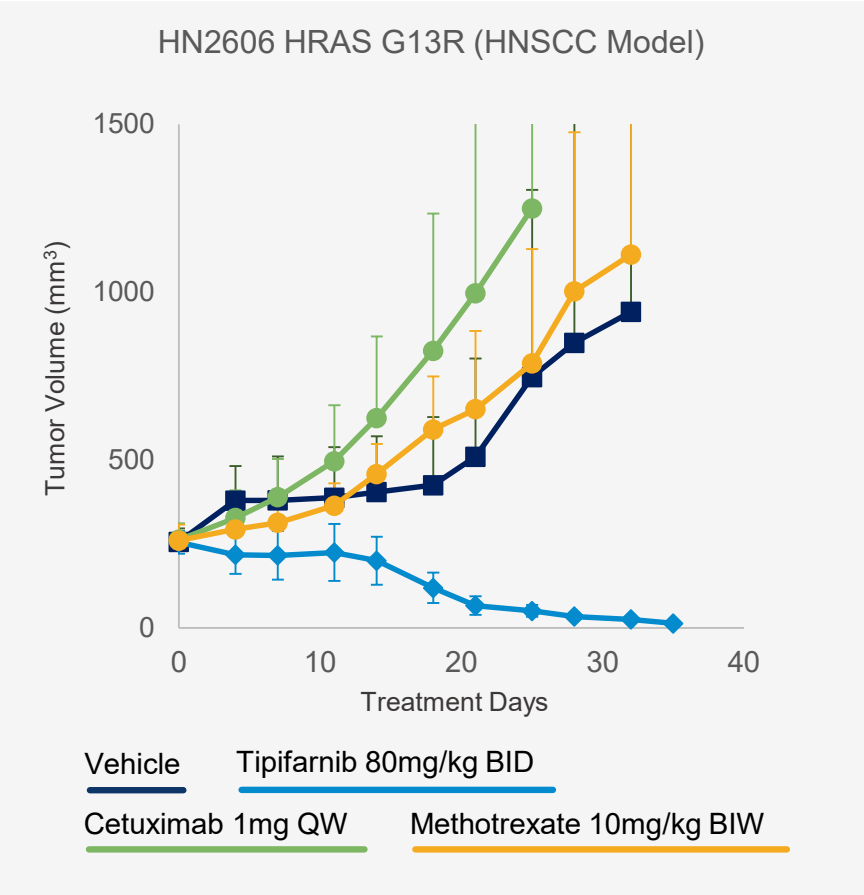
- **Farnesyl transferase (FTase) attaches farnesyl group to proteins**, facilitating localization to the inner cell membrane
- Membrane localization is **required for HRAS signal transduction activity**

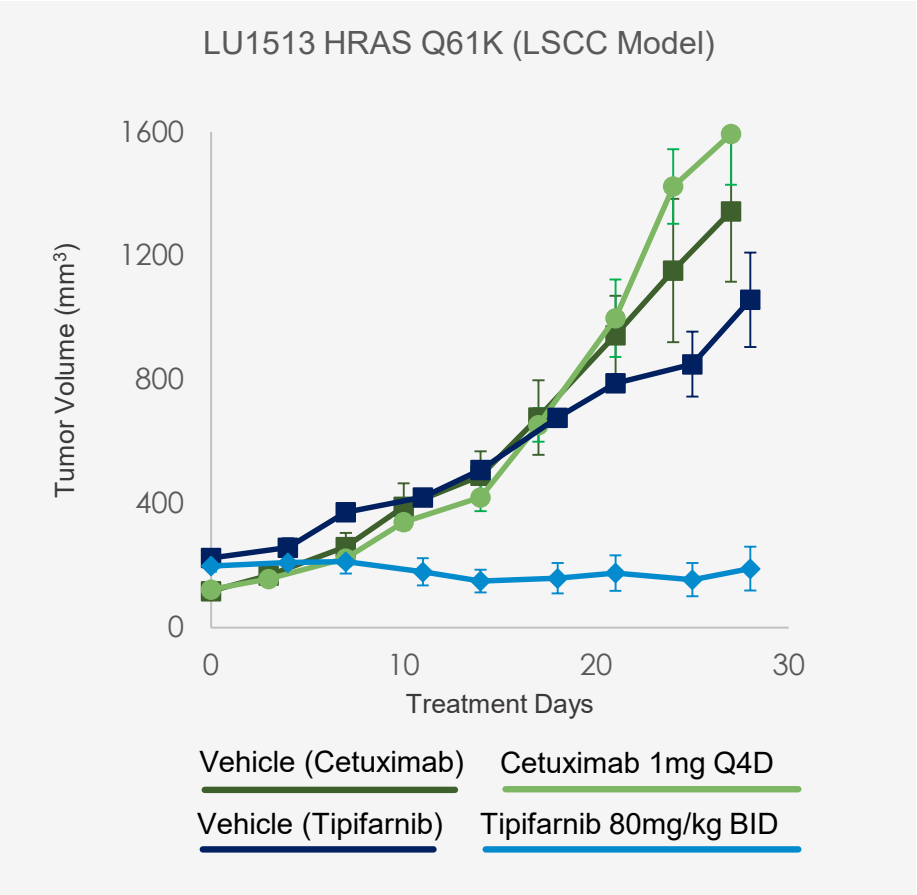
Tipifarnib Inhibits FTase



- Blocking farnesylation **prevents wild-type and mutant HRAS membrane localization**
- NRAS and KRAS are susceptible to redundant forms of prenylation, but **HRAS can only be farnesylated**

Tipifarnib is a Potent Inhibitor of HRAS Mutant Tumors

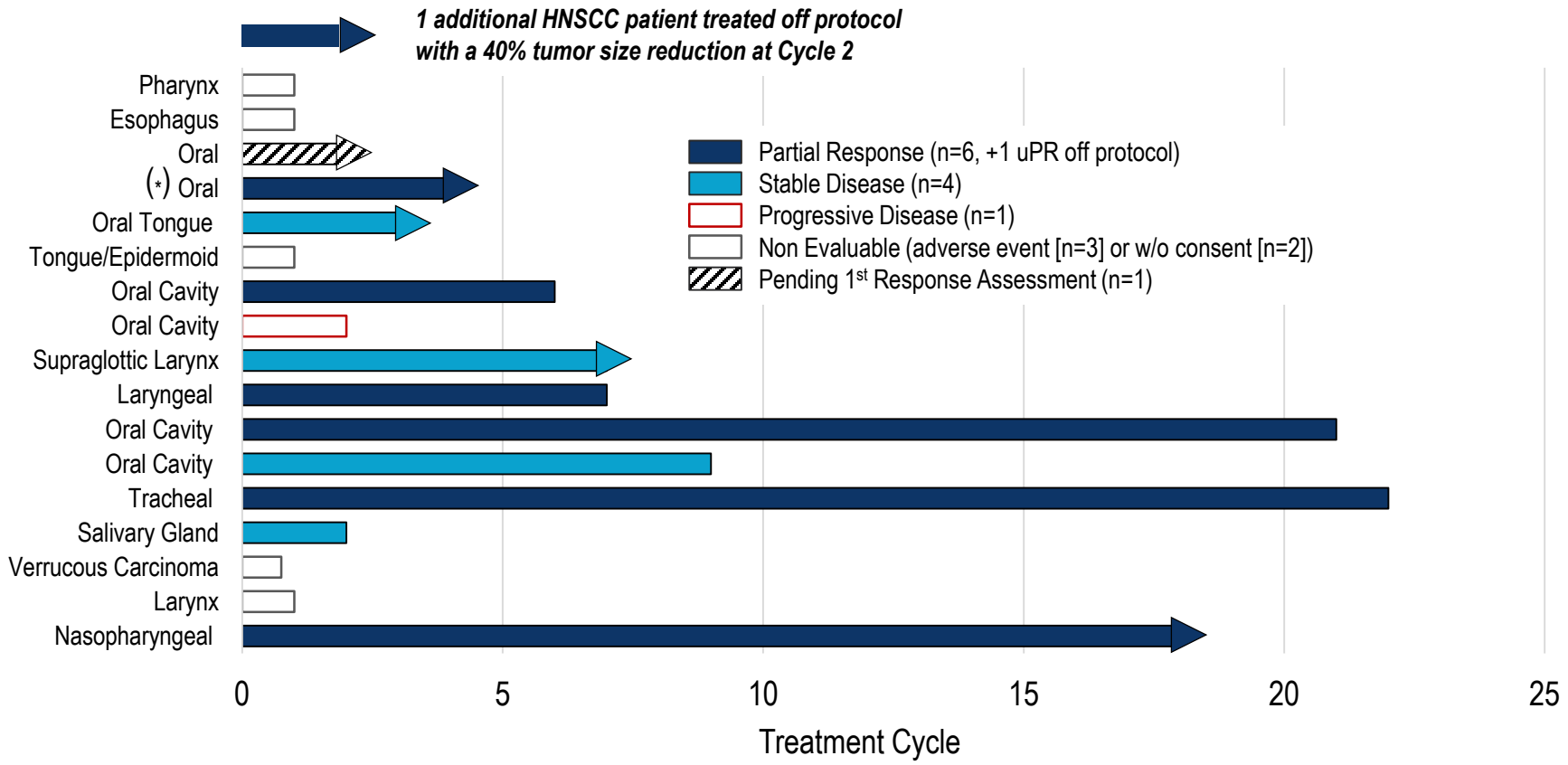




- Regressions observed in preclinical PDX models of SCC carrying the HRAS mutant oncogene
- Stasis or regression observed in other tumor types carrying HRAS mutations

Phase 2 Study of Tipifarnib: HNSCC Patients

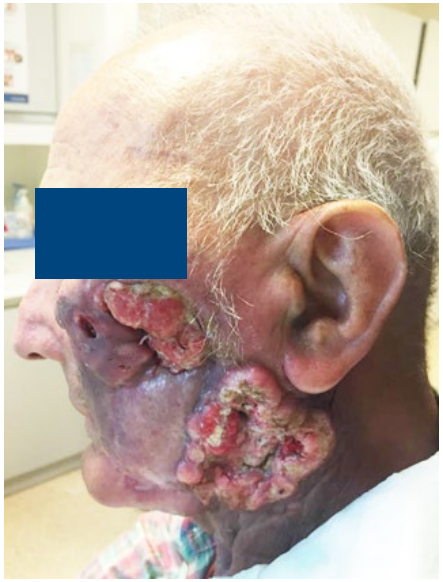
(n=17 on study + 1 patient treated off protocol)



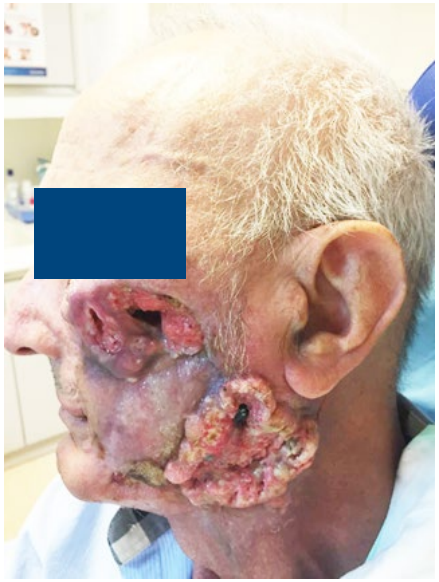
Ho *et al*. European Society for Medical Oncology 2018 Congress #1046O | Preliminary results as of 9/7/18
* Response confirmed on 10/15/18

Resolution of Disfiguring Skin Lesions with Tipifarnib Post-Immunotherapy Failure

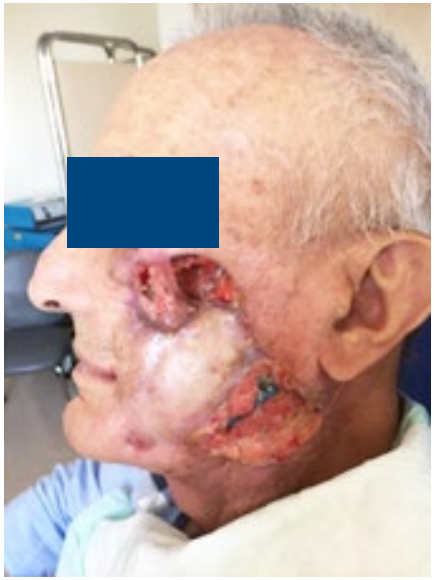
- Patient 012-001: 69-year-old male with recurrent oral cavity SCC
- Prior therapies: TPEx (docetaxel CDDP cetuximab), nivolumab + lirilumab
- Molecular status: HRAS G12S, TP53 R248Q
- 27.5% HRAS mutant allele frequency
- Initial PR (40% tumor reduction) on Cycle 1 Day 15 (7 days tipifarnib + 7 days rest; 56% reduction at Cycle 3



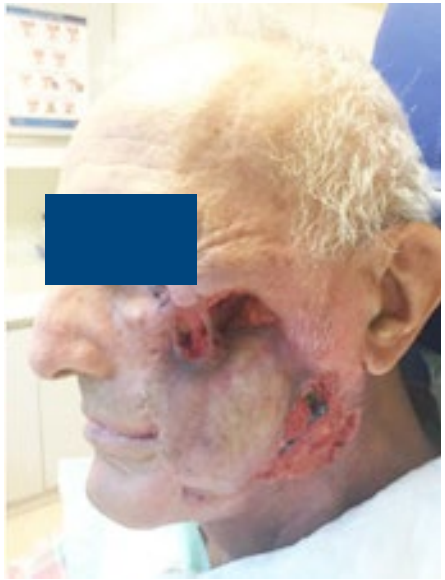
Cycle 1 Day 1



Cycle 1 Day 7



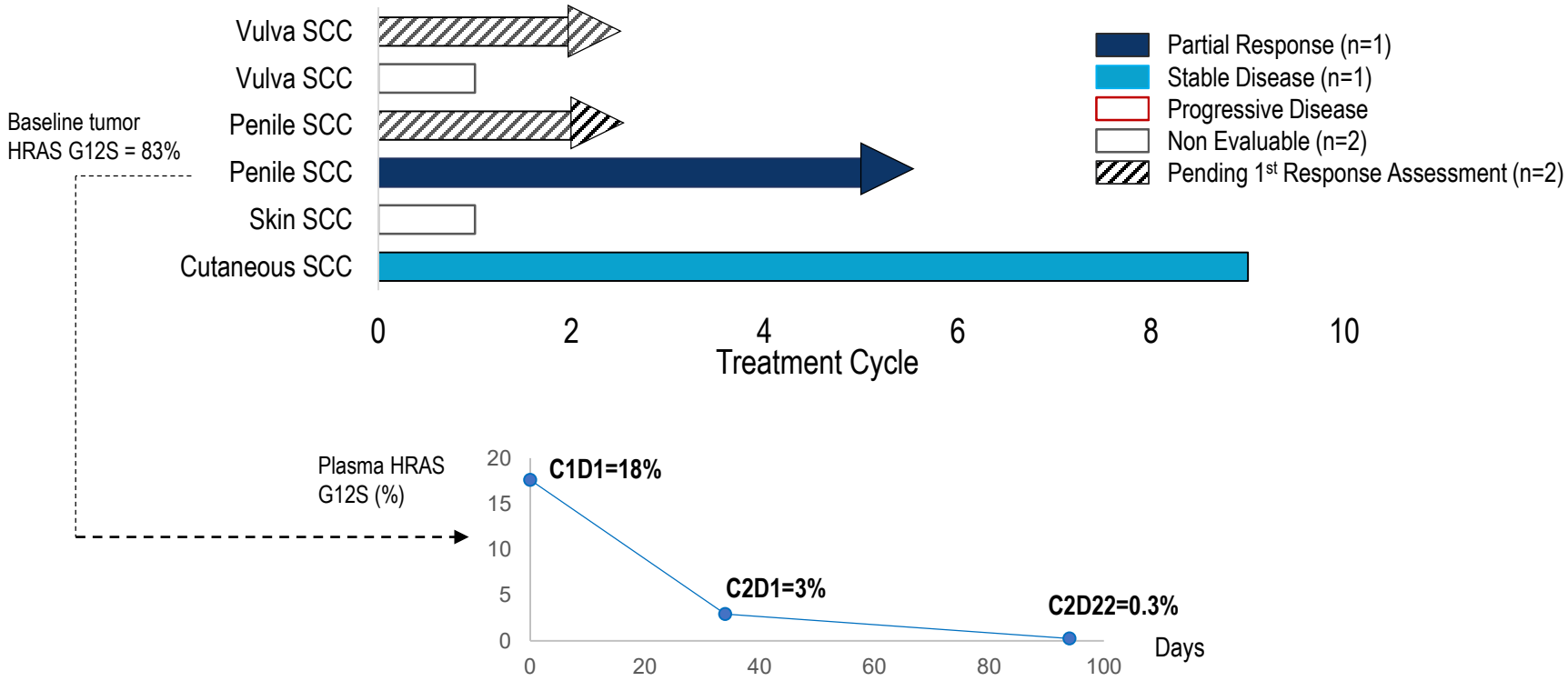
Cycle 1 Day 20



Cycle 2 Day 1

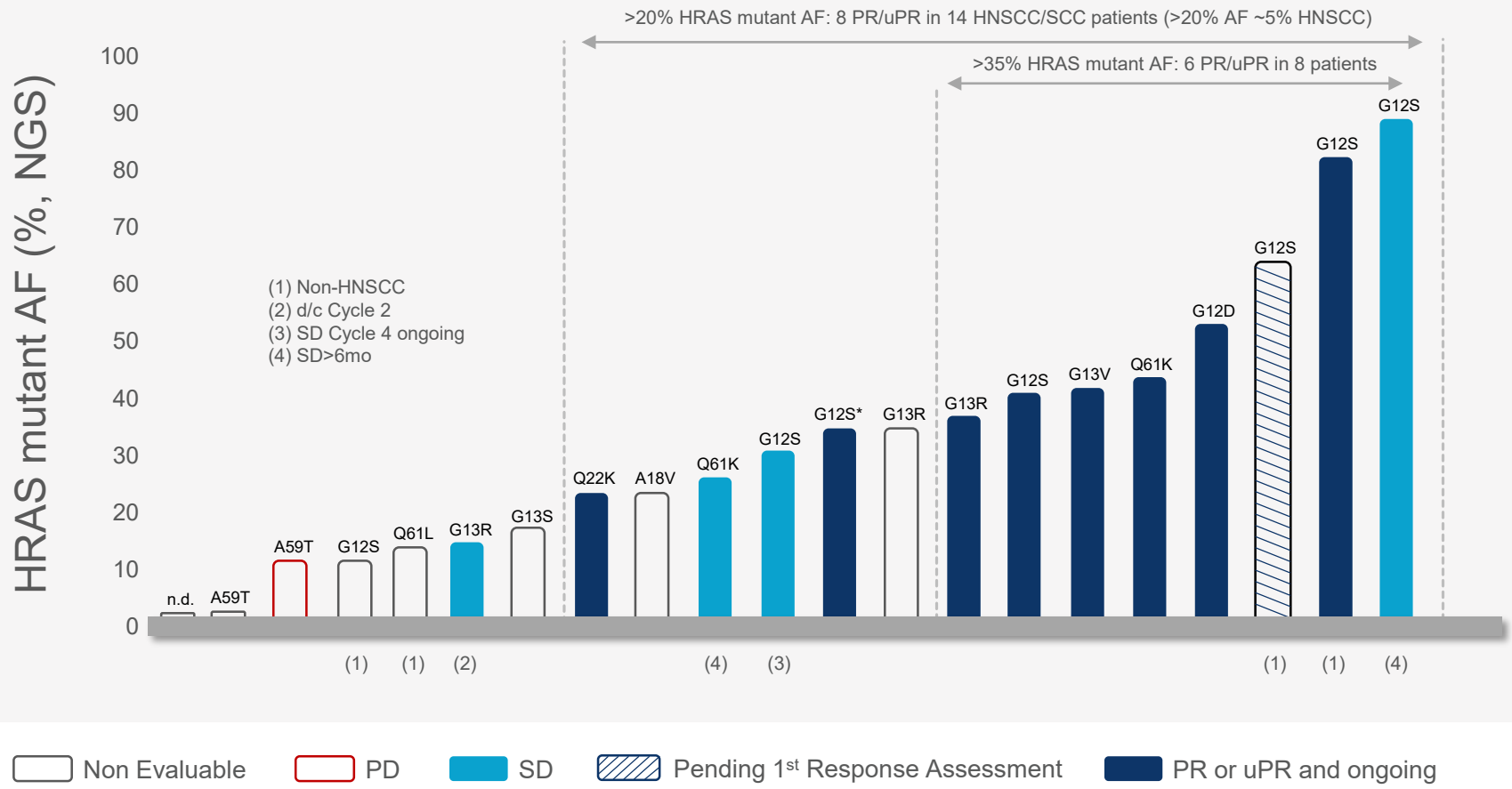
Ho et al. 2018 Multidisciplinary Head and Neck Cancers Symposium #217 | Results based on preliminary data as of 2/8/18
Images provided by Dr. Caroline Even and Dr. Charles Ferte, IGR, Paris

Phase 2 Study of Tipifarnib: Other SCC Patients (n=6)



Association of HRAS Mutant Allele Frequency with Clinical Benefit from Tipifarnib

(HNSCC, SCC, n=21)



Ho *et al*. European Society for Medical Oncology 2018 Congress #1046 | Study KO-TIP-001 patients with HN and non-HN SCC tumors with available HRAS mutant allele data (10/17/18); one additional HNSCC patient was treated off protocol |
* Allele frequency obtained post-ESMO | Pending analysis: 1 HNSCC pending 1st scan, 1 SCC pending 1st scan, 1 SCC SD

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Tipifarnib Development Program in HRAS Mutant HNSCC

RUN-HN
KO-TIP-001

Phase 2
Proof-of-Concept Study

SEQ-HN
KO-TIP-007

Non-Interventional
Screening & Outcomes Cohort

AIM-HN
KO-TIP-007

Registration-Directed Trial

HRAS mutant patients who are not eligible for participation in AIM-HN may be referred to RUN-HN

AIM-HN: Global, multi-center registration directed trial of tipifarnib in HRAS mutant HNSCC

SEQ-HN: Matched control study to identify HRAS mutant HNSCC patients and characterize activity of standard of care

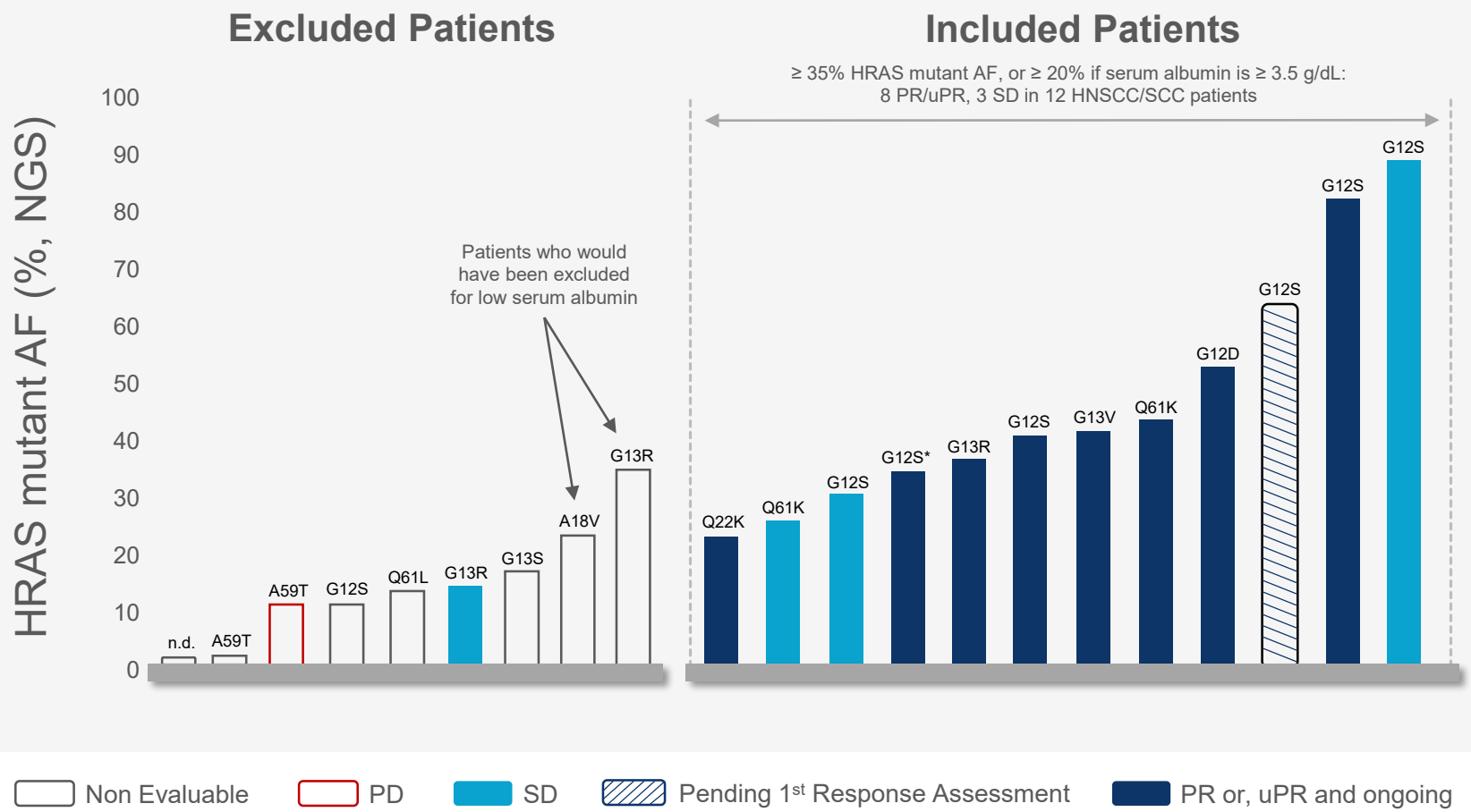
AIM-HN: Trial Design

AIM-HN
KO-TIP-007

- **Global, registration-directed trial**
  - Targeting ~ 100 clinical sites worldwide
  - Anticipate ~ two years to enroll
- **Primary endpoint: Objective Response Rate (ORR) by IRR**
- **Statistical assumptions**
  - At least 59 subjects, 80% power, 15% ORR (null hypothesis) and 30% ORR (response rate of interest)
- **Minimum tumor HRAS mutant allele frequency of 20%**
  - Tumor HRAS mutation with an allele frequency ≥ 35%, or ≥ 20% if serum albumin is ≥ 3.5 g/dL
- **600 mg BID starting dose given daily in alternate weeks**
- **As currently designed, AIM-HN may be adequate to support an NDA seeking accelerated approval (FDA end of Phase 2 meeting)**
  - SEQ-HN data to provide a benchmark of the activity of standard of care in HRAS mutant HNSCC (relevant for potential label discussion and post approval commitments)
- **Trial initiated and open for enrollment in November 2018**

Activity When AIM-HN Criteria Applied Retrospectively to Phase 2 Study

(HNSCC, SCC, n=21)



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* Allele frequency obtained post-ESMO | Pending analysis: 1 HNSCC pending 1st scan, 1 SCC pending 1st scan, 1 SCC SD

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HRAS Mutant Cancers: Market Opportunity

HNSCC Represents Significant Unmet Need[1]

1L	2L
ORR 36%	ORR 13-16%
PFS 5.6 months	PFS ~2 months
OS ~10 months	OS 6-8 months

- Outcome of SOC in unselected populations
- Lower response rate expected in HRAS mutant patients[2]

Populations Based on Annual U.S. Incidence

HRAS Mutant HNSCC	HRAS Mutant All SCCs
2,900-4,700 patients*	7,500+ patients

[1] N Engl J Med. 2008 Sep 11;359(11):1116-27 | Keytruda & Opdivo package inserts | J Clin Oncol. 2007 Jun 1;25(16):2171-7
[2] Journal of Clinical Oncology 2012 30:15_suppl, 5574-5574
* Estimate is between 5-8% of total HNSCC population, depending on allele frequency of HRAS mutations (Source: TCGA, internal data)

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02. *Tipifarnib Using CXCL12 Pathway Biomarkers*

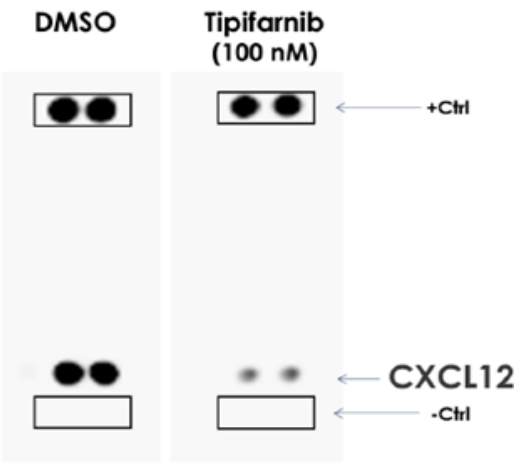
Relevance of CXCL12 Inhibition as a Targeted Therapy

- **Key characteristics of CXCL12**
  - Expressed primarily by immune cells, endothelial cells and stromal fibroblasts that constitute the tumor microenvironment
  - Binds and activates two receptors, CXCR4 and CXCR7
  - CXCL12 and its receptors are key factors linking cancer cells with tumor microenvironment

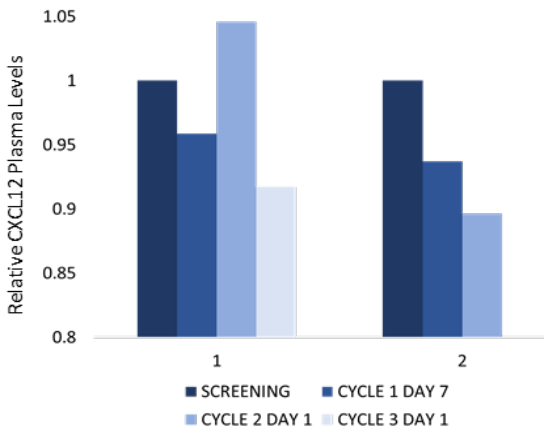
- **Potential role of CXCL12 inhibition in cancer therapy**
  - Inhibition of growth and homing of lymphoid and myeloid tumors[1]
  - Interference with tumor cell metastasis into secondary organs, *e.g.* inhibition of bone recurrence of solid tumors in adjuvant settings – after primary tumor is removed by surgery/chemoradiation[2]
  - Reversion of the tolerogenic effect of a tumor microenvironment rich in immunosuppressive cells such as regulatory T-cells and neutrophils, *e.g.* synergy of CXCL12 and PD-L1 inhibition in pancreatic tumor models[3]

[1] Burger *et al*. 2007. *Br J Haematol*. 137:288-96 | [2] Epstein 2004. *Nat Rev Cancer* 4:901-9 |
[3] Feig *et al*. 2013. *Proc Natl Acad Sci U S A.* 110:20212-7

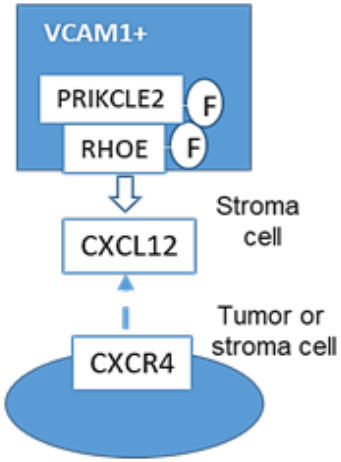
Tipifarnib is a Potent Inhibitor of CXCL12 Secretion by Stromal Cells



Tipifarnib downregulates CXCL12 secretion ex-vivo in CD1 mouse bone marrow stroma cultures



Decrease in CXCL12 plasma levels in two tipifarnib-treated T-cell lymphoma patients (tipifarnib dose 300 mg bid for 21 of 28-day cycles)



Gene expression of the uniquely farnesylated RHOE (RND3) and PRICKLE2 proteins is strongly associated with bone marrow stroma CXCL12 expression, suggesting potential CXCL12-related tipifarnib targets[1]

Gualberto *et al*. AACR 2019 #CT191 | [1] Data from TCGA, AML, Provisional

02a • *Tipifarnib Using CXCL12 Pathway Biomarkers: PTCL / AITL*

PTCL: CXCL12-Expressing Lymphoma with a Significant Unmet Need

	BELEODAQ® (BELINOSTAT)	ISTODAX® (ROMIDEPSIN)	FOLOTYN® (PRALATREXATE)
Efficacy Study	Single Arm[1] N=120	Single Arm[2] N=130	Single Arm[3] N=109
Prior Therapies (range)	2 (1-8)	2 (1-8)	3 (1-12)
Overall Response Rate	**25.8%**	**26.2%**	**27%**
Median PFS/TTP	1.6 months	4.0 months	3.5 months
Median Overall Survival	7.9 months	11.3 months	14.5 months
Dosing	IV infusion[4]	IV infusion[5]	IV push[6]

Approved therapies in relapsed / refractory PTCL approved based on single-arm clinical trials of 130 patients or fewer with response rates in the range of 25-27% and limited duration of clinical benefit in unselected populations

[1] Beleodaq® package insert
[2] Istodax® package insert
[3] Folotyn® package insert
[4] 1,000 mg/m^2 administered over 30 mins by IV infusion once daily on days 1-5 of a 21-day cycle
[5] 14 mg/m^2 administered over a 4-hour period by IV on days 1, 8 and 15 of a 28-day cycle
[6] 30 mg/m^2 administered over 3-5 mins as an IV push once weekly for 6 weeks in 7-week cycles

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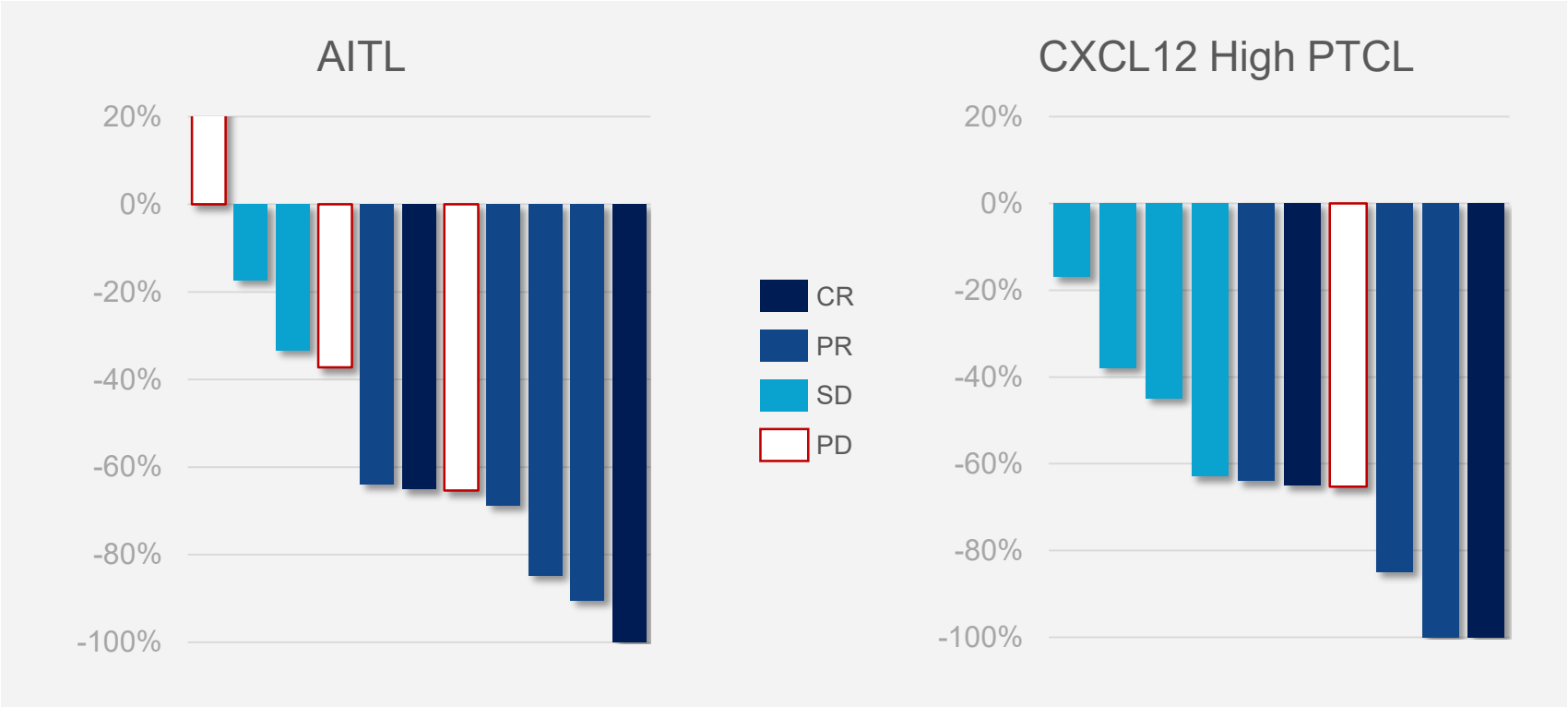
Clinical Activity in Phase 2 Study of Tipifarnib

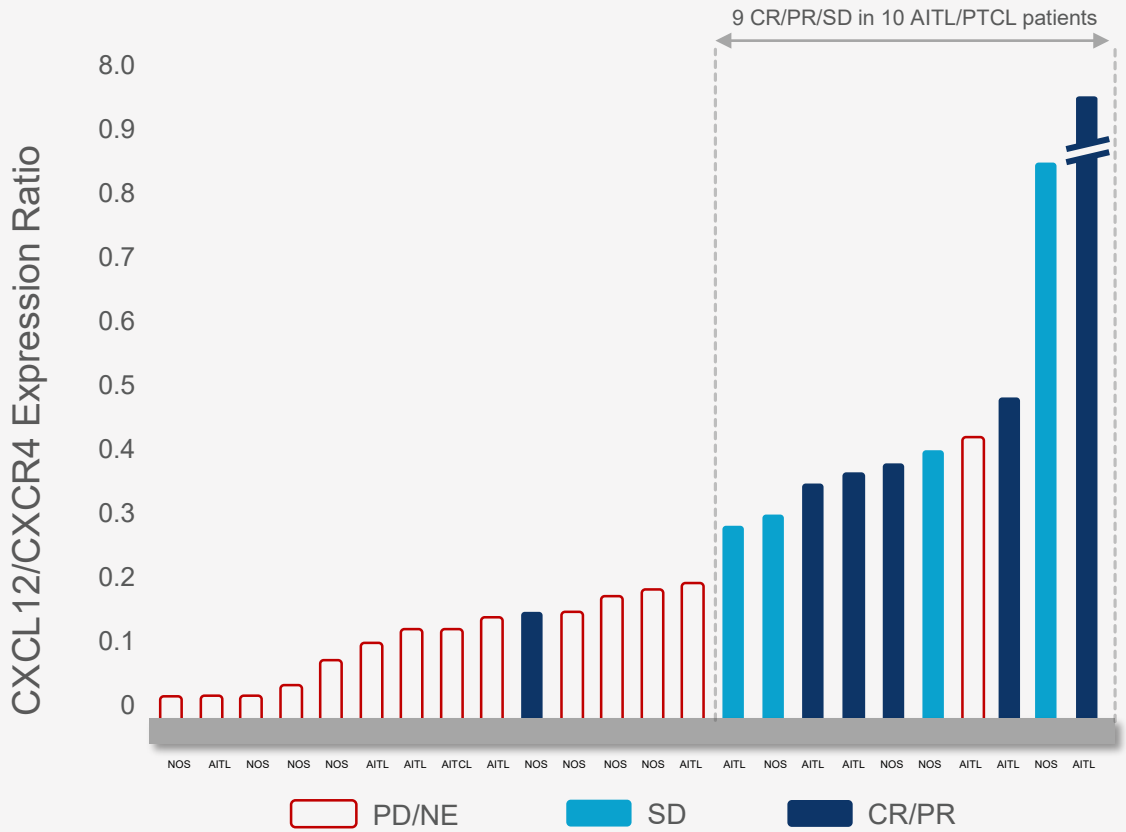
Change in SPD (%)



Witzig *et al*. ASH 2018 #2937 | Preliminary data as of 11/21/18 | Missing measurement data from 2 subjects with best response of PD

SPD: Sum of the products of diameters

Association of High CXCL12 with Clinical Benefit from Tipifarnib in AITL/PTCL

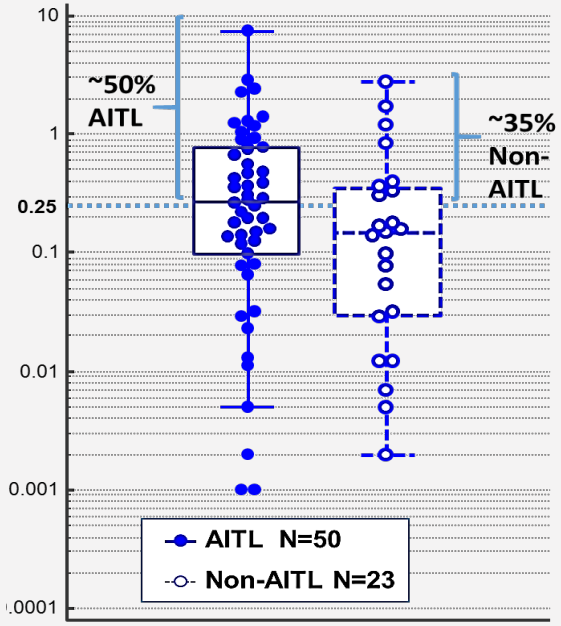


- The High CXCL12/CXCR4 subset of PTCL patients experienced **50% ORR and 90% clinical benefit** with tipifarnib after a median of 3 prior therapies
- High CXCL12/CXCR4 expression ratio had 90% sensitivity and 93% specificity to identify PTCL patients likely to benefit from tipifarnib

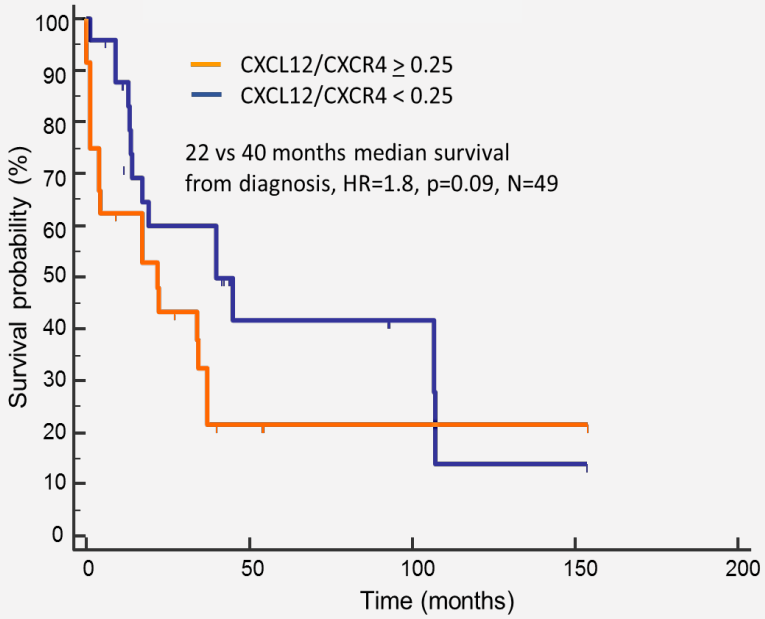
Witzig *et al*. ASH 2018 #2937 | Preliminary data as of 11/21/18 | Expression data generated using RNA-Seq

High CXCL12 Defines Poor Prognosis with Standard of Care Therapy in PTCL

Ratio of CXCL12 to CXCR4 Expression



Standard of Care Treatment

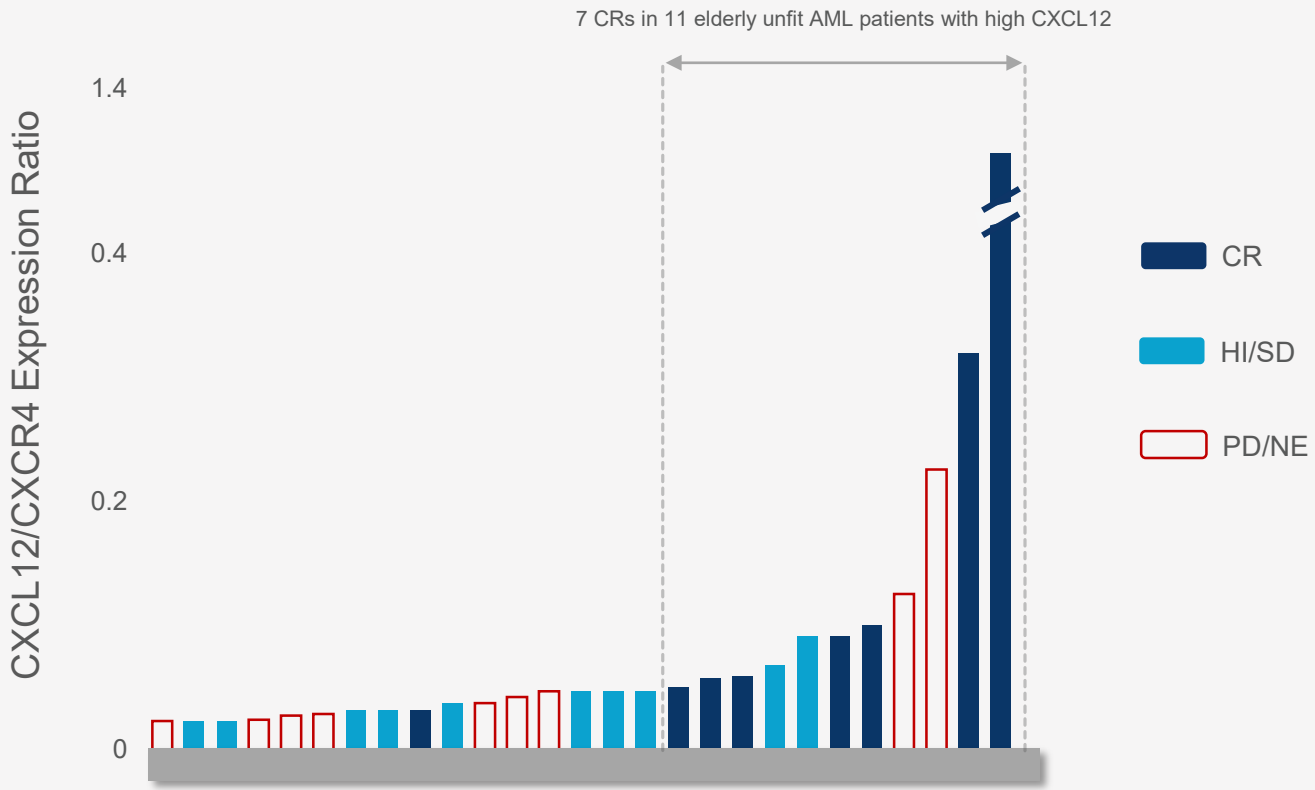


- A trend for worse prognosis was observed in PTCL patients with high CXCL12/CXCR4 expression ratio when treated with standard of care therapy
- Increasing levels of CXCL12 resulted in significantly more negative prognosis for SOC (not shown)
- CXCL12 high subset of patients represents ~40% of PTCL

Witzig *et al*. ASH 2018 #2937

02b • *Tipifarnib Using CXCL12 Pathway Biomarkers: Other Hematologic Malignancies*

Association of High CXCL12 with Activity of Tipifarnib in Elderly Unfit AML



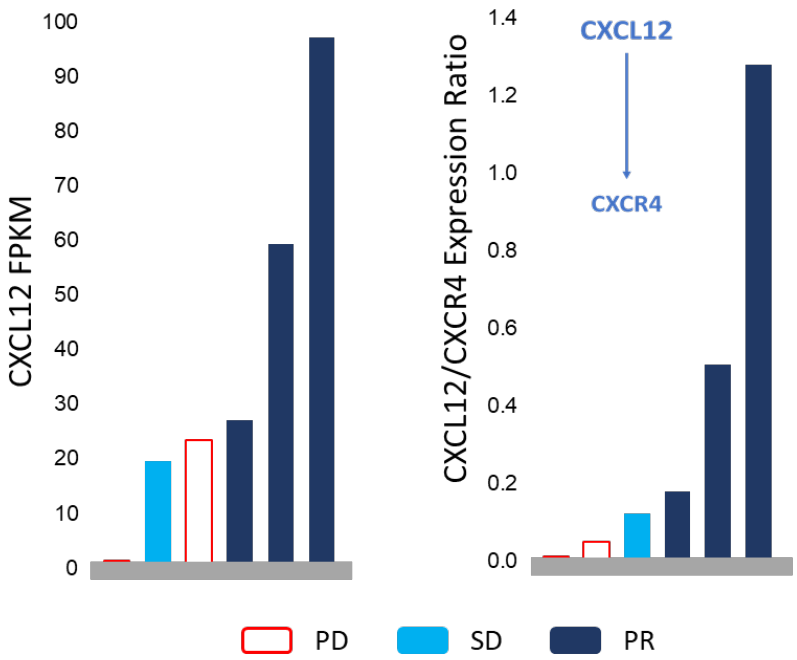
- CTEP20 study: Patient subset – available AML marrow samples with NRAS WT or unknown, N=27 (NCBI GEO, GSE8970)[1]

[1] Raponi *et al*. 2008 *Blood*. Mar 1;111(5):2589-96 | Expression data generated using microarray | HI: Hematologic Improvement

CXCL12 Expression a Potential Marker of Clinical Benefit in DLBCL and CTCL

- Activity of tipifarnib in relapsed/refractory lymphomas was previously investigated in a single-agent Phase 2 trial (N=93)[1]
- Pre-treatment tumor samples and best response data were obtained from 20 patients, including 6 diffuse large B-cell lymphoma (DLBCL), 6 Hodgkin lymphoma and 2 mycosis fungoides
- Six PRs were reported in this subset: 3 in DLBCL, 1 in Hodgkin lymphoma and 2 in mycosis fungoides
- High pre-treatment tumor CXCL12 expression predicted objective response in DLBCL (right)
- Both mycosis fungoides patients with high CXCL12 expression experienced PRs
  - Mycosis fungoides is the most common form of cutaneous T-cell lymphoma (CTCL)
- No relationship between CXCL12 expression and clinical benefit in Hodgkin lymphoma was observed in this dataset

Objective Responses in Tipifarnib-treated DLBCL Patients with High Tumor CXCL12 Expression[2]



02c • *Tipifarnib Using CXCL12 Pathway Biomarkers: Solid Tumors*

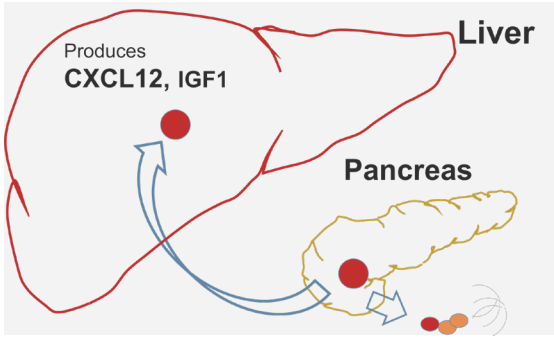
Solid Tumors: Potential CXCL12-Driven Tumor Indication in Pancreatic Cancer

- Elevated CXCL12 expression is known to be a poor prognosis factor in patients with pancreatic, lung and esophageal-gastric cancers[1]
- Kura conducted a retrospective analysis of INT-11, a randomized, double-blind, placebo-controlled Phase 3 trial of gemcitabine + tipifarnib versus gemcitabine + placebo in patients with advanced pancreatic adenocarcinoma previously untreated with systemic therapy
  - Tipifarnib was given at 200 mg bid orally continuously; gemcitabine was given at 1,000 mg/m(2) intravenously weekly x 7 for 8 weeks, then weekly x 3 every 4 weeks; a total of 688 patients were enrolled
  - The median overall survival for the experimental arm was 6.4 vs 6.1 months for the control arm (P =.75). Neutropenia and thrombocytopenia grade > 3 were observed in 40% and 15% in the experimental arm patients versus 30% and 12% in the control arm[2]
- Results were presented at ASCO GI 2019

Gualberto et al. ASCO GI 2019 #275 | [1] Samarendra *et al*. 2017 *Br J Cancer*. Jun 27;117(1):124-135 |
[2] Van Cutsem *et al*. 2004. *J Clin Oncol*. Apr 15;22(8):1430-8

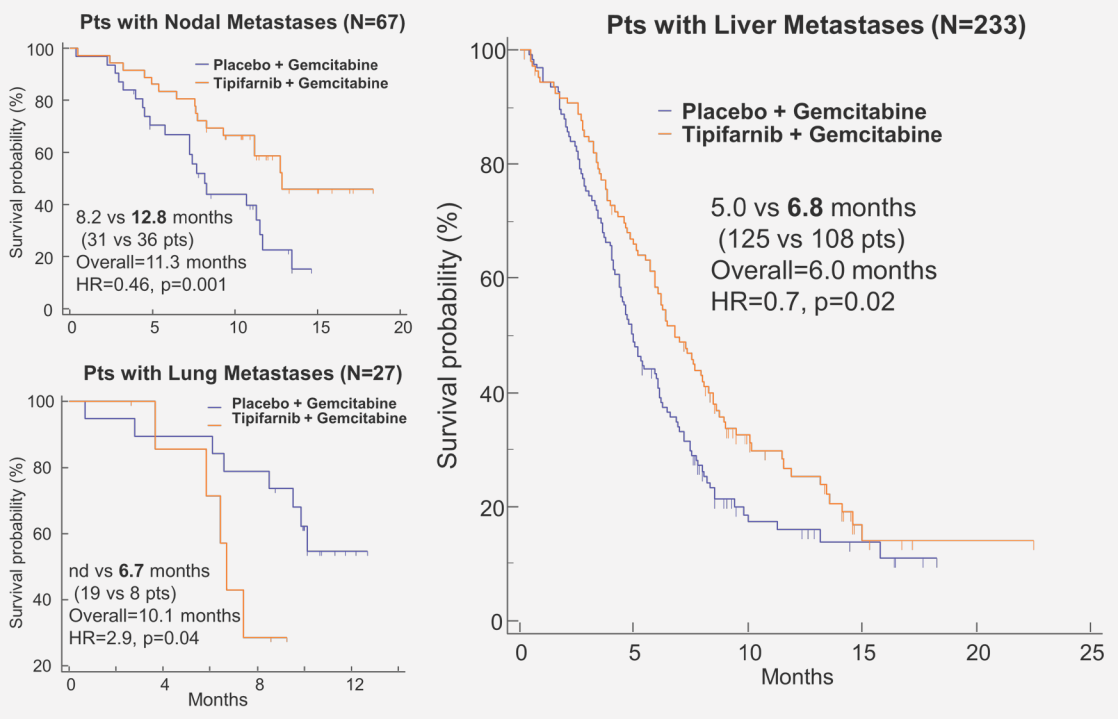
Association between CXCL12 Expression and Clinical Benefit in Pancreatic Cancer

Disease Model for CXCL12 Expressing Sites



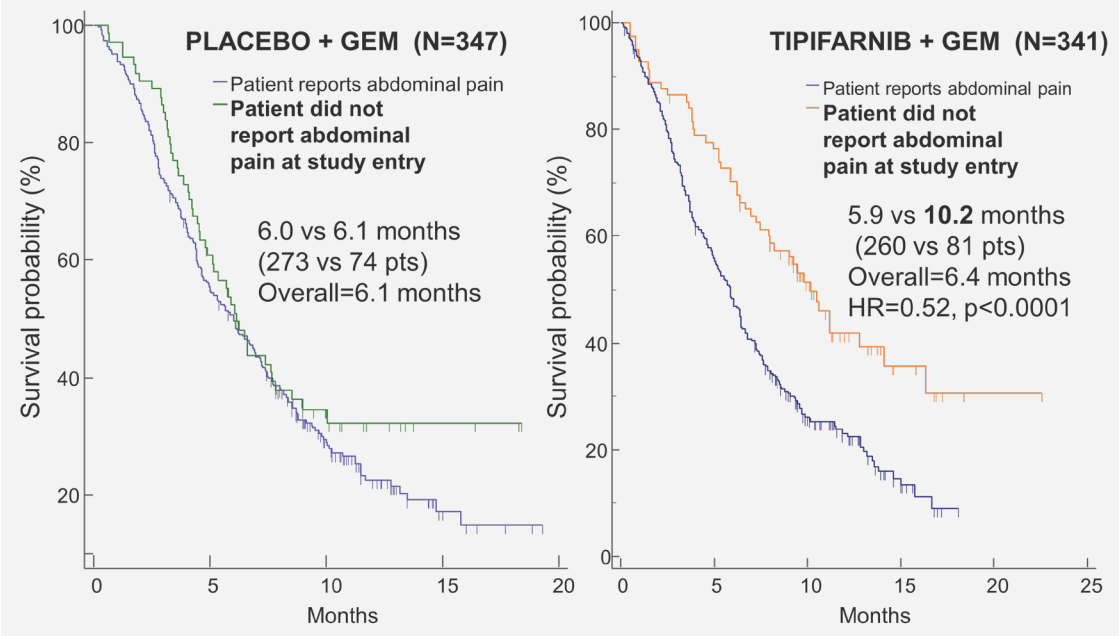
- CXCL12/IGF1 induce tumor homing to liver and lymph nodes[1]
- Lymph nodes and regional para-tumor vessels produce high levels of CXCL12, IGF1

Nodal and Liver Metastases Associated with Clinical Benefit from Tipifarnib

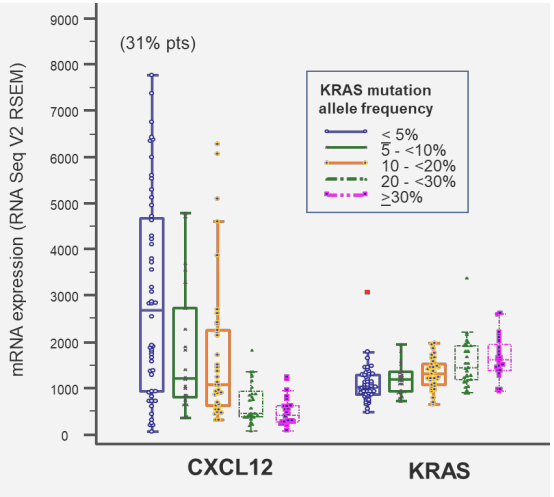


Potential Predictive Value of Absence of Abdominal Pain and Low KRAS mutation

Subset analysis of study INT-11 survival based on expected association between high CXCL12 expression and attenuation of abdominal pain



High CXCL12 Expression in Pancreatic Tumors with ≤ 5% KRAS Mutant Allele Frequency



- Absence of abdominal pain may be a surrogate of tipifarnib activity. High CXCL12 expression attracts CXCR7 expressing Schwann cells resulting in attenuated cancer-associated pain[1]

Gualberto *et al*. ASCO GI 2019 #275 | Gene expression data from TCGA, Provisional

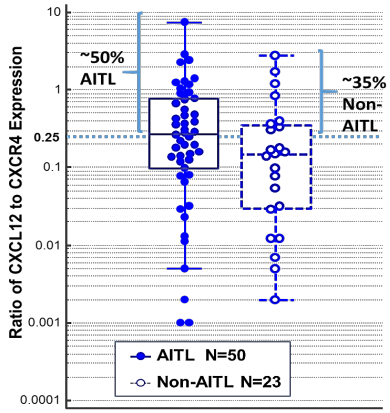
[1] Demir *et al*. 2017 *Proc Natl Acad Sci*. Jan 3;114(1):E85-E94

02d • *Tipifarnib Using CXCL12 Pathway Biomarkers: Opportunity*

CXCL12-High Populations Represented in Indications with High Unmet Need

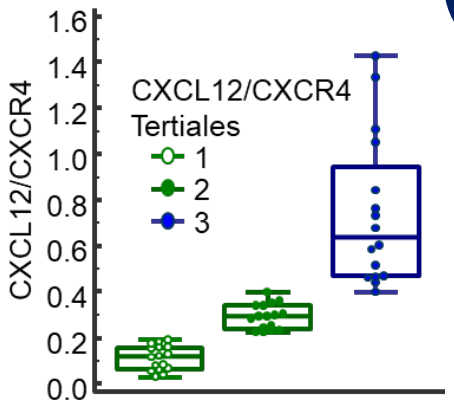
PTCL / AITL[1]

~40%



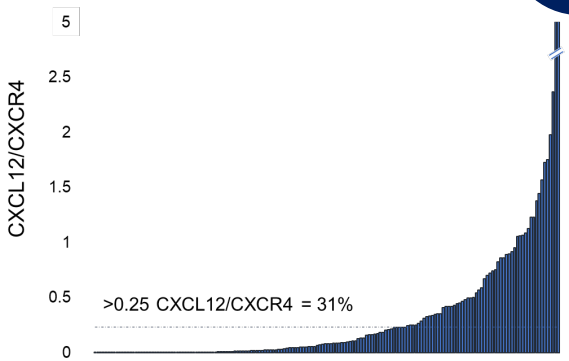
DLBCL[2]

~33%



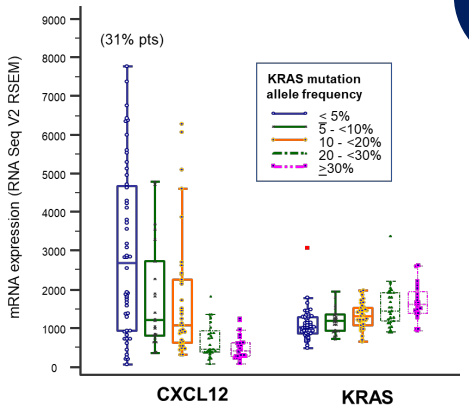
AML[3]

~30%



PANCREATIC[4]

~30%



[1] Witzig ASH 2018 #2937 | [2] Kura Oncology ASH 2018 Data Review | [3] Gualberto ASH 2017 #3957 | [4] Gualberto AACR 2019 #CT191

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CXCL12-Driven Indications

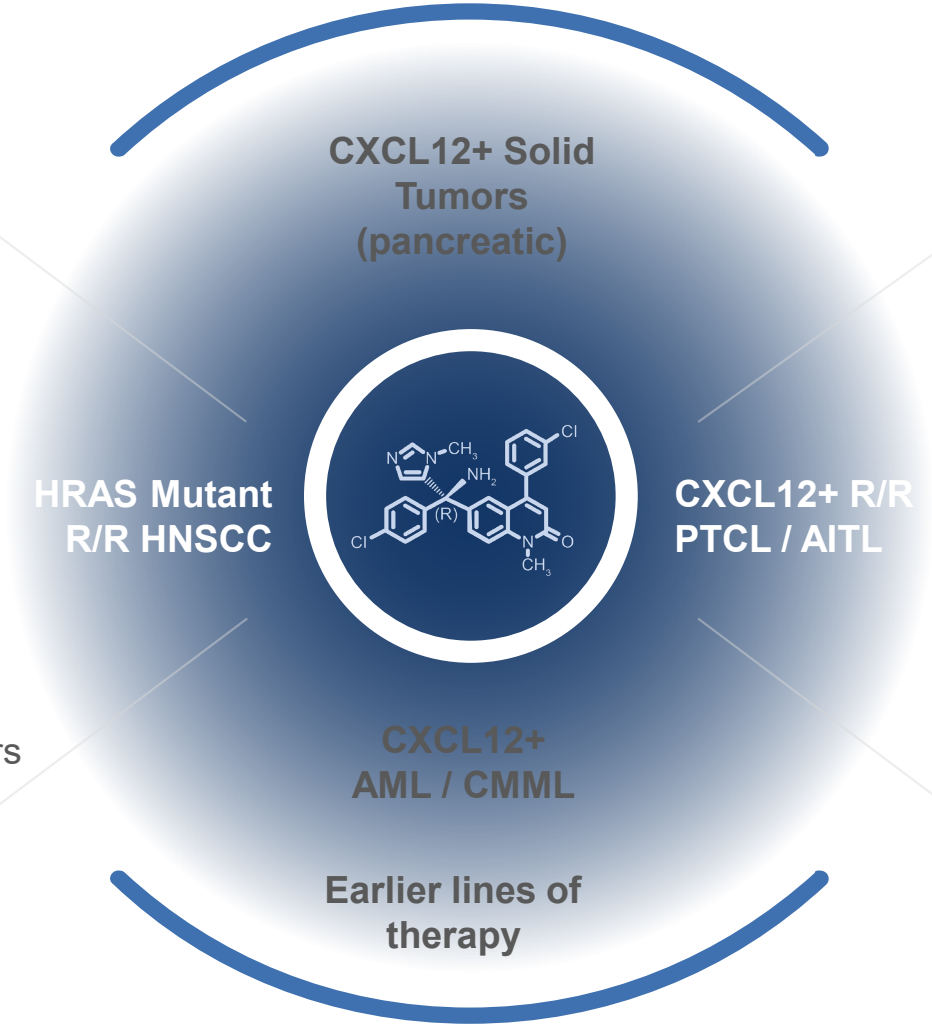
Indication	Est. Annual U.S. Incidence*
Lymphoma	
Diffuse Large B-Cell Lymphoma (DLBCL)	27,650[1]
Peripheral T-Cell Lymphoma (PTCL) / Angioimmunoblastic T-cell Lymphoma (AITL)	3,950[1]
Cutaneous T-Cell Lymphoma (CTCL) / Mycosis Fungoides	1,690[1]
Myeloid Neoplasia	
Acute Myeloid Leukemia (AML)	21,450[2]
Chronic Myelomonocytic Leukemia (CMML)	1,100[2]
Solid Tumor	
Pancreatic Cancer	56,770[2]

* Not adjusted for CXCL12-high subset | [1] Teras *et al*. 2016 *CA Cancer J Clin*. Nov 12;66(6):443-459 | [2] American Cancer Society

Cornerstone Proof-of-Concepts Support Expansion to Additional Indications

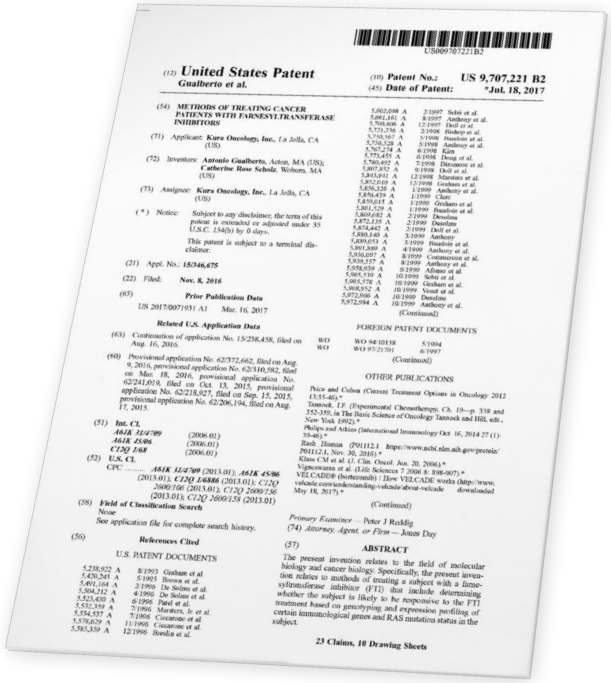
Tipifarnib

Farnesyl transferase (FT) inhibitor



Biomarker Strategies Enlarge Patent Estate for Therapeutic Uses of Tipifarnib

- U.S. patent 9,707,221 issued in July 2017 provides exclusivity for tipifarnib in **HRAS mutant HNSCC indication to 2036**
- Corresponding patents beginning to issue in foreign countries
- U.S. patent 9,956,215 issued in May 2018 provides exclusivity for tipifarnib in certain **CXCL12-expressing cancers to 2037**
- U.S. patent 10,137,121 issued in November 2018 provided exclusivity for tipifarnib **in AITL to 2037**
- Additional patent applications pending in the U.S. and foreign countries for tipifarnib in other biomarkers and disease indications
- Patents illustrate potential of broader strategy to generate intellectual property related to use of drug candidates in biomarker-defined populations



US009707221B2

(12) **United States Patent**
Gualberto et al.

(10) **Patent No.: US 9,707,221 B2**
(45) **Date of Patent: *Jul. 18, 2017**

(54) **METHODS OF TREATING CANCER PATIENTS WITH FARNESYLTRANSFERASE INHIBITORS**

(71) Applicant: **Kura Oncology, Inc.**, La Jolla, CA (US)

(72) Inventors: **Antonio Gualberto**, Acton, MA (US); **Catherine Rose Scholz**, Woburn, MA (US)

(73) Assignee: **Kura Oncology, Inc.**, La Jolla, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/346,675**

(22) Filed: **Nov. 8, 2016**

(65) **Prior Publication Data**

US 2017/0071931 A1 Mar. 16, 2017

Related U.S. Application Data

(63) Continuation of application No. 15/238,458, filed on Aug. 16, 2016.

(60) Provisional application No. 62/372,662, filed on Aug. 9, 2016, provisional application No. 62/340,582, filed on Mar. 18, 2016, provisional application No. 62/241,019, filed on Oct. 13, 2015, provisional application No. 62/218,927, filed on Sep. 15, 2015, provisional application No. 62/206,194, filed on Aug. 17, 2015.

(51) **Int. Cl.**
A61K 31/47/09 (2006.01)
A61K 45/06 (2006.01)
C12Q 1/68 (2006.01)

(52) **U.S. Cl.**
CPC ***A61K 31/47/09*** (2013.01); ***A61K 45/06*** (2013.01); ***C12Q 1/6886*** (2013.01); *C12Q 2600/106* (2013.01); *C12Q 2600/156* (2013.01); *C12Q 2600/158* (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

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VELCADE (bortezomib) | How VELCADE works (http://www.velcade.com/understanding-velcade/about-velcade downloaded May 18, 2017) *

(Continued)

Primary Examiner — Peter J Reddig
(74) *Attorney, Agent, or Firm* — Jones Day

(57) **ABSTRACT**

The present invention relates to the field of molecular biology and cancer biology. Specifically, the present invention relates to methods of treating a subject with a farnesyltransferase inhibitor (FTI) that include determining whether the subject is likely to be responsive to the FTI treatment based on genotyping and expression profiling of certain immunological genes and RAS mutation status in the subject.

23 Claims, 10 Drawing Sheets

03 • *KO-947 (ERK Inhibitor)*

KO-947: Potent Inhibitor of ERK1/2

- **Summary**
  - Potent, selective small molecule inhibitor of ERK1/2
  - Demonstrates prolonged pathway modulation in preclinical tumor models
  - Multiple tumors, including SCCs and KRAS mutant adenocarcinomas, identified as sensitive to KO-947 as monotherapy in preclinical models
  - Mechanism-based and SOC combinations under evaluation

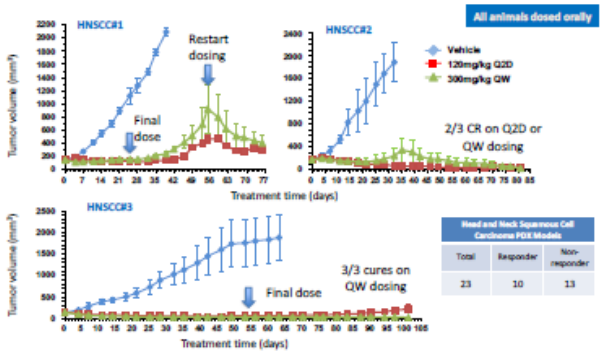
KO-947

ERK inhibitor

- **Clinical Development and Status**
  - Unique pharmacology enables intermittent dosing schedules
  - Potential biomarkers, including 11q13 amplifications in SCCs, for sensitive subsets have been identified
  - Phase 1 dose-escalation trial ongoing
  - Initial Phase 1 clinical data anticipated in 2019

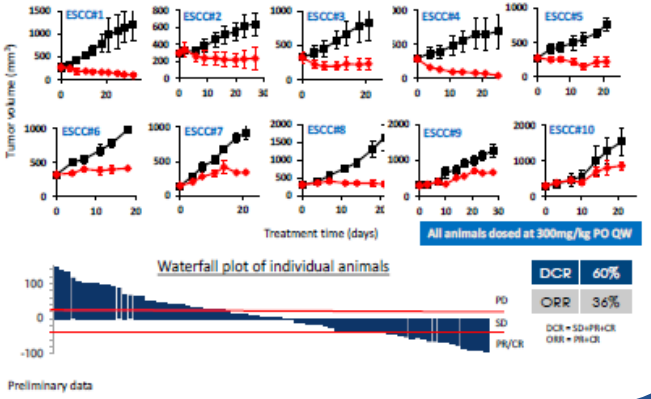
KO-947 Demonstrates Robust Single-Agent Activity in Preclinical Studies

KO-947 induces complete responses and regressions of large tumors in head and neck squamous cell carcinoma



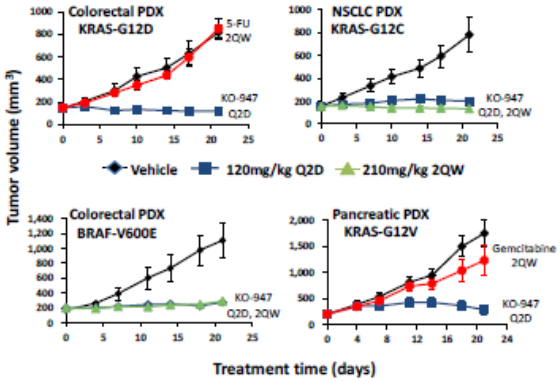
Head and Neck Squamous Cell Carcinoma PDX Models		
Total	Responder	Non-responder
23	10	13

KO-947 is highly active in PDX models of esophageal squamous cell carcinoma



DCR	60%
ORR	36%

KO-947 is active in a subset of KRAS- or BRAF-mutant colon, lung and pancreatic PDX models



Burrows *et al*. AACR 2017 #5168/11

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04 • *KO-539 (Menin-MLL Inhibitor)*

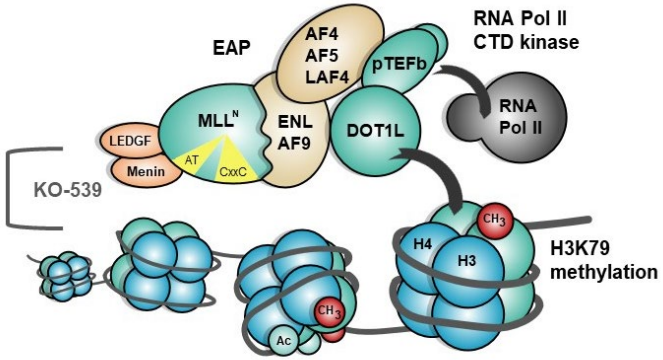
KO-539: Potent Inhibitor of Menin-MLL Interaction

- **Summary**
  - Potent, selective small molecule inhibitor of the menin-MLL interaction
  - Robust antitumor activity observed in mixed lineage leukemias rearranged (MLL-r) as well as disseminated NPM1mut and DNMT3Amut AML PDX models
  - Preliminary data suggests anti-leukemic activity by induction of myeloid differentiation in AML blasts
  - **Menin-MLL inhibitors have the potential to treat approximately 50% of acute leukemias**

KO-539

Menin-MLL inhibitor

- **Status**
  - IND application cleared in Q1 2019
  - Initiation of Phase 1 study anticipated in mid-2019

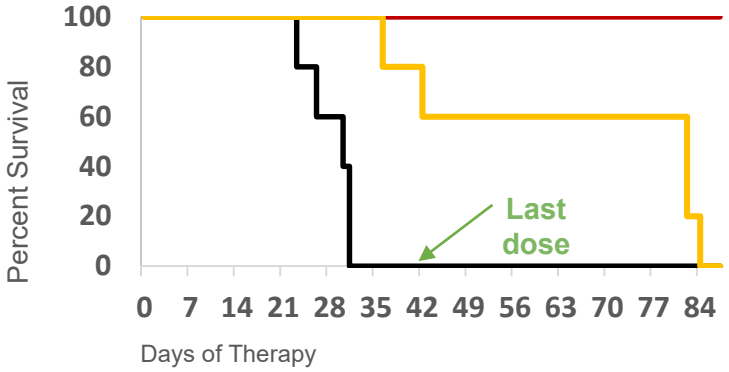


The menin-MLL complex appears to be a central node in epigenetic dysregulation driven by several distinct oncogenic driver mutations important in diverse leukemias and myeloproliferative disorders

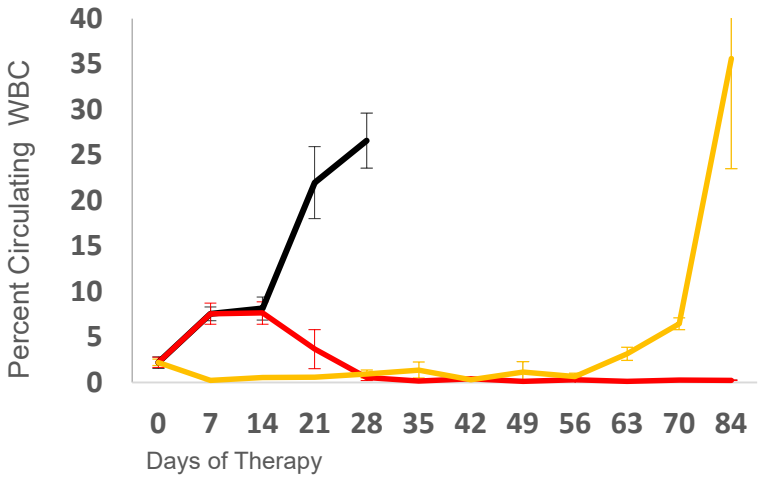
KO-539 Produces Lasting Complete Remissions in a NPM1/DNMT3A/IDH2/FLT3-Mutant AML Model

AM7577 Model

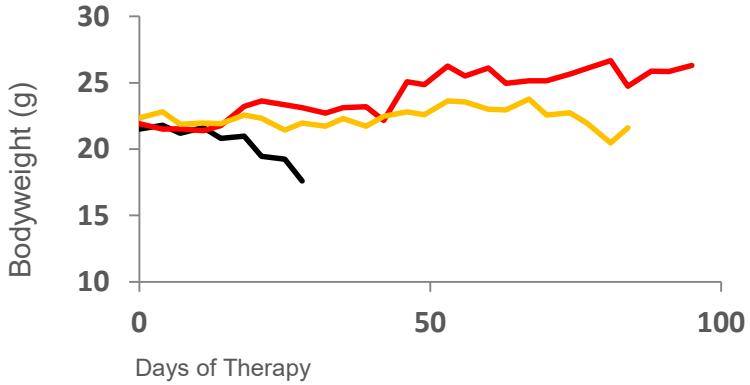
Overall survival



CD45+ human AML blasts



Tolerability



Vehicle

KO-539 100 mg/kg QD

Quizartinib 3 mg/kg QD

Burrows *et al*. AACR-NCI-EORTC 2017 LB-A27

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Anticipated Milestones & Financial Highlights

Program		Milestones	Status
Tipifarnib Farnesyl Transferase Inhibitor	HRAS Mutant Indications	Initiation of registration-direct1ed trial in HNSCC	✓
		Additional data from Phase 2 trial in HNSCC and other SCCs	2H 2019
	CXCL12 Pathway Indications	Patents for tipifarnib in AITL and CXCL12+ PTCL/AML	✓
		Proof-of-concept in AITL	✓
		Additional data from Phase 2 trial in CXCL12+ PTCL	June 2019
		Additional data from Phase 2 trial in CMML	2019
KO-947 ERK Inhibitor		Potential biomarker of activity in squamous cell carcinomas	✓
		Data from Phase 1 dose-escalation trial	2019
KO-539 Menin-MLL Inhibitor		FDA clearance of IND application	✓
		Initiation of Phase 1 trial	Mid-2019

Financial Highlights	
	Nasdaq: KURA
	Shares outstanding: 38.2M basic, 4.3M options*
	Cash, cash equivalents and short-term investments: $165.5M*

* As of March 31, 2019

KURA ONCOLOGY

Developing Precision Medicines for the Treatment of Cancer