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# Chronic Myeloid Leukemia Webinar

NASDAQ: TERN

**July 25, 2023**

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# Opening Remarks

**Erin Quirk, M.D.,** President & Head of R&D Terns

# Terns Pipeline: Rational Drug Design to Improve on Validated MoAs

| 3 Clinically Validated Mechanisms | 3 Indications with Unmet Need |
|---|---|
| **1** **TERN-701: Allosteric BCR-ABL inhibitor**<br>• U.S. Ph 1 initiation in 2H23; interim top-line readouts from initial cohorts in 2024 | **Chronic Myeloid Leukemia**<br>• Orphan indication supporting ~$5B market[1] across multiple similar active-site TKIs |
| **2** **TERN-501: THR-β agonist**<br>• DUET top-line data expected in 3Q23; primary endpoint of MRI-PDFF at week 12 for 501 vs. pbo | **NASH**<br>• No approved drugs to date<br>• Potentially differentiated CV / GI profile versus peer THR-β molecules[2] |
| **3** **TERN-601: Oral/small-molecule GLP-1RA**<br>• Ph 1 obesity trial initiation in 2H23, QD dosing to assess weight loss and PK; initial data in 2024 | **Obesity**<br>• ~$30B market[3] limited by supply / cost of peptides<br>• Oral drugs expected to expand market access potential |

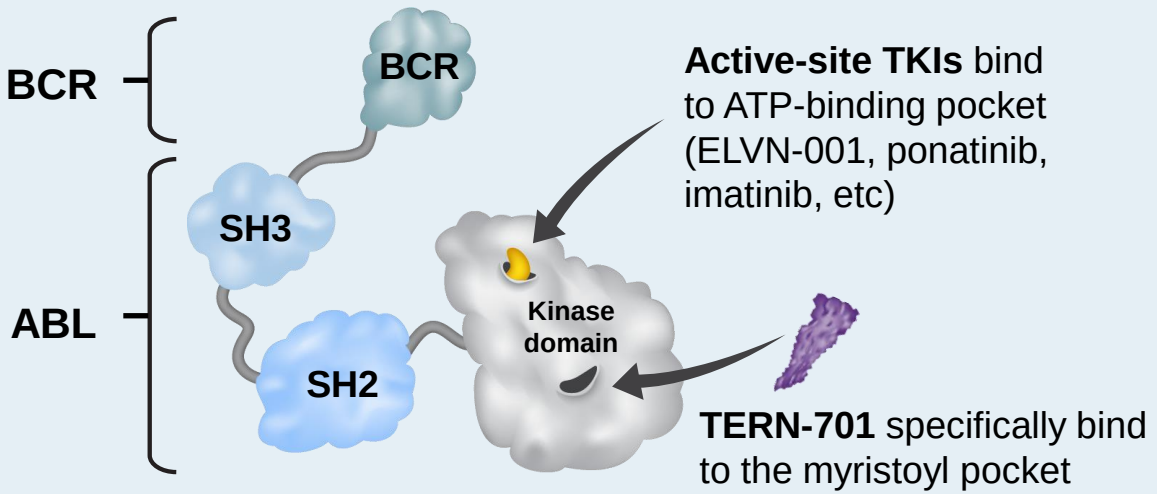
**3 Key Characteristics**

- **Oral administration**
- **Small-molecule**
- **Internally-discovered**

1. Factset estimates for 2023E; 2. Based on publicly available data; comparisons were not done on a head-to-head basis and includes cross-trial and/or cross-phase comparisons; 3. EvaluatePharma 2026E consensus estimates

# TERN-701: Terns' Allosteric TKI for CML

**Active BCR-ABL1 ➔ Cell proliferation / reduced apoptosis**




**Inactive BCR-ABL1 ➔ Cell death**

- CML is an **orphan indication** with **sizeable market ($5B+)** and a need for **multiple agents**
- **Frequent switching** occurs between TKIs, most commonly due to intolerance
- **Allosteric** BCR-ABL TKIs have significant (~2x) efficacy improvement over older standard-of-care active-site inhibitors and are better tolerated
- 1st approved allosteric TKI, asciminib, expected to be a **blockbuster in 3L CML** and is being developed for 1L
- TERN-701 is an **internally-developed allosteric** TKI with an expected profile ≥ asciminib
- Phase 1 trial in CML patients initiated by Hansoh in 2Q 2022 in China; **Terns' Phase 1 clinical trial initiation targeted in 2H 2023**

Note: 1L: 1st line; 3L: 3rd line; TKI: tyrosine kinase inhibitor
Source: Réa et al Blood 2021, NVS 2Q 2022 Earnings, Factset estimates

# Experienced Leadership Team with Deep Industry Expertise

- Emil Kuriakose, M.D. joined in May 2023 as chief medical officer of Terns oncology. Dr. Kuriakose; 10+ years of drug development
- Previously chief medical officer at Calithera Biosciences, led the transition of two mid-stage clinical programs with subsequent rapid initiation of two phase 2 studies.
- Previously, Dr. Kuriakose served as global clinical program lead at Novartis Institutes for BioMedical Research (NIBR),
- Fellow at Weill Cornell Medical College, and as a research fellow at Memorial Sloan Kettering Cancer Center
- Dr. Kuriakose earned an M.D. from SUNY Stony Brook University School of Medicine and a B.S. in Neuroscience from New York University.

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# Agenda & KOL Introductions

**Emil Kuriakose, M.D.,** CMO, Oncology

# Agenda

| | |
|---|---|
| • KOL Introduction | Emil Kuriakose, M.D., CMO, Oncology |
| • Chronic Myeloid Leukemia Overview | Jorge Cortes, M.D., Georgia Cancer Center |
| • Fireside Chat: Allosteric vs. Active-Site TKIs | Michael Mauro, M.D., MSKCC & Emil Kuriakose, M.D. |
| • TERN-701 Overview / Update | Emil Kuriakose, M.D. |
| • Q&A | Sen Sundaram, CEO, Erin Quirk, M.D., Emil Kuriakose, M.D. & Jorge Cortes, M.D. |

# KOL Bios

**Jorge Cortes, M.D.**
Director, Georgia Cancer Center
Cecil F. Whitaker Jr. GRA Eminent Scholar Chair in Cancer
Augusta University

- Prior to joining Augusta University, Dr. Cortes was at The University of Texas MD Anderson Cancer Center where he held numerous roles including Deputy Department Chair of the Leukemia department, Chair of AML and CML Sections, Deputy Division Chair for MDACC Network.
- His clinical interest focuses on new drug development and the management of patients with MDS, acute and chronic leukemias, and MPNs and has authored more than 1,000 peer-review original research manuscripts.
- Dr. Cortes has over 230 grants and contracts where he was principal investigator and has led the approval of 4 drugs currently available for patients with leukemia.

**Michael Mauro, M.D.**
Leader, Myeloproliferative Neoplasms Program, Leukemia Service
Memorial Sloan Kettering Cancer Center

- Before joining MSK, Dr. Mauro was on the faculty of Oregon Health and Sciences University for 13 years.
- There he directed the CML clinical trial program and was involved in the early development and sentinel clinical study of targeted therapy for CML from imatinib (Gleevec) onwards.
- Dr. Mauro's clinical expertise is in treating patients with CML as well as other myeloproliferative disorders with a focus in therapy optimization, novel therapies, treatment free remission and pregnancy/fertility.

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# Chronic Myeloid Leukemia Overview

**Jorge Cortes, M.D.**, Georgia Cancer Center

# Updates in CML Management

Jorge Cortes, MD
Director, Georgia Cancer Center

GEORGIA CANCER CENTER
AUGUSTA UNIVERSITY

# Disclosure Information

- **Grant or research support (to my institution) from *BMS, Novartis, Pfizer, Sun Pharma, Takeda***
- **Paid Consultant for *Novartis, Pfizer, Sun Pharma, Takeda, Terns***

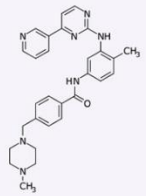
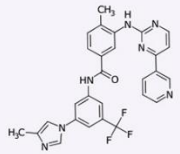
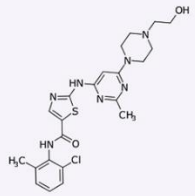
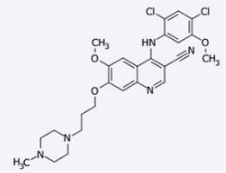
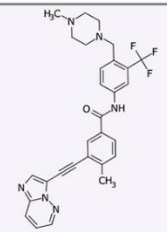
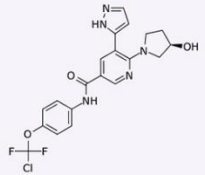
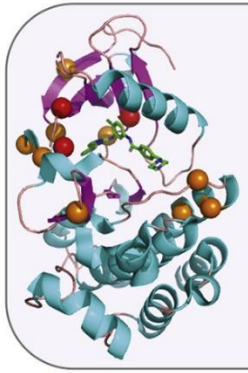
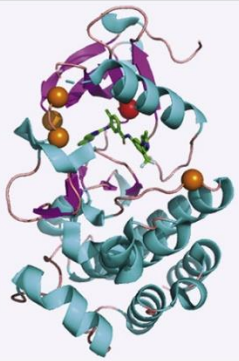
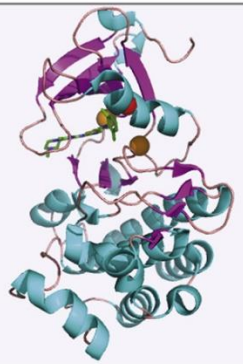
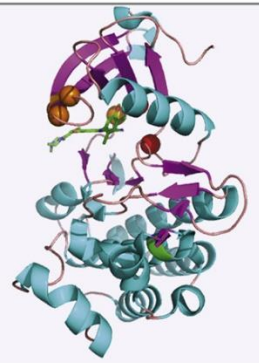
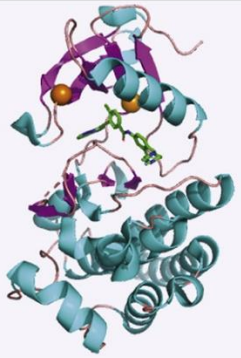
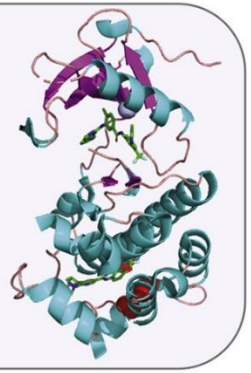
# CML: The Current Status

- Six TKI approved
- High rates of response
- Low rates of transformation
- Near-normal life expectancy
- TFR: a reality in standard practice

# However…

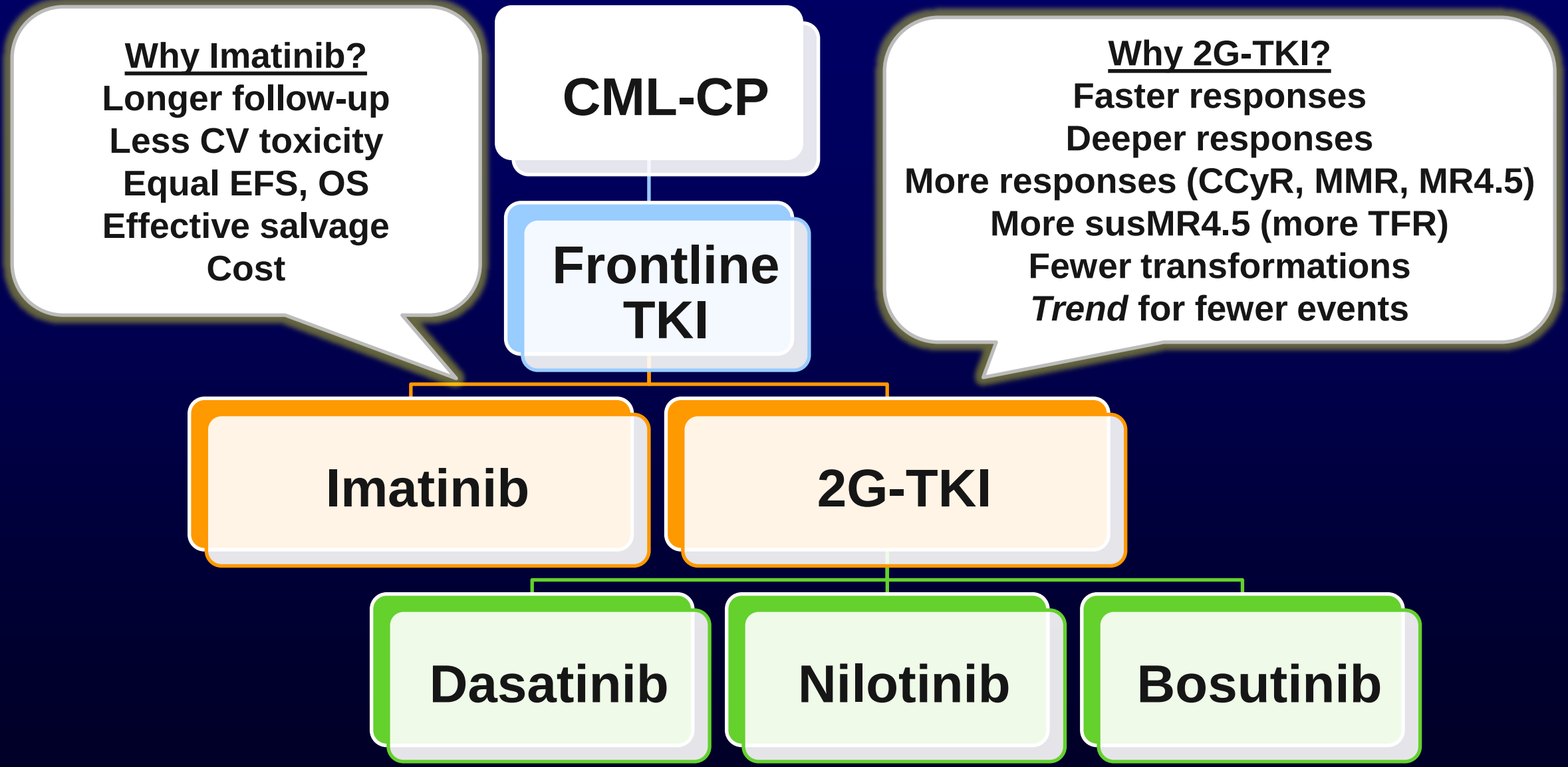
- ~40% change therapy by 5 yrs
- ~60% achieve MR4.5 by 10 yrs
- ~50% have sustained MR4.5 by 10 yrs
- ~50% resume therapy after TFR
- CCyR with 2GTKI ~40% after imatinib resistance
- 2nd line TKI discontinuation ~50-80% by 2 yrs
- 3rd line TKI *BCR::ABL1* <1% ~45%
- 3rd line TKI discontinuation ~40-50% by 2 yrs
- Arterio-occlusive events with most TKI

# BCR-ABL1 Tyrosine Kinase Inhibitors

| Inhibitor | Imatinib | Nilotinib | Dasatinib | Bosutinib | Ponatinib | Asciminib |
|---|---|---|---|---|---|---|
| Chemical Structure |  |  |  |  |  |  |
| Crystal Structure |  |  |  |  |  |  |
| Binding Conformation | Inactive | Inactive | Active | Both | Inactive | Myristoyl Pocket |
| Resistance | Y253 Q252<br>E255 F317<br>T315 M351<br>M244 M355<br>L248 F359<br>G250 H396 | T315<br>L248<br>Y253<br>E255<br>F359 | T315<br>V299<br>F317 | T315<br>V299<br>L248<br>G250<br>E255<br>F317 | | A337<br>W464<br>P465<br>V468<br>I502 |

Modified from Braun et al. Cancer Cell 2020; 37: 530-42

# Selecting Frontline TKI



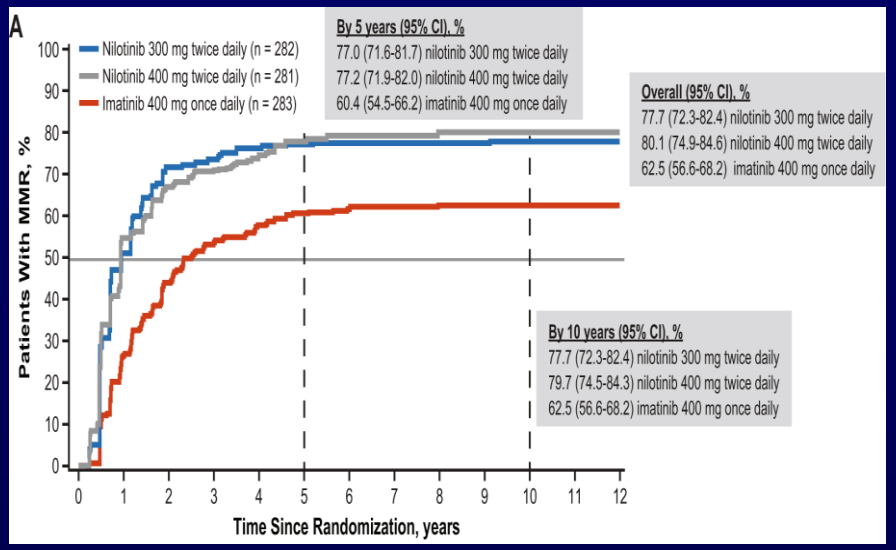
# Outcome Across 1st Line CML Studies

| response at, % | DASISION | | ENESTnd | | BFORE | | TOPS | |
|---|---|---|---|---|---|---|---|---|
| | DAS 100 | IMA 400 | NIL 300 | IMA 400 | BOS 400 | IMA 400 | IMA 800 | IMA 400 |
| MMR 3m | 8 | 0.4 | 9 | 1 | 4.1 | 1.7 | 12 | 3 |
| MMR 12m | 46[a] | 28[a] | 44 | 22 | 47 | 37 | 47 | 40 |
| CCyR 12m | 77 | 66 | 80 | 65 | 77 | 66 | 70 | 66 |
| AP/BP | 2.3 | 5.0 | 1 | 6 | 2.2 | 2.6 | 1.9 | 3.2 |
| PFS | 94 | 92 | 96 | 94 | NR | NR | 97 | 94 |
| OS | 95.3 | 95.2 | 97 | 96 | 99 | 97 | 99 | 98 |

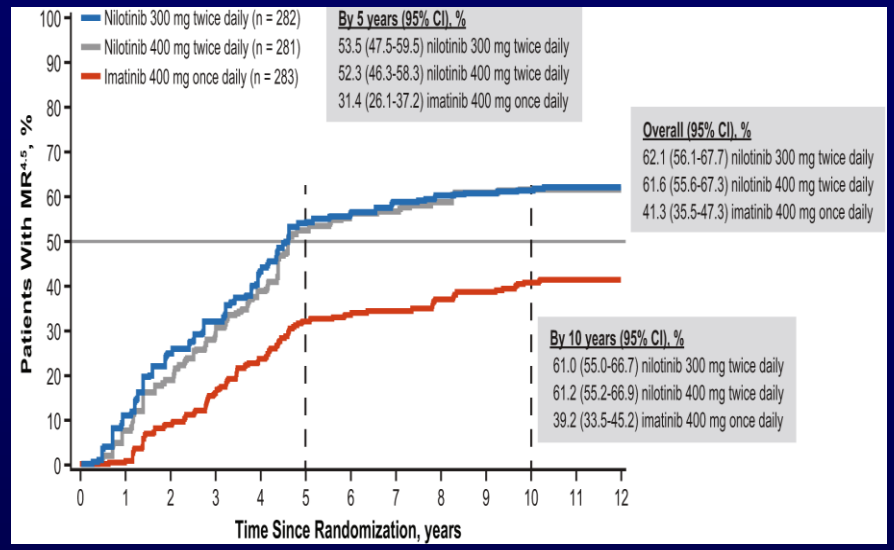
[a] MMR by 12 mo

# Cumulative Incidence of Molecular Response – ENESTnd 10-Yrs

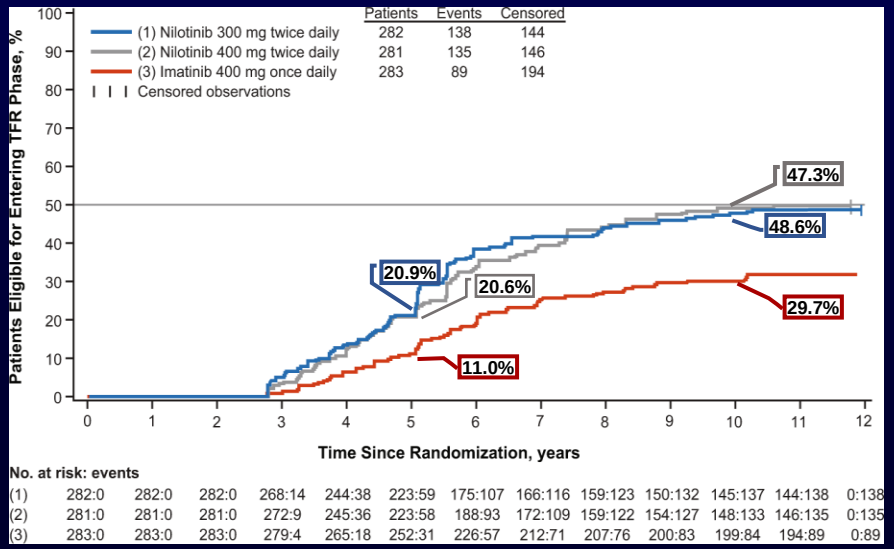
## Cumulative Incidence of MMR




## Cumulative Incidence of MR$^{4.5}$



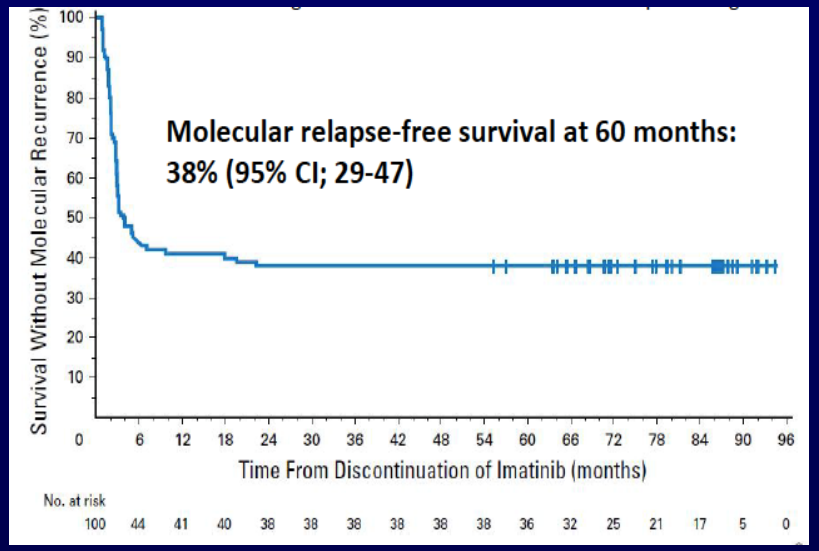

## Cumulative Incidence of sDMR



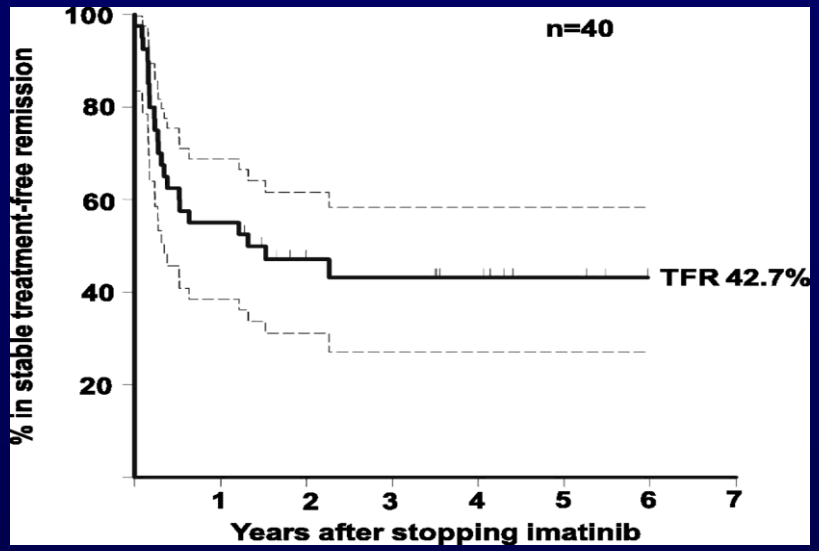

Kantarjian et al. Leukemia 2021; 35: 440-53

# Treatment-Free Remission

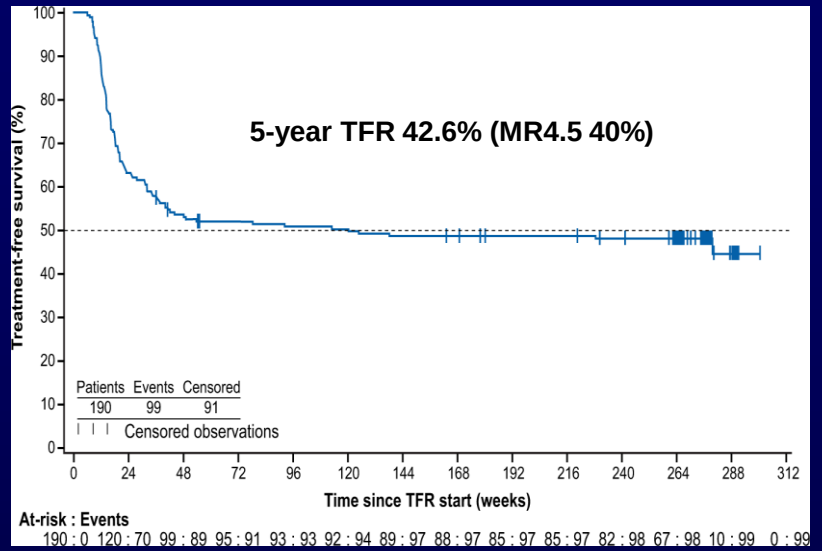
## STIM[1]



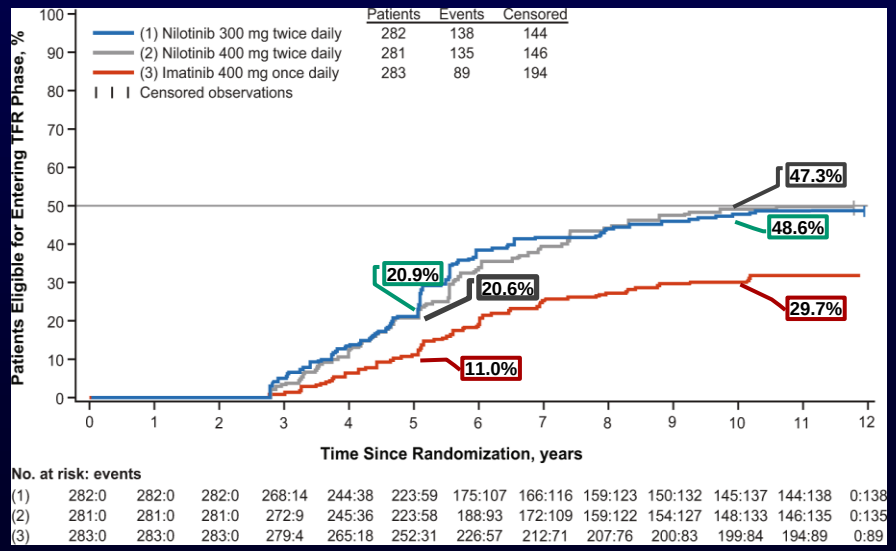

## TWISTER[2]




## ENESTfreedom[3]




## ENESTnd[4]




## BFORE[5]

- 2-year sustained MR4: bosutinib 32.5% vs imatinib 26.5% (OR 1.33 [95% CI, 0.92, 1.93])

**~47% eligible**
**X**
**~60% TFR**
**~28% Success**

[1]Etienne et al. JCO 2017; 35: 298-305; [2]Ross et al. Blood 2013; 122: 515-22; [3]Radich et al. Leukemia 2021; 35: 1344-55; [4]Kantarjian et al. Leukemia 2021; 35: 440-53; [5]Brümmendorf TH, et al. *Blood.* 2020;136(Suppl 1): Abstract 46

# Treatment Discontinuation by TKI

| | DASISION | | ENESTnd | | BFORE | |
|---|---|---|---|---|---|---|
| | Dasatinib | Imatinib | Nilotinib | Imatinib | Bosutinib | Imatinib |
| 2 yrs | 23 | 25 | 26 | 33 | 29 | 31 |
| Efficacy | 9 | 11 | 9 | 17 | 5 | 15 |
| Safety | 9 | 5 | 9 | 10 | 19 | 11 |
| 5 yrs | 39 | 37 | 39 | 50 | 40 | 42 |
| Efficacy | 11 | 14 | 13 | 25 | 6 | 18 |
| Safety | 21 | 9 | 12 | 14 | 25 | 13 |
| 10 yrs | - | - | 53[a] | 48[b] | - | - |
| Efficacy | - | - | 5[a] | 6[b] | - | - |
| Safety | - | - | 22 | 35 | - | - |

[a] 62% including those who switched to imatinib or increased to nilotinib 400 mg BID (14% for efficacy)
[b] 65% including those who switched to niltionib or increased imatinib dose (24% for efficacy)

Cortes et al. JCO 2016; 34: 2333-40; Hochhaus et al. Leukemia 2016; 30: 1044-54; Kantarjian et al. Blood 2012; 119: 1123-9;
Kantarjian et al. Lancet Oncology 2011; 12: 841-51; Cortes et al. J Clin Oncol 36, 2018 (suppl; abstr 7002); Brümmendorf et al. ASH 2020; abstract #46

# 2nd Generation TKI in CML CP Post-Imatinib Resistance

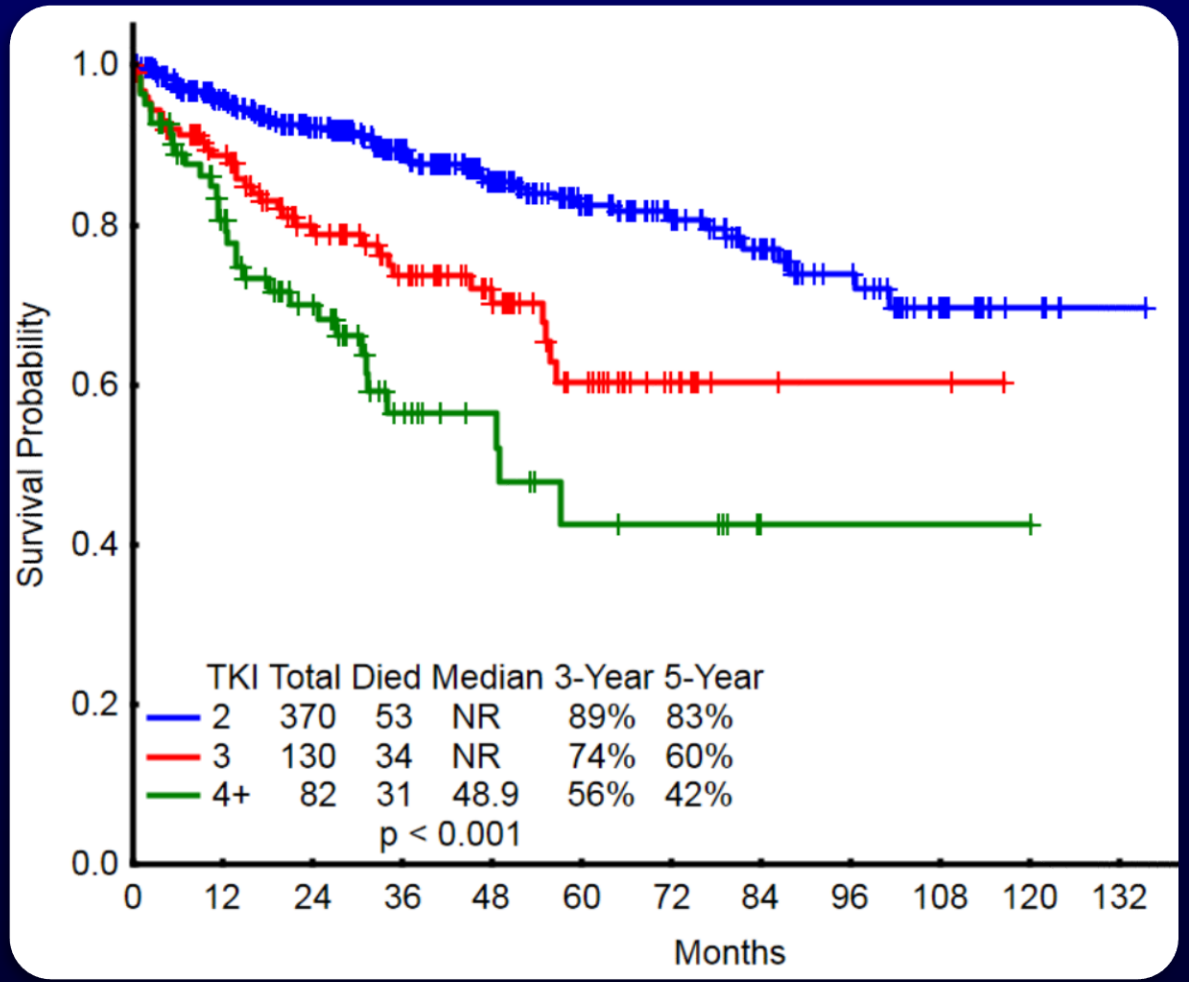
| Response | Percentage | | |
|---|---|---|---|
| | Dasatinib† | Nilotinib‡ | Bosutinib |
| FU (mo) | >24 | >24 | >24 |
| CHR | 89 | 77 | 85 |
| MCyR | 59 | 56 | 57 |
| CCyR | 44 | 41 | 41 |
| 24 mo PFS* | 80% | 64% | 79% |
| 24 mo OS* | 91% | 87% | 92% |

† 7-yr MMR 43%, PFS 42%, OS 65%; discontinued 78%
‡ 4-yr PFS 57%, OS 78%; discontinued 70%
* All patients (resistant + intolerant)

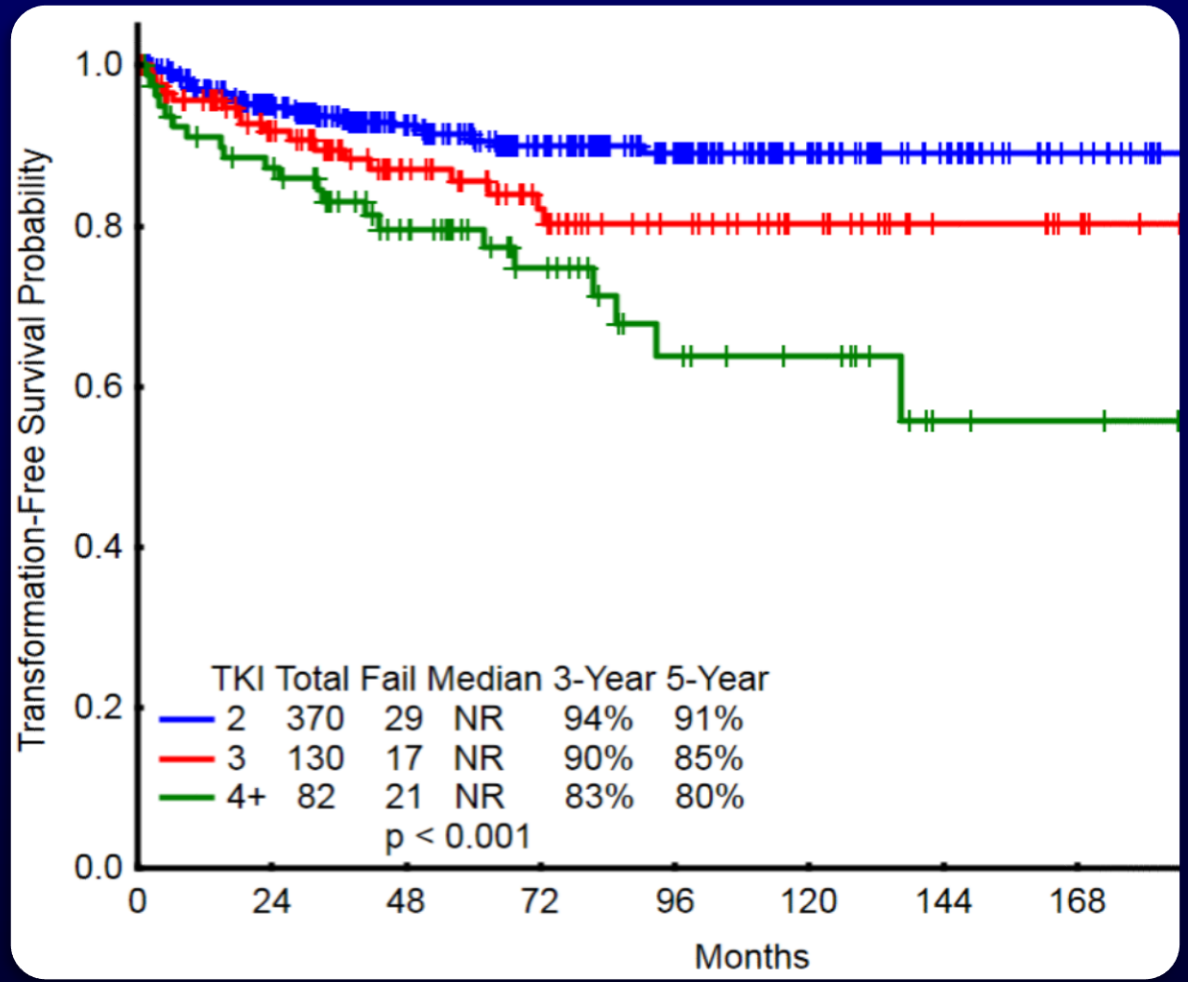
Shah et al. Haematologica 2010; 95: 232-40; Shah et al. Am J Hematol 2016; 91: 869-74
Kantarjian et al. Blood 2011; 117: 1141-45; Giles et al. Leukemia 2013; 27: 107-112
Cortes et al. Blood 2011; 118; 4567-76; Gambacorti-Passerini et al. Am J Hematol 2014; 89: 732-42

# Long-Term Outcome After Multiple TKI

## Overall Survival




## Transformation-Free Survival




Akosile et al. Blood 2015; 126: 1587

# 2G-TKI as 3rd-Line Treatment for CML-CP

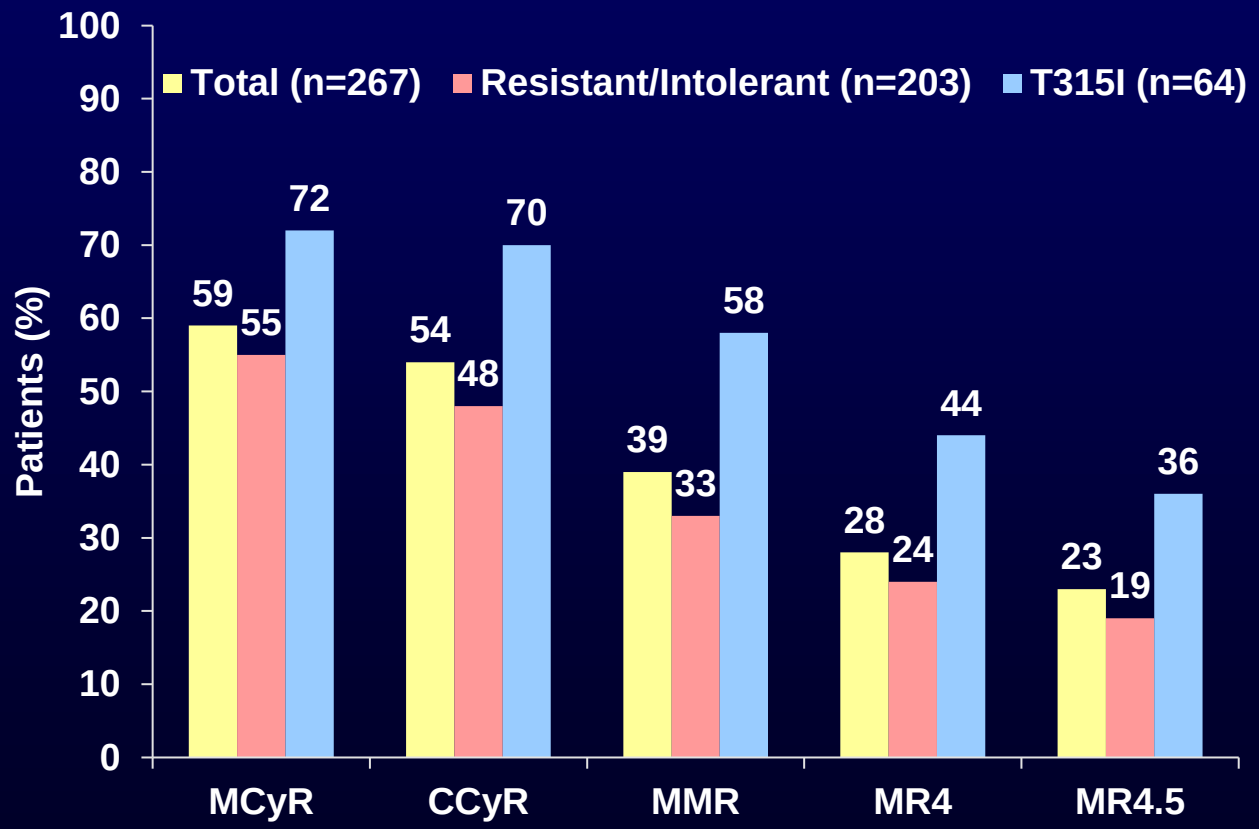
| Study | TKI (n) | CCyR | MMR | EFS/PFS/TTF | OS |
|---|---|---|---|---|---|
| Garg 2009 | Das (16) | 31 | 12 | Median FFS 20 m | Median 20 |
| | Nil (9) | 11 | 33 | | |
| Ribeiro 2015 | Das (5), Nil (13) | 13 | 24 | 5-y EFS 22%<br>5-y PFS 54% | 5-y 86% |
| Lomaia 2015 | Das (30), Nil (18), Bos (5) | 21 | NA | NA | 2-y 67% |
| Giles 2010 | Nil (39) | 24 | NA | Median TTF 19.5 m<br>18-m PFS 59% | 18-m 86% |
| Cortes 2011 | Any (29) | 24 | NA | NA | NA |
| Ibrahim 2010 | Das or Nil (26) | 35 | 19 | 30-m EFS 46% | 30-m OS 47% |
| Cortes 2016 | Bos (119) | 28 | 15 | 4-y progression or death 24% | 4-y OS 78% |
| Hochhaus 2019 | Bos (61) | 84 | 64 | NA | NA |

Modified from Hochhaus et al. Leukemia 2020; 34: 1495-1502

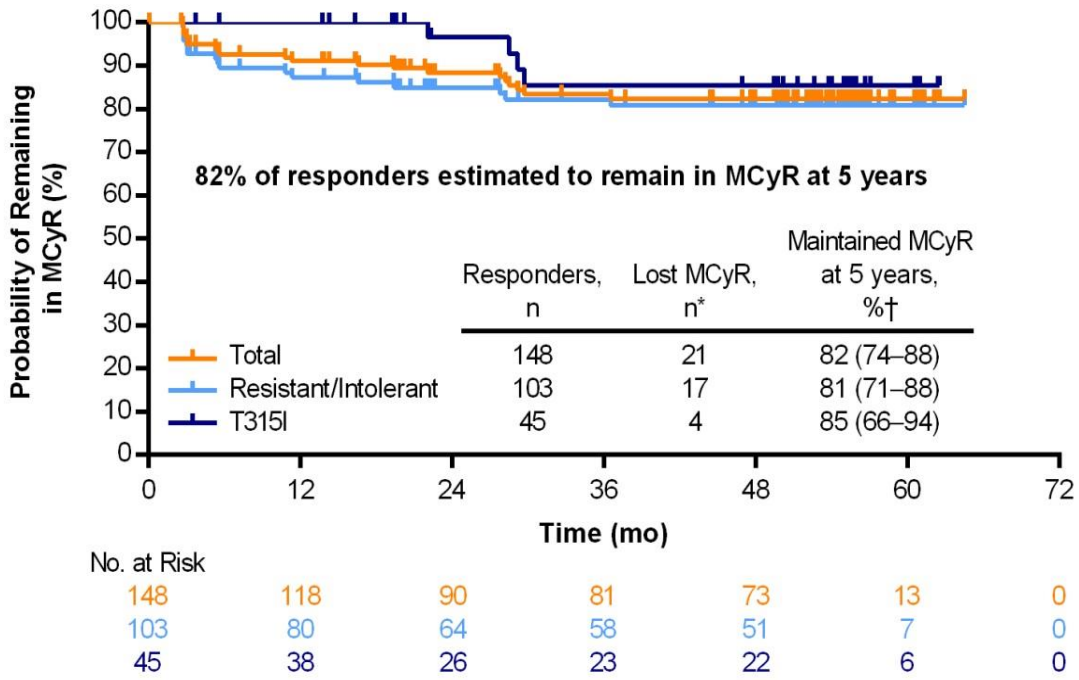
# Efficacy of Ponatinib in CP-CML

- **Median times to MCyR 2.8 (1.6–24.5) mo, CCyR 2.8 (1.6–35.7) mo, and MMR 5.5 (1.8–32.9) mo**

## Responses at Any Time




## Duration of MCyR




Cortes et al. Blood 2018; 132: 393-404

# Vascular Occlusive Events in Ponatinib Phase 2 Trial: 60-Month Final Report

| | CP-CML (n=270) | | Total (n=449) | |
|---|---|---|---|---|
| | AE | SAE | AE | SAE |
| Cumulative exposure, patient-years | 615.7 | | 826.0 | |
| AOEs, n (%) | 84 (31) | 69 (26) | 111 (25) | 90 (20) |
| Cardiovascular | 42 (16) | 33 (12) | 59 (13) | 44 (10) |
| Cerebrovascular | 35 (13) | 28 (10) | 41 (9) | 33 (7) |
| Peripheral vascular | 38 (14) | 31 (11) | 48 (11) | 38 (8) |
| Exposure-adjusted* incidence of ATEs | 14.1 | 10.9 | 13.8 | 10.6 |
| VTEs, n (%) | 15 (6) | 13 (5) | 27 (6) | 23 (5) |
| Exposure-adjusted* incidence of VTEs | 2.1 | 1.8 | 2.8 | 2.4 |

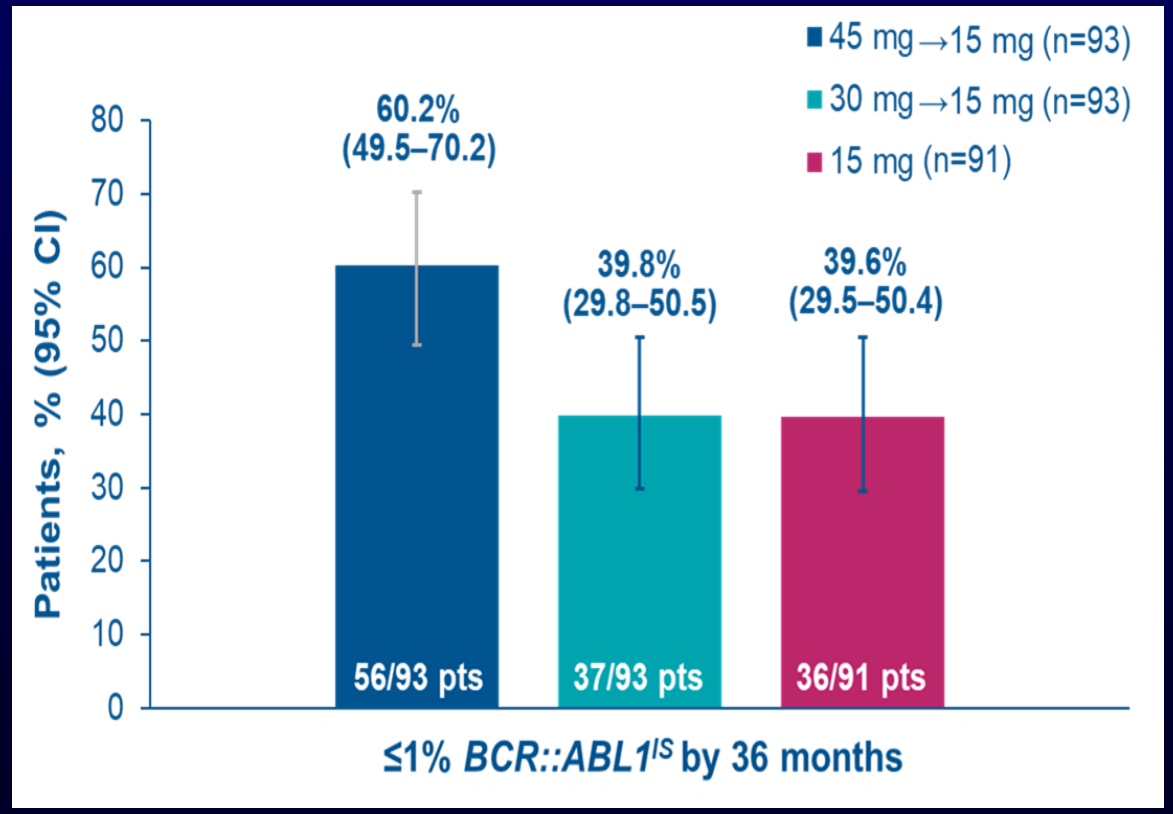
- Median (range) time to ATE onset in CP-CML: 14.1 (0.3-44.0) mo
- Median (range) time to VTE onset in CP-CML: 22.3 (2.0-40.2) mo
- 46 CML-CP and 57 overall had >1 AOE

*Number of patients with events per 100 patient-years.
Median follow-up time was 42.3 months.

Cortes et al. Blood 2018; 132: 393-404; Cortes JE, et al. EHA 2015; abstract P234

# Efficacy and Safety of Ponatinib: The OPTIC Approach

- CML-CP with resistance/intolerance to ≥2 TKI or with T315I
- Randomized to starting dose of 45, 30 or 15 mg
- Dose reduction to 15 mg after achievement of BCR-ABL1 ≤1%
- Prospective adjudication of AOEs by independent, blinded committee
- Primary endpoint BCR::ABL1 ≤1% at 12 Months:
  - 44.1% @ 45 mg, 29.0% @ 30 mg, 23.1% @ 15 mg ($p < 0.017$)



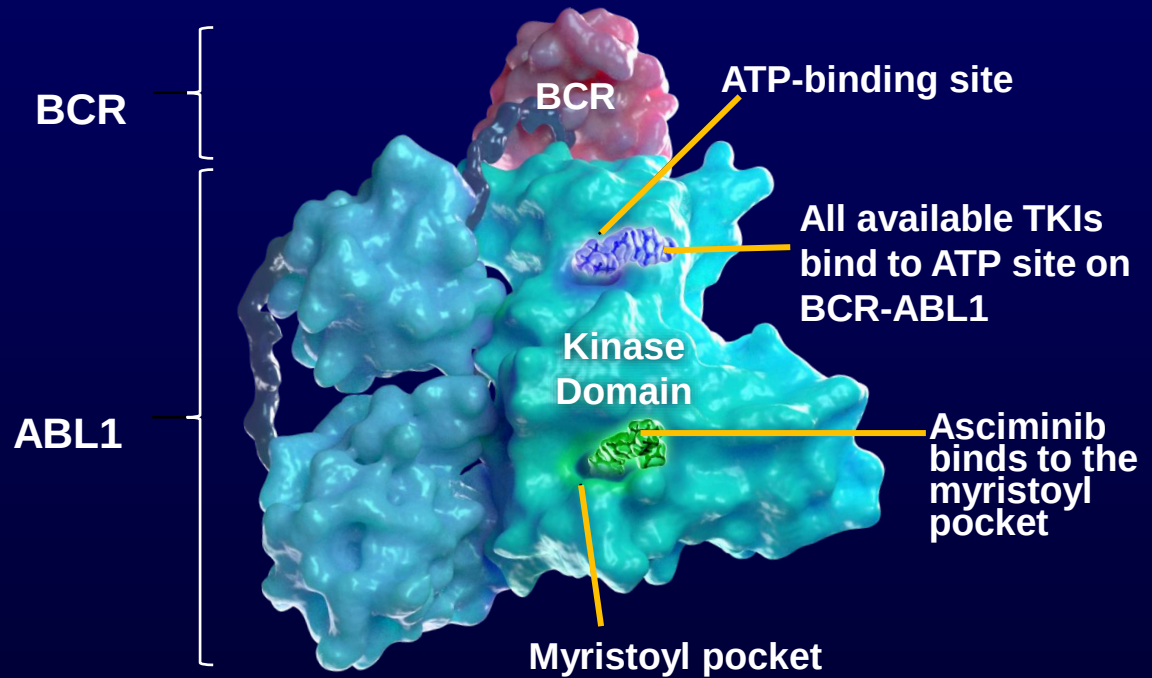

| | 45 mg → 15 mg (N=94) | 30 mg → 15 mg (N=94) | 15 mg (N=94) |
|---|---|---|---|
| **TE-AOEs — %** | | | |
| Any AOE | 12 | 6 | 4 |
| Grade ≥3 TE-AOEs | 6 | 6 | 4 |
| Exposure-adjusted rate (95% CI) | 4.5 (1.7–7.3) | 3.0 (0.6–5.5) | 1.9 (0.04–3.8) |
| **Dose modifications for AOE — n (%)** | | | |
| Discontinuation | 6 | 4 | 1 |
| Reduction | 0 | 2 | 0 |
| Interruption | 3 | 3 | 2 |

Cortes et al. Blood 2021; 138: 2042-50; Cortes et al. ASH 2022; abstract #620

# Asciminib
## *Background*

- T315I confers resistance to all approved ATP-competitive TKIs except ponatinib; compound mutations involving T315I can also confer resistance to ponatinib[a-c]
- Asciminib has a different mechanism of action from available TKIs.
  - First-in-class STAMP (Specifically Targeting the ABL1 Myristoyl Pocket) inhibitor[c-f]
  - Early results showed clinical activity and favorable safety profile in patients with T315I mutations[f,g]
  - Updated efficacy and safety results from the expansion cohort in patients with T315I-mutated CML treated with asciminib 200 mg twice daily

- Assembled Inactive Conformation[c]




a. Hochhaus A, et al. *Leukemia*. 2020;34:966-984. b. Byrgazov K, et al. *Haematologica*. 2018;103:e10-e12. c. Manley PW, et al. *Leuk Res*. 2020;98:106458. d. Wylie AA, et al. *Nature*. 2017;543:733-737. e. Schoepfer J, et al. *J Med Chem*. 2018;61:8120-8135. f. Hughes TP, et al. *N Engl J Med*. 2019;381:2315-2326. g. Rea D, et al. *Blood*. 2018;132(Suppl 1): Abstract 792.

# Phase 1 Asciminib – Response in R/R CML-CP

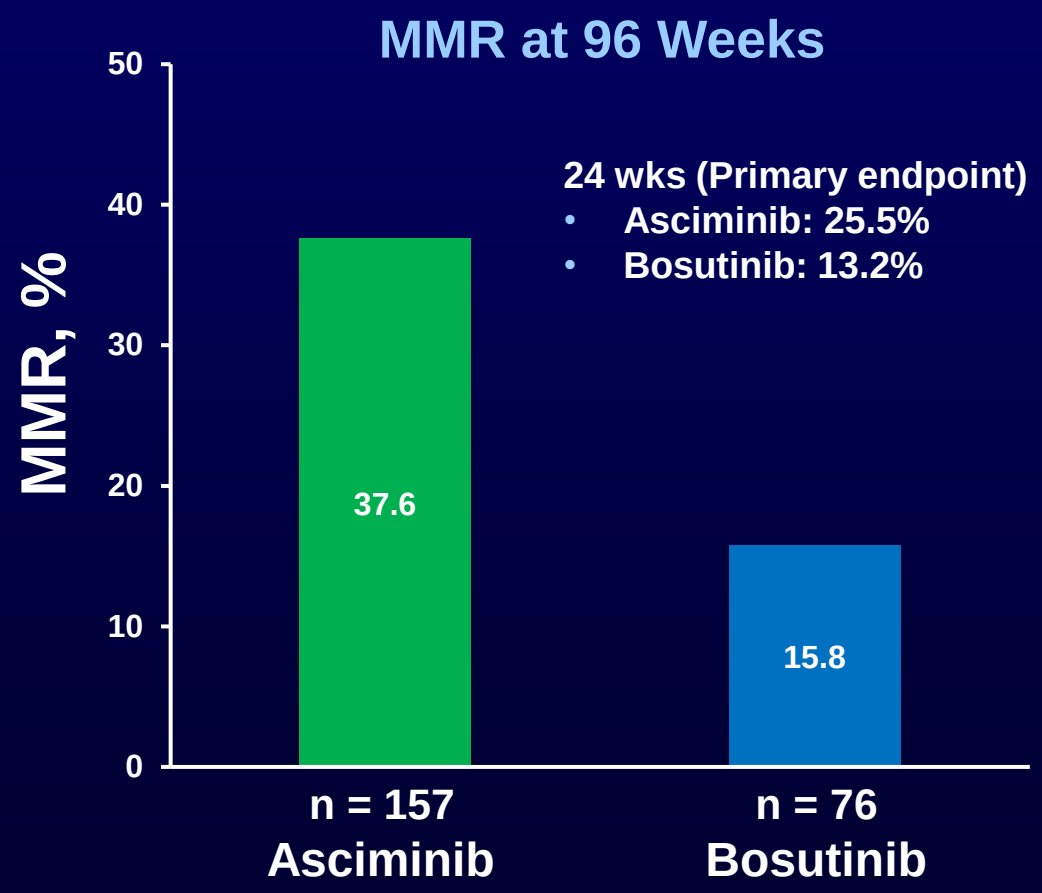
| MMR — n/N‡ (%) | Non-T315I | | | T315 | | |
|---|---|---|---|---|---|---|
| | Overall | Achieve | Maintain | Overall | Achieve | Maintain |
| | (N = 113)† | | | (N = 28)† | | |
| ≤2 prior TKIs | N = 34 | | | N = 12 | | |
| By 6 months | 13/25 (52) | 5/15 (33) | 8/10 (80) | 4/10 (40) | 3/9 (33) | 1/1 (100) |
| By 12 months | 15/25 (60) | 7/15 (47) | 8/10 (80) | 4/9 (44) | 3/8 (38) | 1/1 (100) |
| >2 prior TKIs | N = 79 | | | N = 16 | | |
| By 6 months | 24/74 (32) | 14/64 (22) | 10/10 100) | 1/10 (10) | 1/10 (10) | 0 |
| By 12 months | 29/66 (44) | 19/56 (34) | 10/10 (100) | 1/9 (11) | 1/9 (11) | 0 |
| Resistant and/or intolerant of ponatinib | N = 18 | | | N = 11 | | |
| By 6 months | 7/17 (41) | 3/13 (23) | 4/4 (100) | 1/7 (14) | 1/7 (14) | 0/0 |
| By 12 months | 8/14 (57) | 4/10 (40) | 4/4 (100) | 1/6 (17) | 1/6 (17) | 0/0 |

- 91 evaluable pts at 12 mo: 30/40 (75%) with baseline BCR-ABL1$^{IS}$ ≤1% achieved MMR by 12 mo vs 14/51 (27%) with BCR-ABL1$^{IS}$ >1%.

Hughes T, Mauro M, Cortes J, et al. NEJM 2019; 381: 2315-26

# ASCEMBL – Asciminib vs Bosutinib in R/R CML CP

- 233 pts previously treated with ≥2 TKIs randomized 2:1 to asciminib 40 mg BID or bosutinib 500 mg QD
- T315I and V299L excluded




- Median wks to MMR: asciminib 12.7 vs bosutinib 14.3
- Median wks exposure: asciminib 43.4 (0.1-129.9), bosutinib 29.2 (1.0-117.0)
- Other efficacy endpoints:
  - CCyR: 40.8% v 24.2% (96 w: 45.1% v 19.4%)
  - MR4: 10.8% v 5.3%
  - MR4.5: 8.9% v 1.3%
- TEAEs ≥G3 >2%: thrombocytopenia 22%, neutropenia 19%, hypertension 6.4%, ↑ lipase 3.8%
- AOEs (per 100 pts-years): asciminib 3.0, bosutinib 1.4



Hochhaus et al. Leukemia 2023; [ePub ahead of print]; Rea et al. Blood 2021; 138: 2031-2041

# Asciminib for T315I CML
## *Response*

- Asciminib 200 mg twice daily

| Patients, n (%) | MMR | MR4 | MR4.5 |
|---|---|---|---|
| All patients (n = 49) | 23 (46.9) | 13 (26.5) | 10 (20.4) |
| Ponatinib naive (n = 21) | 12 (57.8) | 8 (38.1) | 7 (33.3) |
| Ponatinib pretreated (n = 28) | 8 (28.6) | 5 (17.9) | 3 (10.7) |

- Median time to MMR: 12.1 weeks (range, 4 to 48 weeks)
  - K-M-estimated MMR duration at 144 wks: 87% (95CI: 68.4%, 100%)
- AOEs 5.8%



Cortes JE, et al. *Blood.* 2020;136 (Suppl 1): Abstract 650.

# *ASCEMBL - BCR::ABL1* Mutations[a] at the End of Treatment

Patients discontinuing treatment due to lack of efficacy or disease progression

| n (%) | Asciminib (n=39) | Bosutinib (n=30) |
|---|---|---|
| No mutations detected at end of treatment | 22 (56.4) | 20 (66.7) |
| Missing assessments at end of treatment | 1 (2.6) | 3 (10.0) |
| Mutations detected at end of treatment | 16 (41.0) | 7 (23.3) |
| Newly emerging mutations at end of treatment | 10 (25.6) | 2 (6.7) |
| ATP-binding site | • M244V (n=3)[b]<br>• E355G (n=1)[c]<br>• F359V (n=1)<br>• T315I (n=1) | • T315I (n=1)<br>• V299L (n=1) |
| Myristoyl pocket | • A337T (n=3)<br>• P465S (n=1) | None |
| Mutations at baseline and end of treatment | 6 (15.4) | 5 (16.7) |
| ATP-binding site | • F317L (n=2)<br>• F359C/V (n=3)<br>• Y253H (n=1) | • M244V (n=2)<br>• E255V (n=1)<br>• F317L (n=1)<br>• Q252H (n=1) |

[a] Determined by Sanger sequencing, mutation analysis was performed on week 1 day 1 and at the end of treatment. In case mutations were detected on week 1 day 1, additional assessments were performed every 12 weeks during the study.
[b] 1 patient had Y253H and F486S mutations at baseline that were not detected at the time of discontinuation.
[c] Patient had the F317L mutation at baseline, which was not detected at the time of discontinuation.

Hochhaus et al. EHA 2022

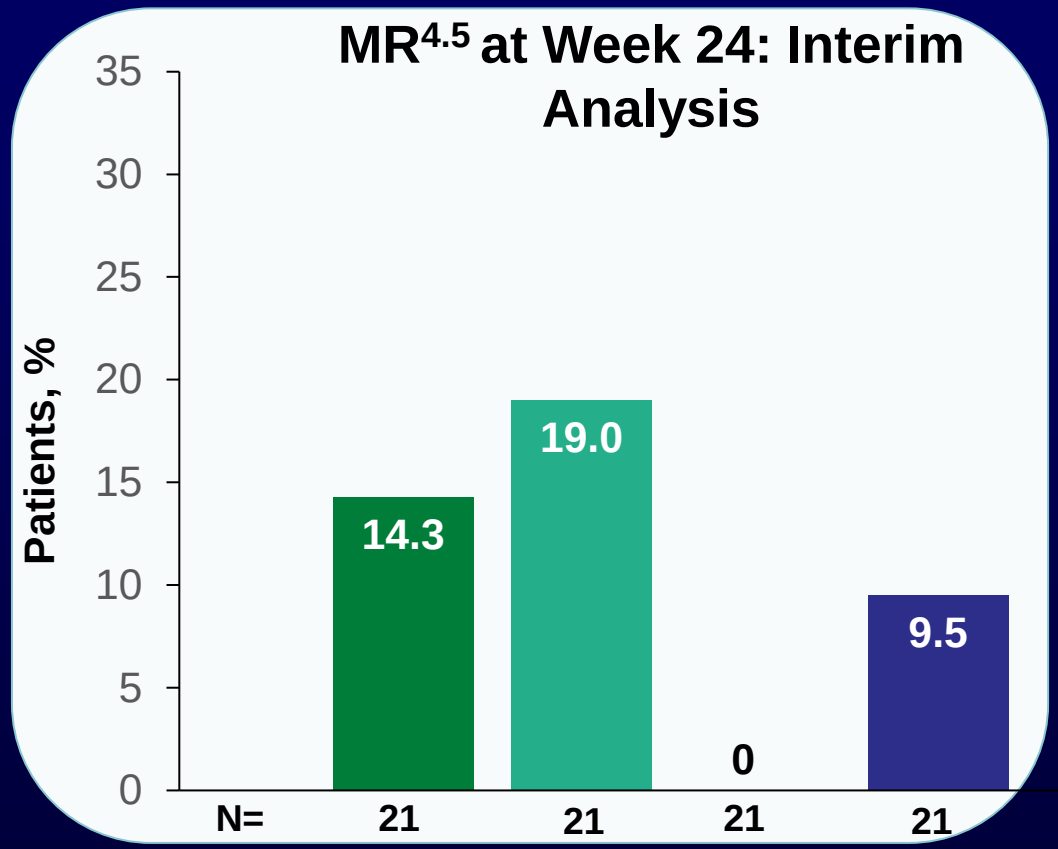
# What is the Role of 3GTKIs?

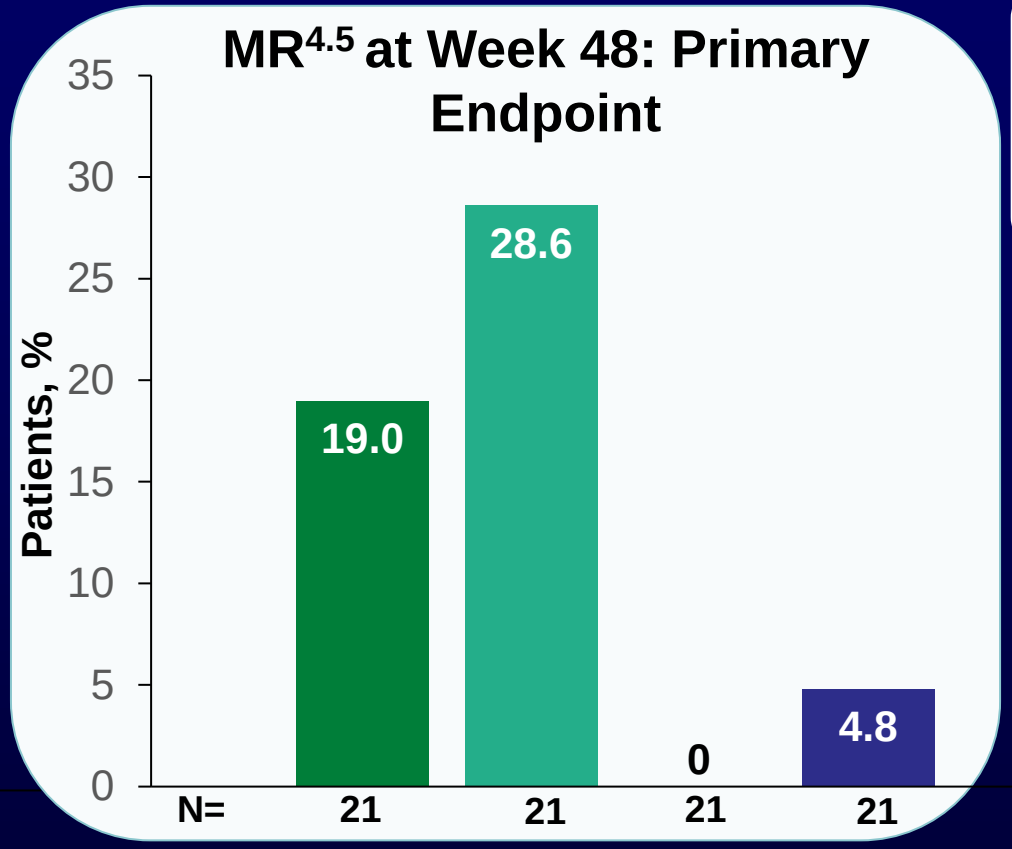
| Clinical Setting | The data | What I would like to see |
|---|---|---|
| 3rd+ line | • Excellent efficacy<br>• Minimal/improved toxicity | • Comparison ponatinib v asciminib<br>• Longer term safety (AOEs) |
| T315I | • Ditto | • Ditto |
| Add-on to improve DMR (Asciminib) | • Promising preclinical data | Established (other ongoing) |
| 2nd line | • None | Hopeful CyR >60%, |
| Frontline | • None | • Clinical trials (MR4.5 >75%, AOEs ≤Bosutinib<br>Needed |

**Other questions:**

- What is the right dose of asciminib?
- Phase 2 data for vodobatinib, olverembatinib
- Incidence of AOEs for all (comprehensive)
- Do combinations of TKIs with different MOA have a role?

# ASC4MORE - MR$^{4.5}$ at Weeks 24 and 48





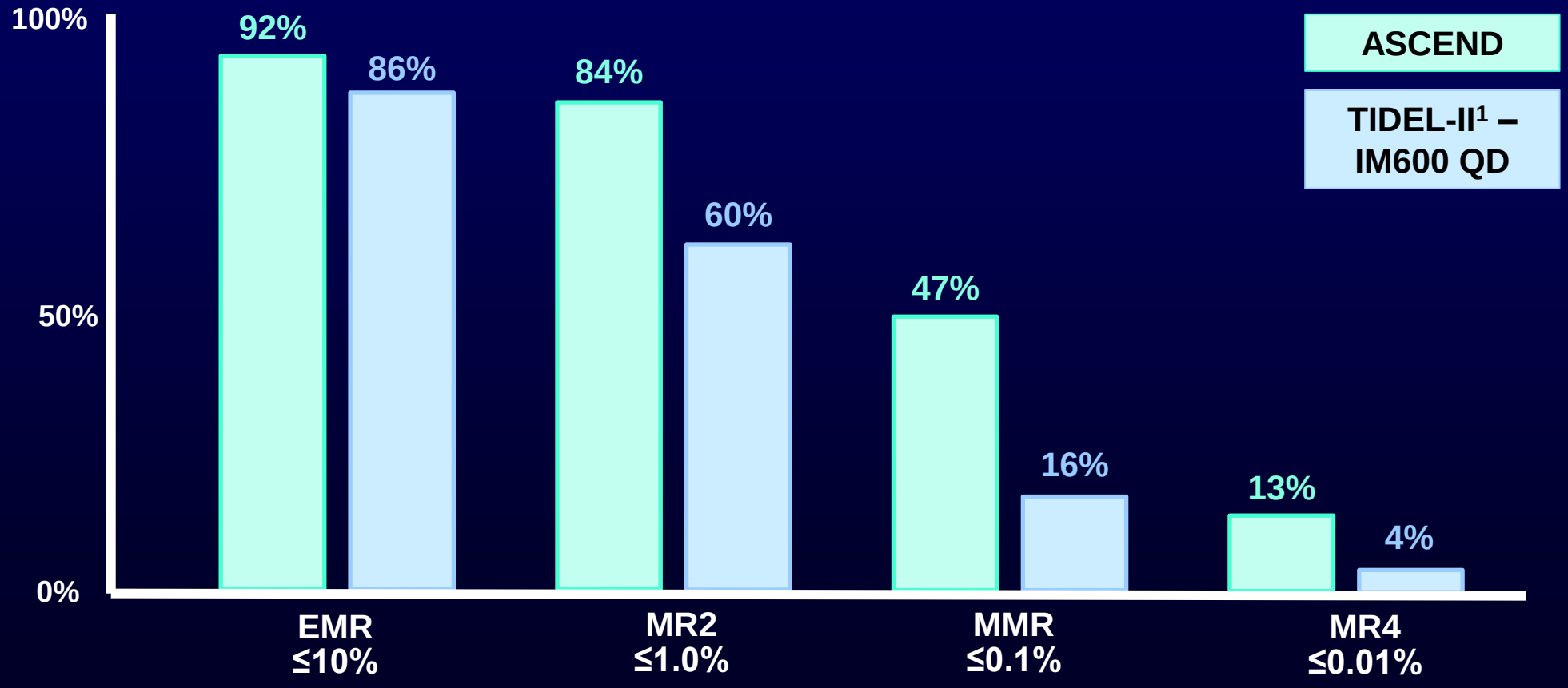
- More patients were able to achieve MR$^{4.5}$ with asciminib add-on to imatinib vs continued imatinib or switch to nilotinib
- No patients in the continued imatinib arm were in MR$^{4.5}$ at week 48, although more patients in this arm were in MMR at baseline than in the asciminib add-on arms



Cortes et al. ASH 2022

# Asciminib for Frontline CML – ASCEND
## Molecular Response at 3 Months N=76

- Previously untreated CML CP
- Starting dose: Asciminib 40 mg BID
- If hallmarks not met, escalate to 80 mg BID; then add imatinib, dasatinib or nilotinib
- Co-primary endpoints: *BCR::ABL1* ≤10% at 3 months, ≤ 0.1% at 12 months




[1]Yeung et al Blood 2015

Yeung et al. ASH 2022; abstract #79

# Are we done?

| Scenario | Action | But | Solution |
|---|---|---|---|
| Imatinib resistance | Change to 2GTKI | ~40% CCyR | 3GTKI? |
| 1L 2GTKI resistance | Change to another 2GTKI | ~20% CCyR | 3GTKI |
| | 3GTKI | No data, no label | Studies |
| Suboptimal | Monitor closely | Not much | Long-term DASCERN (maybe) |
| Resistance ≥2 TKI or T315I | Change PON/ASC | • MMR ~40%<br>• Dose?<br>• AOEs | Additional studies<br>New agents? |
| Intolerance | Change to other TKI | • Cross-discontinuation or cross-AEs?<br>• Class effect AEs<br>• The nagging: thrombocytopenia, AOEs, lipase, LFTs | • Manage AEs<br>• New TKIs? (probably not) |
| Low-grade toxicity | Manage AEs | • Some are chronic<br>• Relatedness? | • Better understanding and management<br>• Studies |

# Remaining Challenges in CML

- Frontline: improve sMR4.5 rates
- Combinations: which, when, who (and mostly, if)
- Second line
  - After 2GTKI
  - After imatinib
- ACA, other molecular abnormalities
- Third line & T315I: not enough options?
- Dose and schedule
- AP/BP: do we care?

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# Fireside Chat:
# Allosteric vs. Active-Site TKIs

**Michael Mauro, M.D.**, MSKCC
**Emil Kuriakose, M.D.**

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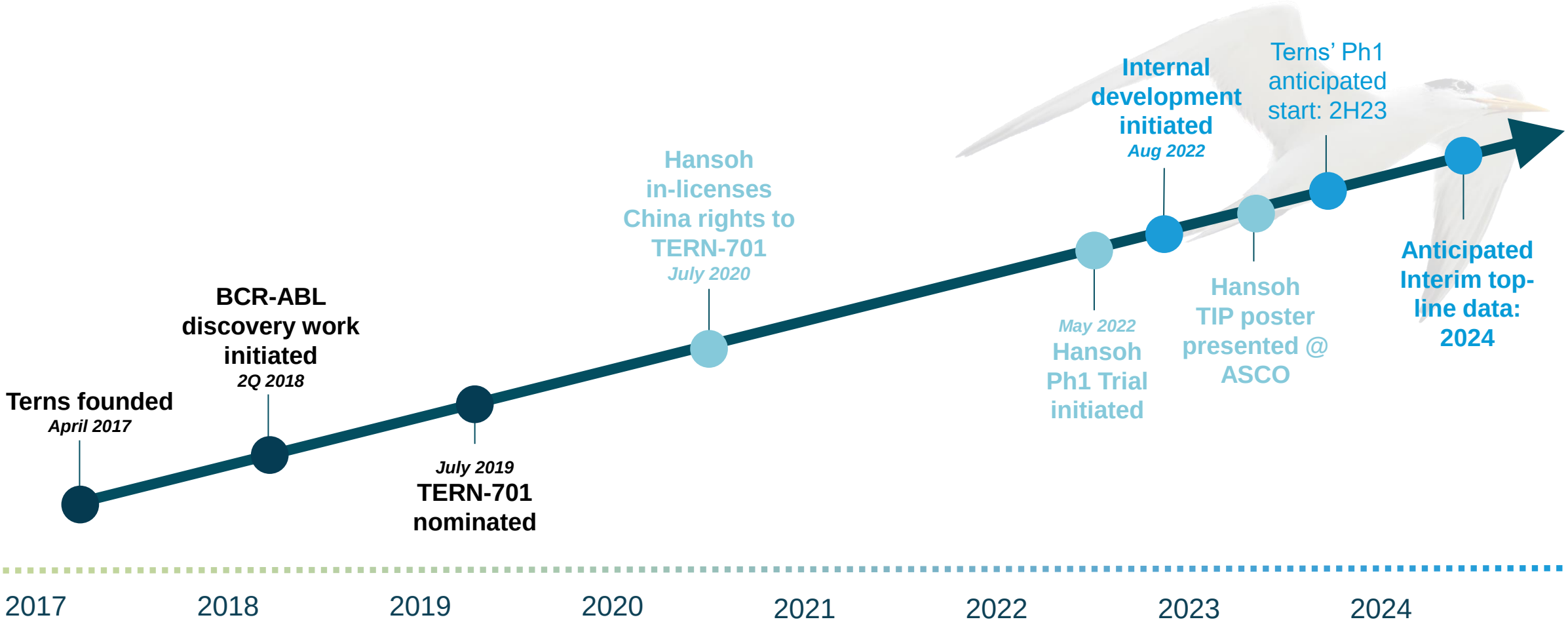
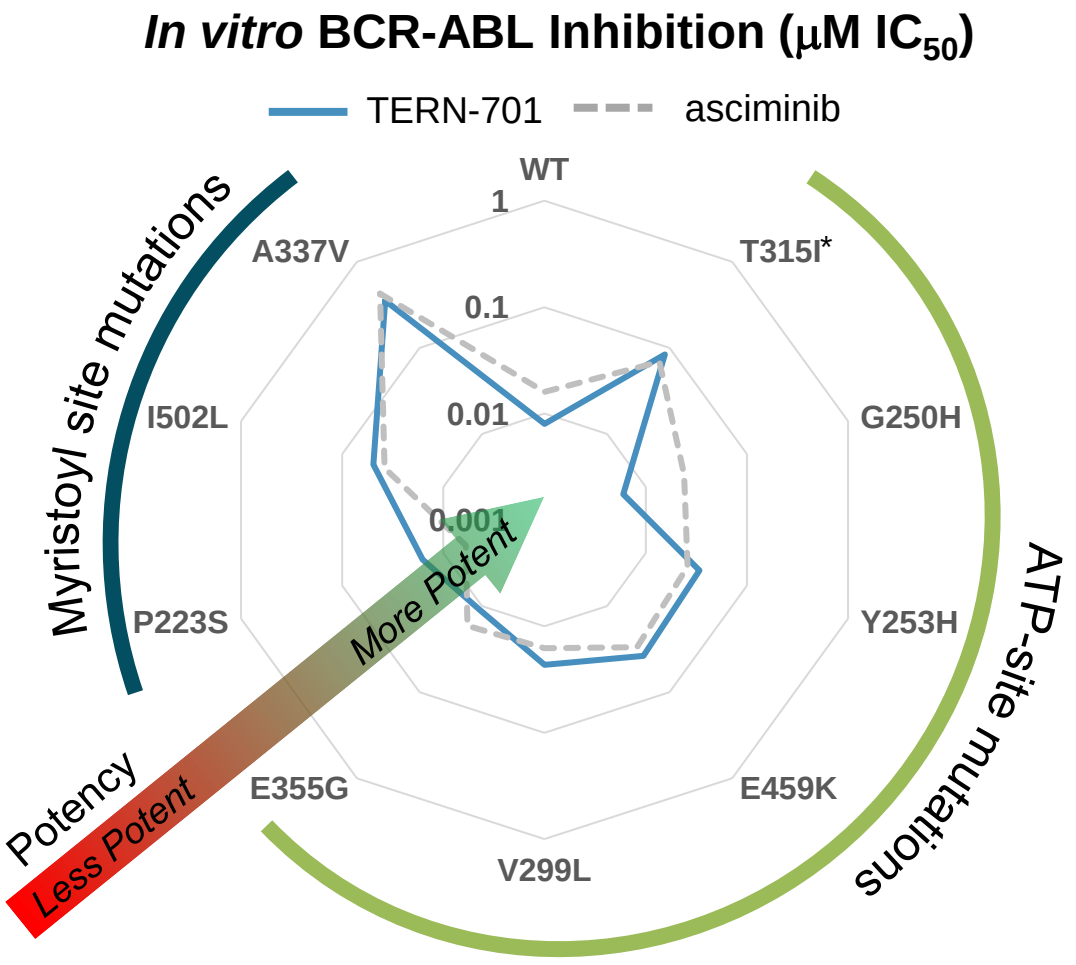
# TERN-701 Overview / Update

**Emil Kuriakose, M.D.**

# TERN-701: Our Internally Discovered Allosteric TKI of BCR-ABL for the Treatment of CML



# TERN-701 Potency Suggests Anti-Tumor Activity Comparable to asciminib; With Opportunities to Differentiate




In non-clinical assays, **TERN-701 has a similar profile to asciminib** and is highly potent against:

- wild type BCR-ABL, and
- most-common mutations occurring in patients treated with active-site TKIs

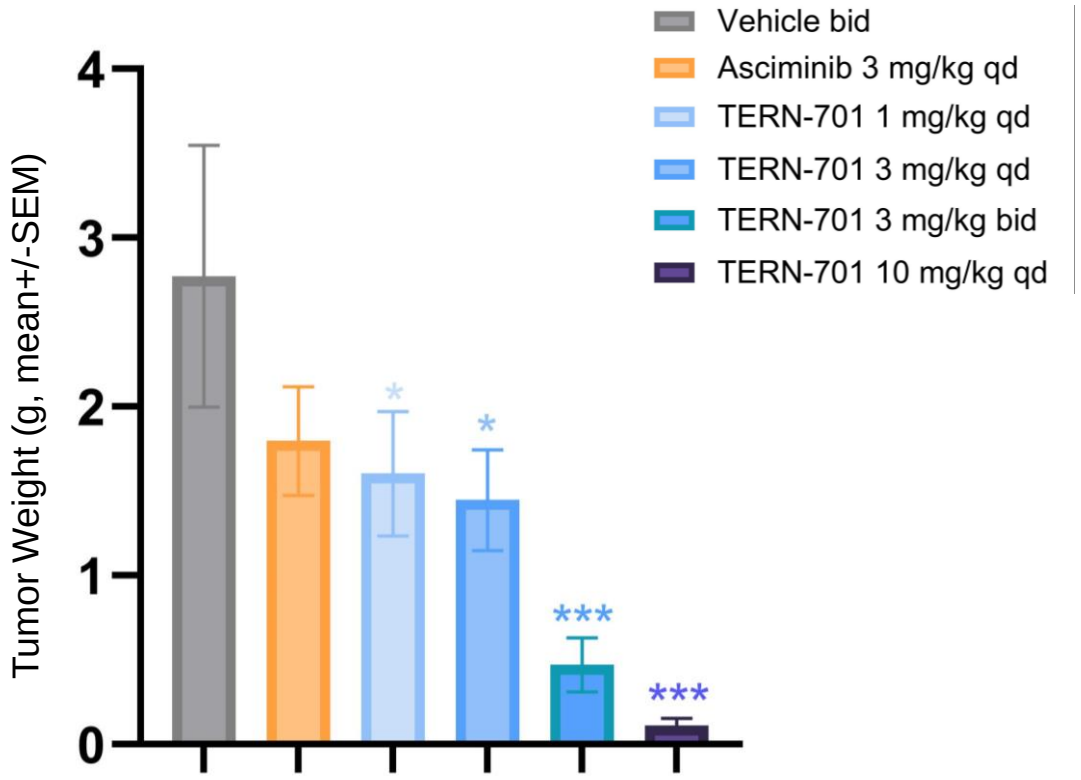
**TERN-701** could have simplified dosing & fewer drug-drug interactions vs asciminib

Note: WT (wild-type) and BCR-ABL mutations were evaluated in an ABL auto-phosphorylation assay
* T315i mutation was evaluated in a cell proliferation assay

# In Preclinical Models of CML, TERN-701 Showed a Greater Anti-Tumor Effect vs. asciminib at Equivalent Doses & Dosing Frequency

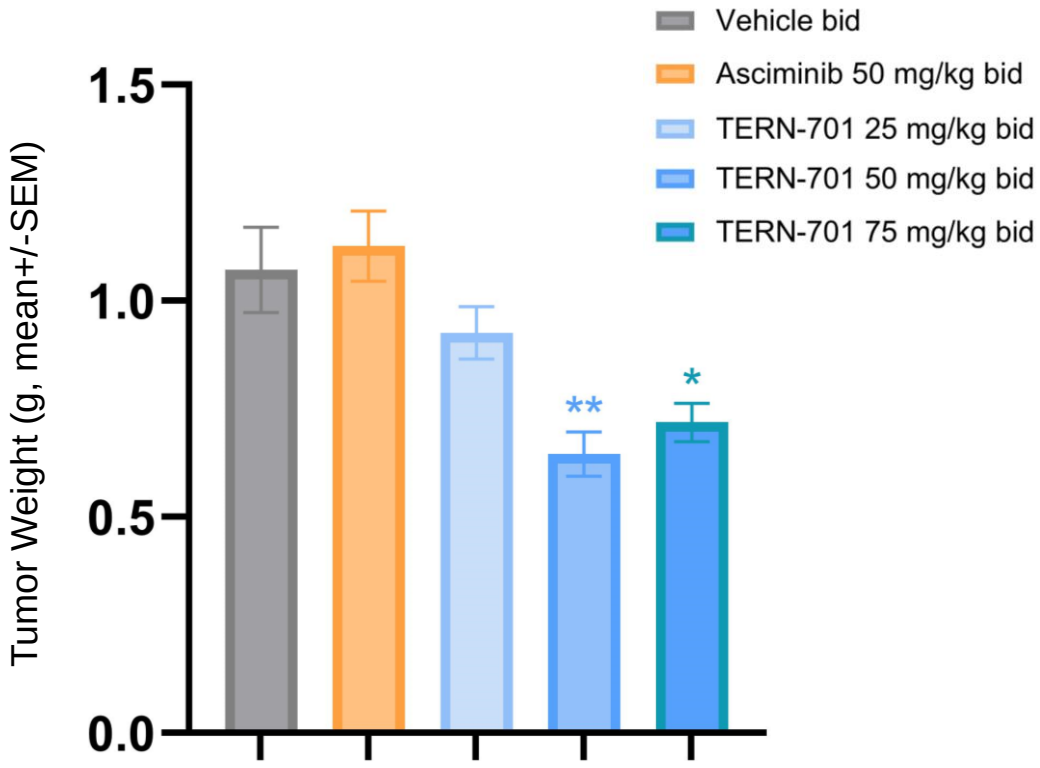
## K562 Xenograft

*(Day 14)*




## Ba/F3 BCR-ABL1-T315I Xenograft

*(Day 15)*

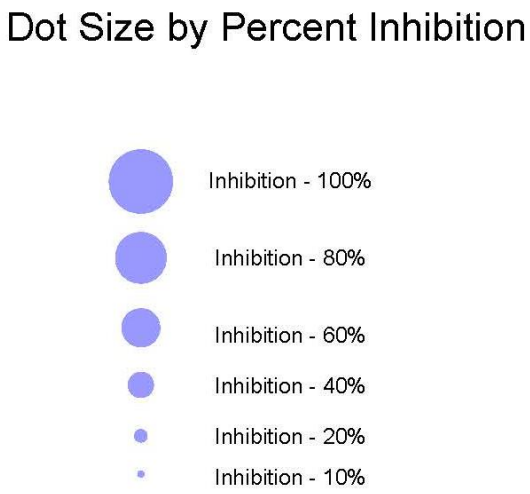


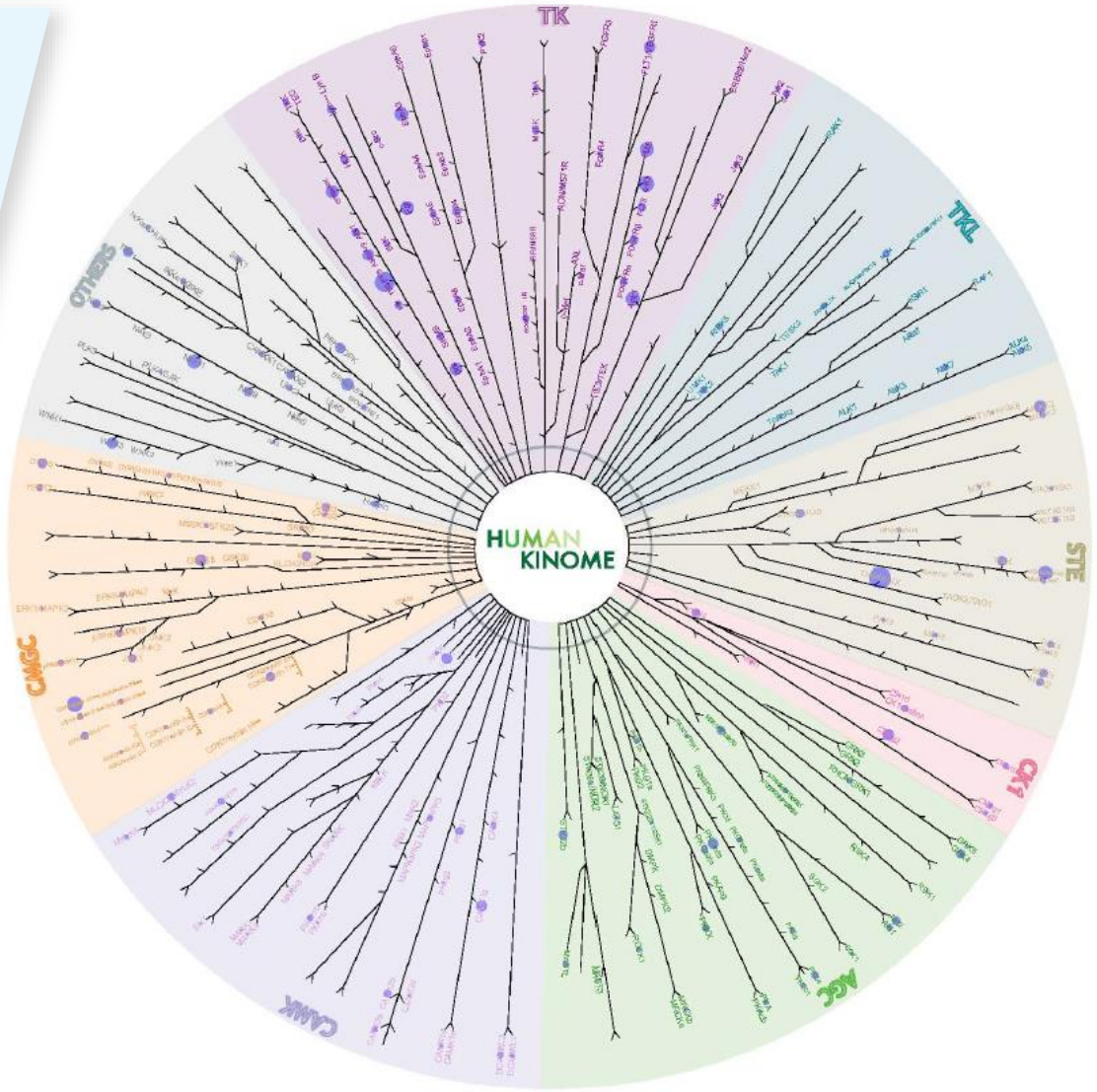

Note: NOD-SCID (K562) and BALB/c nude mice (Ba/F3T315I) were implanted with CML cells, randomized, and administered the indicated TKIs once tumor volumes reached a mean size of 110 mm. Mean tumor weights for each of the treatment groups at the conclusion of the study. All error bars represent the SEM. *p<0.05, **p<0.01, ***p<0.001.
1. asciminib was utilized as the free base, TERN-701 was formulated as an optimized salt form
Source: ASPET TERN-701 poster

# TERN-701 Also Demonstrated High Selectivity on a Broad Kinase Panel, Suggesting Reduced Potential for Off-Target Activity

**TERN-701** was assessed at 1 µM against a panel of 375 kinases

No kinase, including wild-type ABL1, was inhibited by >50% → reduced potential for TERN-701 off-target activity




Source: ASPET TERN-701 poster

# Hansoh Study to Evaluate Efficacy of TERN-701 in CML

*~100 patient China trial will provide full efficacy evaluation & other key insights to **accelerate** Terns' development; status update across dose escalation cohorts presented at ASCO 2023*

**TERN-701**

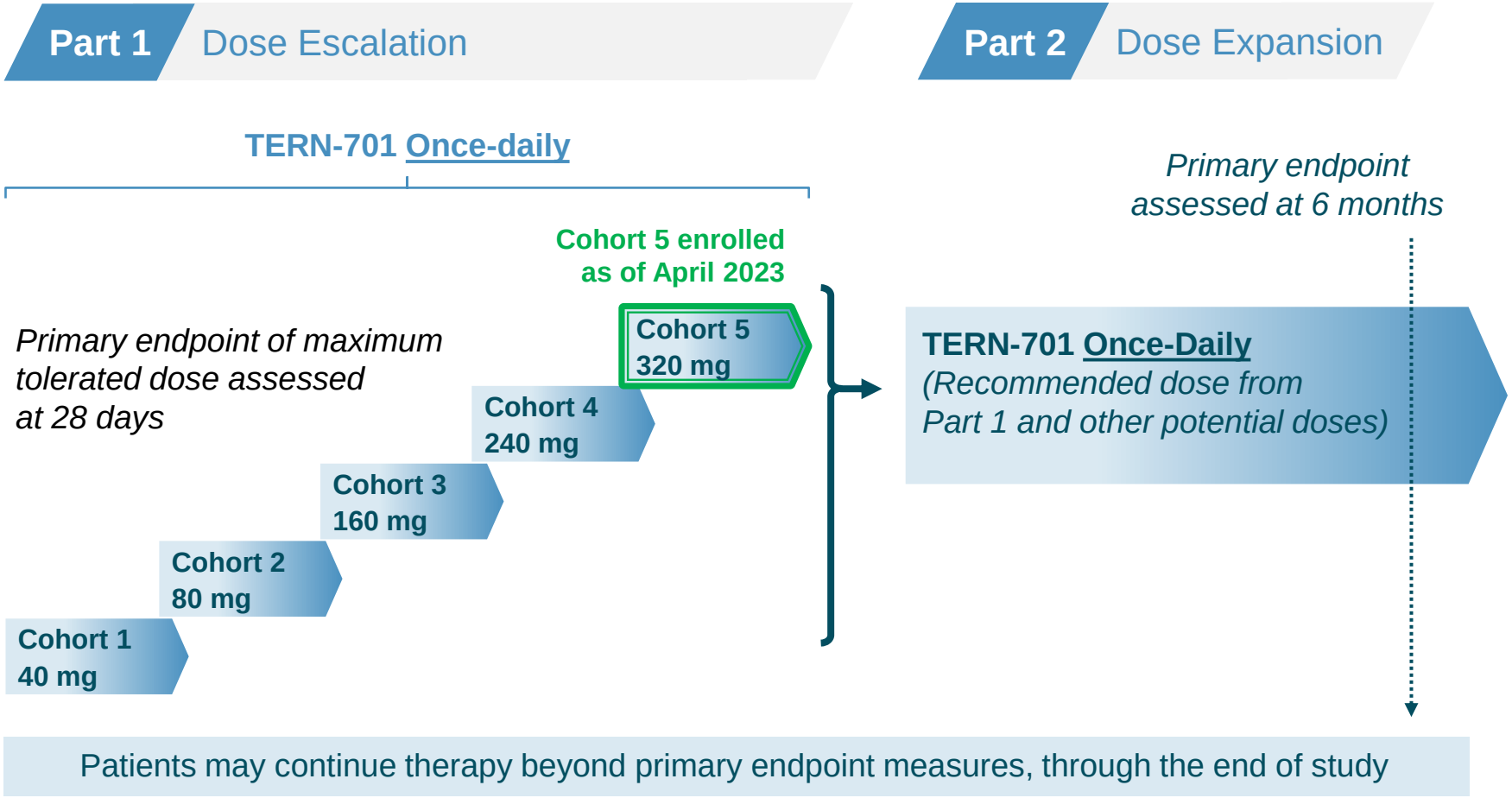
## Trial Design

*Population (n=~100)*

- CML patients (Ph+)
- Resistant or intolerant to active-site TKIs

*Endpoints For Part 2*

- Cytogenetic response
- Major molecular response
- Safety, tolerability
- PK




Source: clinicaltrials.gov
Note: TERN-701 is referred to by Hansoh Pharmaceuticals as HS-10382

# Terns' Draft Phase 1 Trial Design

*Aims to leverage Hansoh Phase 1 trial data to evaluate dose ranges expected to be both safe & therapeutic*

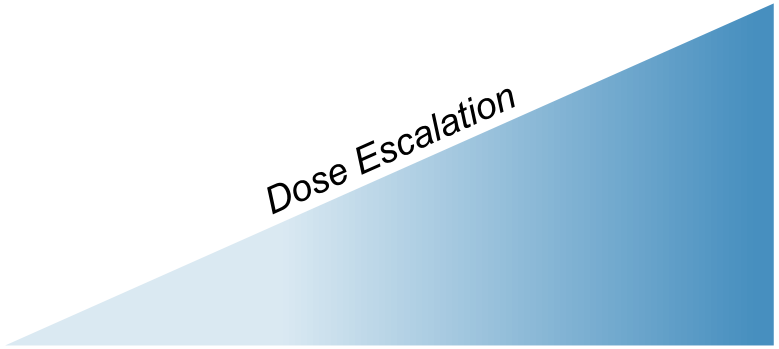
**TERN-701**

## Study Population

- Chronic phase CML patients treated with at least one prior TKI
- Treatment failure or intolerance on current TKI

**Part 1** Dose Escalation

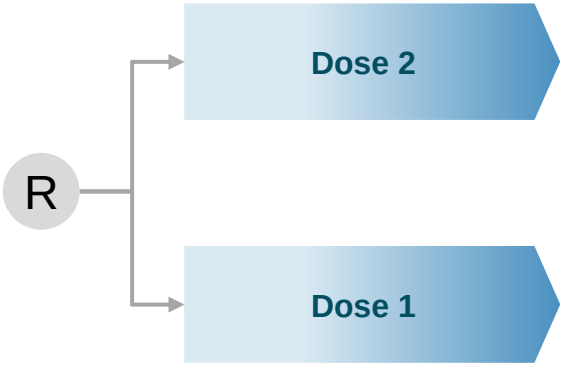
**TERN-701 Once-daily (N=20-30)**




RDE Selection*

**Part 2** Dose Expansion

**TERN-701 Once-daily (N≤80)**




Patients may continue therapy beyond primary endpoint measures, through the end of study

*RDE = recommended doses for expansion.

# Potential for POC and Expansion Data in 2024 / 2025

**1H23**

**CMC activities**

**Completed manufacturing** of initial material to support Phase 1 study start

**2H23**

**Terns Phase 1 start in U.S., E.U., other Terns territories**

**Phase 1 dose escalation / expansion**

*(Initial data expected 2024)*

**Phase 1 ~1-2 yrs***

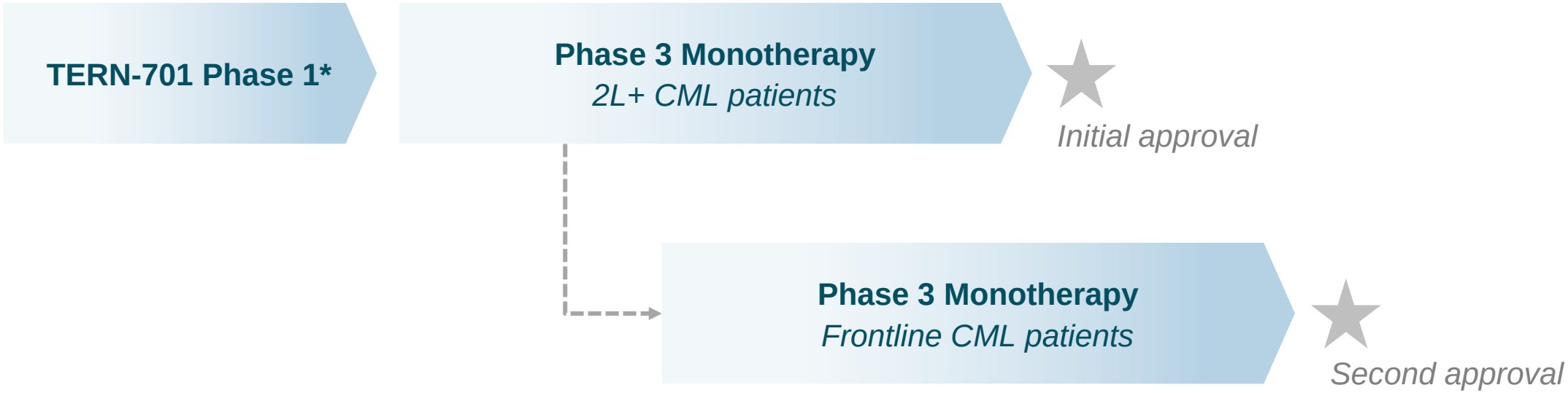
**Phase 3 Registrational CML 2-3 years***

**Evaluating multiple options for pivotal trial(s)**

*Trial durations estimated based on enrollment projections from asciminib development program

# Potential Option for TERN-701 Monotherapy Registration Path in Earlier Line CML Patients

- Potential for initial approval as 2L+ therapy in patients failing frontline treatment with active site TKI
- Clinical development of TERN-701 in newly diagnosed CML patients is feasible despite anticipated approval of asciminib in frontline setting




Note: 2L+; 2nd line and later.
*Dose escalation/dose expansion study

# TERN-701 is Addressing a Sizeable, and Still Unmet, Market Opportunity in CML with Novel Allosteric TKI

- CML is an **orphan indication** with **sizable market** and a need for **multiple agents**
- **Frequent switching** occurs between TKIs, most commonly due to intolerance
- Allosteric BCR-ABL TKIs have significant (~2x) efficacy improvement over older standard-of-care active-site inhibitors and are better tolerated
- 1st approved allosteric TKI, asciminib, expected to be a blockbuster in 3L CML and is being developed for 1L
- TERN-701 is an **internally-developed allosteric** TKI with an expected profile ≥ asciminib
- Phase 1 trial in CML patients initiated by Hansoh in 2Q 2022 in China; **Terns' Phase 1 clinical trial initiation targeted in 2H 2023**

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# Q&A

**Sen Sundaram**
**Erin Quirk, M.D.**
**Emil Kuriakose, M.D.**
**Jorge Cortes, M.D.**

# Mission. Vision. Core Values.

## MISSION

To advance transformative medicines that address serious diseases

## VISION

To pioneer significant innovations across the lifecycle of drug development

TRUST
EVOLVE
RESPECT
NURTURE
SOAR

**Trust**: empowered and accountable to do the right thing

**Evolve**: learning and growing from our successes, failures and changes in the environment

**Respect**: celebrating the diversity of our backgrounds, opinions and experiences

**Nurture**: fostering internal and external relationships

**Soar**: aiming high and being your best