Zandelisib: A PI3Kδ Inhibitor with Highly Differentiated Pharmaceutical Properties

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NASDAQ: MEIP

Forward-Looking Statements

- This presentation contains, and our officers and representatives may from time to time make, statements that are "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Examples of forward-looking statements include, among others, statements regarding our development strategy; potential advantages of our product candidates; the initiation and completion of preclinical and clinical studies and the reporting of the results thereof; the timing of regulatory submissions and actions; the sufficiency of our existing cash; and all other statements relating to our plans, objectives, expectations and beliefs regarding future performance, operations, financial condition and other future events (including assumptions underlying or relating to any of the foregoing).
- These forward-looking statements rely on a number of assumptions concerning future events and are subject to a number of risks, uncertainties, and other factors, many of which are outside of our control. Important factors that could cause our actual results and financial condition to differ materially from those indicated in forward-looking statements include, among others: uncertainties relating to the initiation and completion of preclinical and clinical studies; whether preclinical and clinical study results will validate and support the safety and efficacy of our product candidates; the outcome of regulatory reviews of our product candidates; varying interpretation of research and development and market data; the impact of the COVID-19 pandemic on our industry and individual companies, including on our counterparties, the supply chain, the execution of our clinical development programs, our access to financing and the allocation of government resources; risks and uncertainties relating to intellectual property and the other factors discussed under the caption "Item 1A. Risk Factors" in our most recent annual report on Form 10-K and our most recent quarterly report on Form 10-Q.
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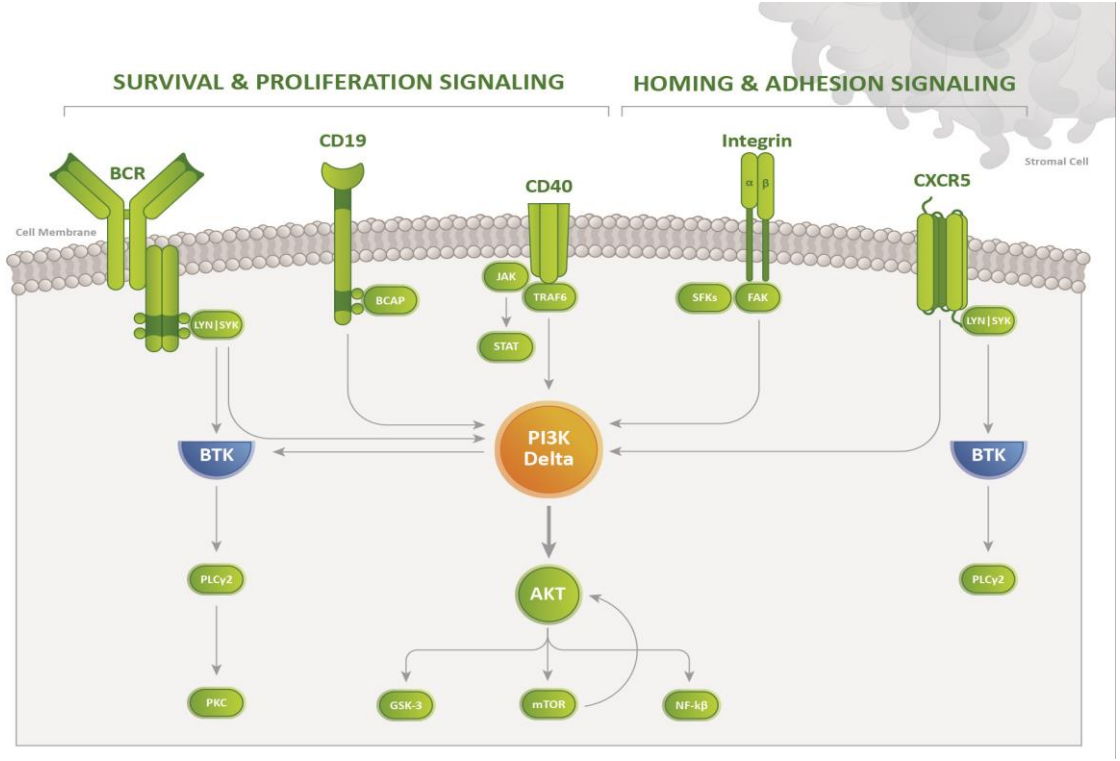
Zandelisib (ME-401): Targeting a Mechanism at a Crossroads of B-cell Malignancy Signaling

- PI3Kδ is highly expressed in lymphoid cells and is critical for the survival, proliferation and homing of malignant B cells
- Zandelisib is an oral, once-daily, selective inhibitor of PI3Kδ in clinical development for the treatment of B-cell malignancies



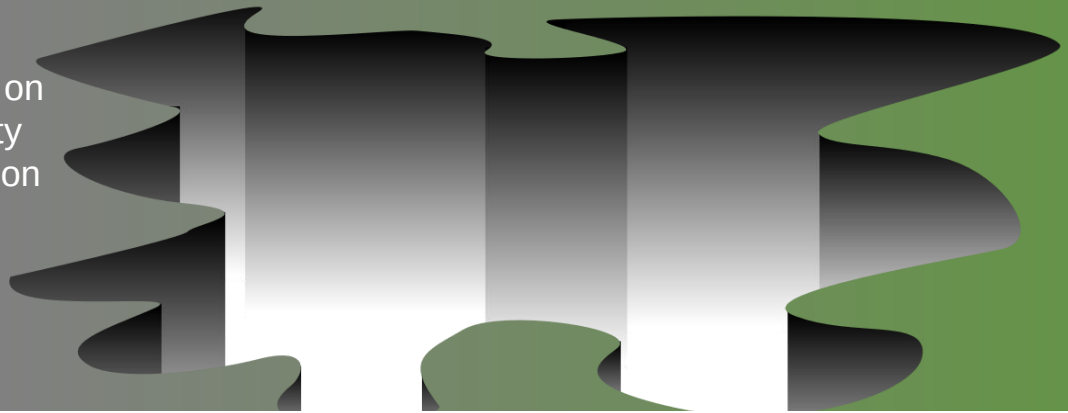
Zandelisib: Potential to Bridge the Gap Between the History of PI3Kδ and its Promise

The Challenge:

Realize utility of target on B-cells but limit toxicity associated with target on T-regs

The Gap

Inability of earlier PI3Kδ inhibitors to realize clinical potential of target due to toxicity



The Promise:

Therapeutic with strong efficacy that is also well-tolerated

Zandelisib: Potential to Bridge the Gap Between the History of PI3Kδ and its Promise

Zandelisib:
Bridging The Gap

The Challenge:

Realize utility of target on B-cells but limit toxicity associated with target on T-regs

- High volume of distribution
- Tumor Accumulation
- Selective inhibition
- Trough Plasma >EC90
- Tumor penetration
- Binding kinetics

The Promise:

Emerging Zandelisib Profile

- **High Response Rates**
  83% ORR (r/r FL)
- **Durable to Date**
  DOR Not Reached
  Median follow-up: 13.2 mo. (r/r FL)
- **Well-tolerated**
  7% Discontinuation Rate due to TEAE*

Zandelisib data reported from ongoing Phase 1b study of 57 patients, including r/r FL (36) and other B-cell malignancies (21). Data cutoff presented: April 13, 2020.

Zandelisib: Superior Volume of Distribution and Cell Penetration Offer a Differentiation Explanation

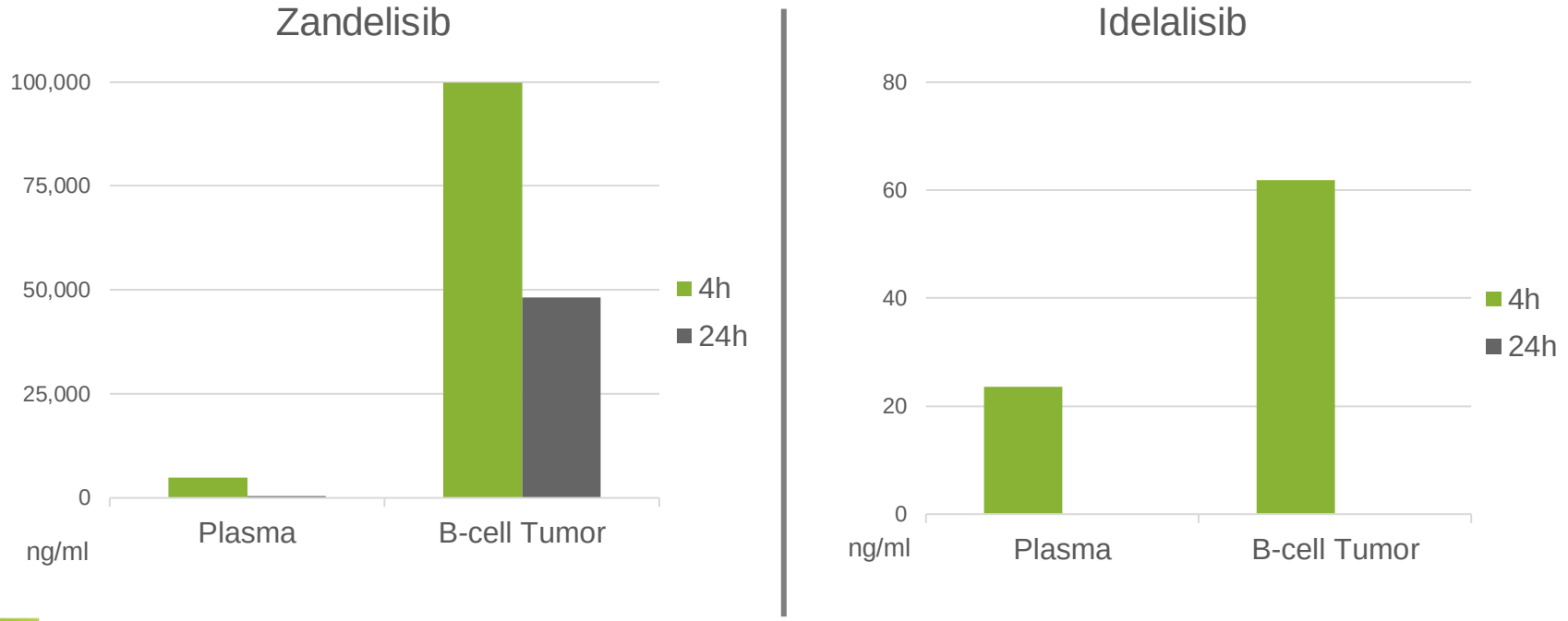
	Zandelisib	Copanlisib (Intravenous)	Idelalisib	Duvelisib	Parsaclisib	Umbralisib
High V_{SS}						
V_{SS} (L)	~700[1]	871	23.0	28.5	~40[2]	N/A
AUC (ug*h/ml)	<1	1.6	11	7.9	~6	~8
Cell Penetration						
Cellular Association[3]	61%	68%	~10%	~10%	19%	--
In Vivo Biologic Activity IC_{50} (nM)[4]	1	NA	150	115	NA	NA

1. Assumes average body weight of 70kg. 2. Incyte reported that "PK analysis has demonstrated that Parsaclisib distributes with body water. 3. Derived from blood/plasma ratio. 4. Inhibition of basophil activation, except for Parsaclisib which is inhibition of pAKT formation in SUDHL5 cells after incubation in blood from patients.

Sources: Zandelisib: Moreno, et. al. Clinical Therapeutics (2018) and Moreno et. al., Targeted Oncology (2019). **Copanlisib**: CDER Multi-Discipline Review; Package insert. **Idelalisib**: CDER Clinical Pharmacology and Biopharmaceuticals Review; CHMP assessment report. **Duvelisib**: CDER Multi-Discipline Review; Package insert. **Parsaclisib**: Torres, et. al., Blood (2019). **Umbralisib**: Burris, et. al., Lancet Oncology (2018).

Zandelisib: Preferential Retention in Tumors

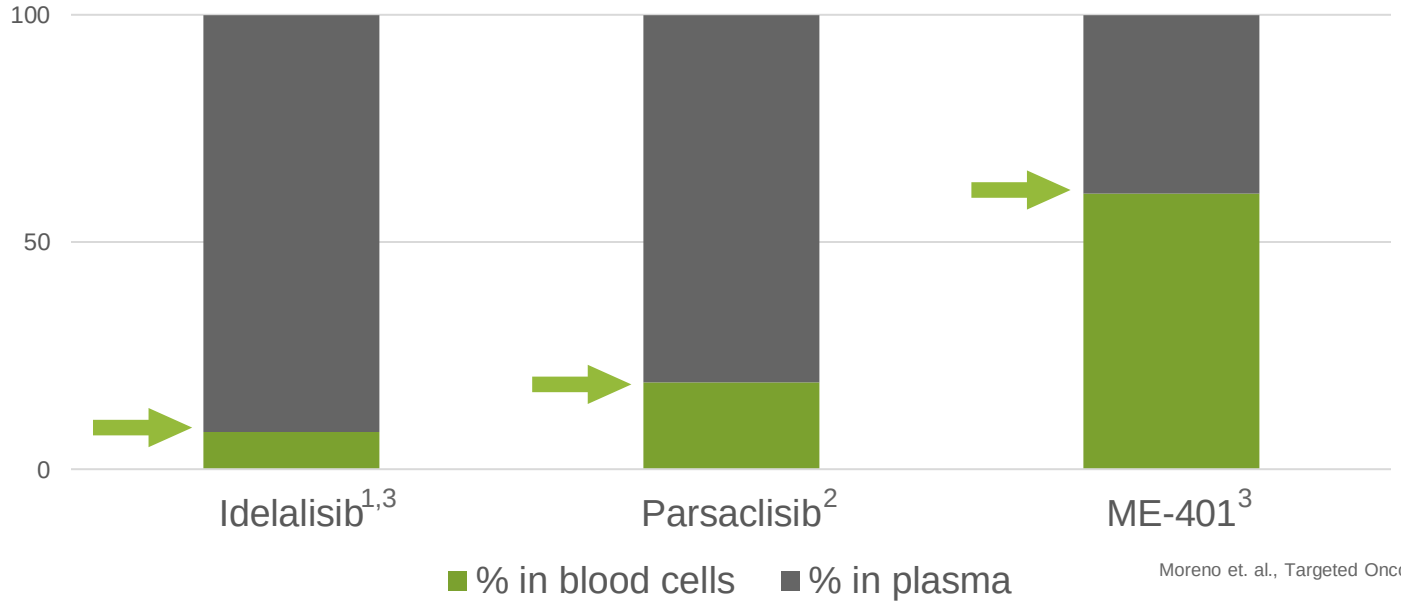
Preferential Retention in Murine B-cell Tumors



Moreno et. al., Targeted Oncology (2019).

Zandelisib: Superior Blood Cell Penetration

% Of Drug in Plasma vs. Blood Cells Based on Blood/Plasma Ratios



Moreno et. al., Targeted Oncology (2019).

1. Idelalisib package insert. 2.Torres, et. Al., Blood 2013 122:5570; 3. Moreno et. al., Targeted Oncology (2019).

Zandelisib: Selective Inhibition of PI3Kδ

	PI3K-δ	PI3K-α	PI3K-β	PI3K-γ
Mean IC_{50} (nM)	≤5	5491	335	2533
Fold selectivity		>1000	>65	>500

- Does not significantly inhibit other kinases in the Kinomescan
- Does not significantly inhibit other proteins in broad-spectrum selectivity screening

MEI data on file

Zandelisib: Differentiated Binding Kinetics vs. Idelalisib

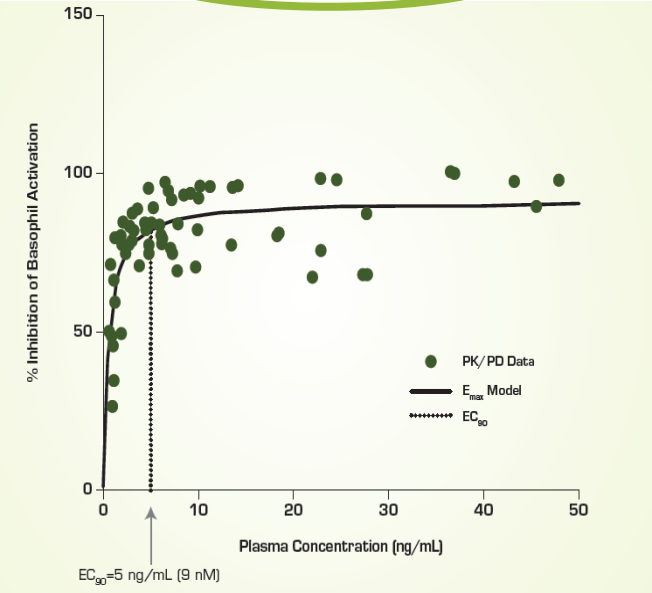
Compound	k_a (1/Ms)	k_d (1/s)	K_D (M)	$t_{1/2}$	Residence Time
Zandelisib	1.72E+06	5.20E-05	3.03E-11	3.7 h	5.5 h
Idelalisib	6.53E+06	7.25E-03	1.11E-09	1.6 min	2.3 min

Moreno et. al., Targeted Oncology (2019).

Zandelisib: Potent Activity in Basophil Activation Test (BAT)

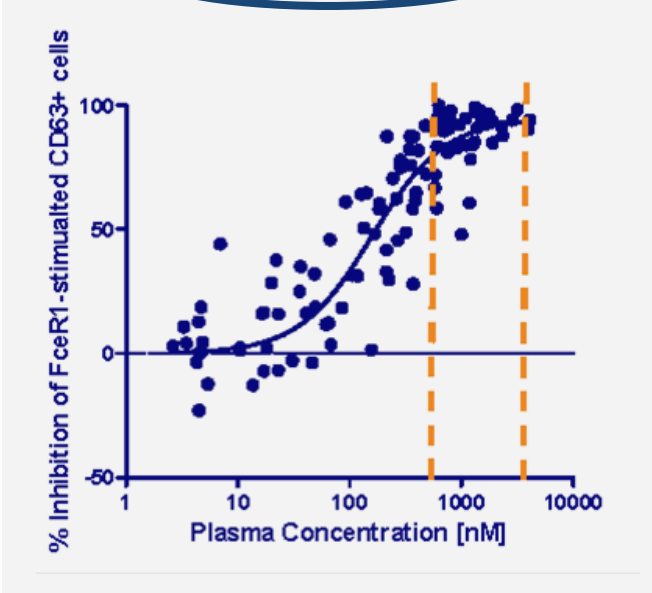
Zandelisib

EC_{90} = 9 nM[1]



Idelalisib

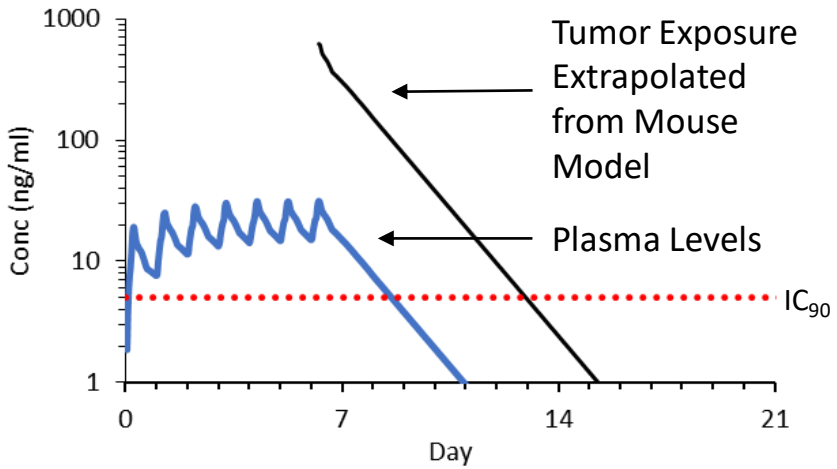
EC_{90} >500 nM[2]



1. Moreno, et. al. Clinical Therapeutics (2018) 2. ORCA Meeting, 2011

Rationale for Zandelisib Intermittent Schedule

MEI Modeling of 1 Week On, 3 Weeks Off Dosing



Zandelisib

- Plasma levels > IC_{90} for 9/28 days
- Plasma underestimates tissue levels
- Significantly higher levels expected in tumor vs plasma

MEI data on file.

Zandelisib Differentiation Supports Potential to Redefine the Class as Single Agent and in Combination Therapies

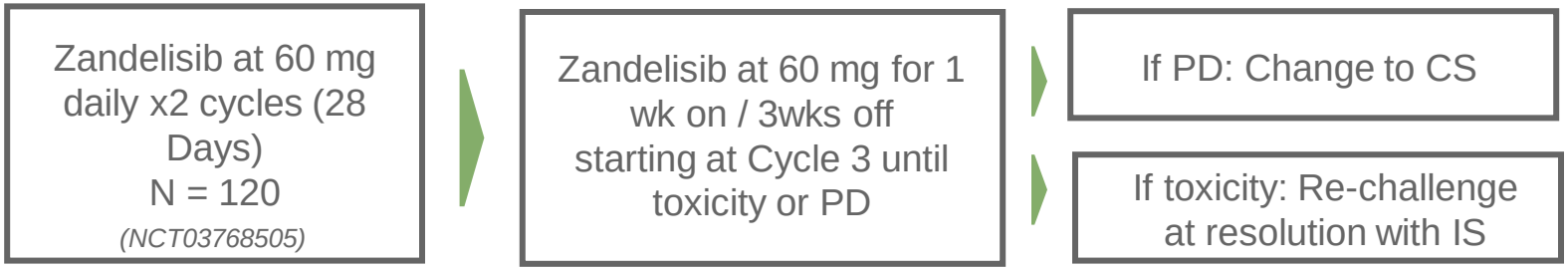
Zandelisib:
Volume of distribution
Cell penetration
Tumor accumulation

Differentiated Pharmacologic Profile

High Potency at Low Plasma Concentrations

- Dose schedule flexibility providing potential to maintain clinical utility while minimizing adverse events of special interest common to other PI3Kδ agents
- Unlocks possibilities for single agent and therapeutic combination approaches

Phase 2 TIDAL Trial to Support Accelerated Approval Marketing Application – The Initial Opportunity in r/r FL

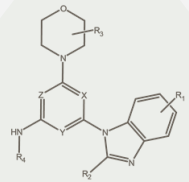


- Histologically confirmed diagnosis of FL, Grade 1, 2, or 3a
- FL, relapsed or refractory to 2 prior systemic therapies including an anti-CD20 antibody and chemotherapy
- No prior therapy with PI3Kδ inhibitors
- No histological transformation to an aggressive lymphoma

Zandelisib: Best-in-Class Potential

High Response Rates:
83% ORR (r/r FL)

Durable Responses to Date:
DOR Not Reached
Median follow-up: 13.2 mo. (r/r FL)



Zandelisib

Well-tolerated:
7% Low Discontinuation Rate for any TEAE*

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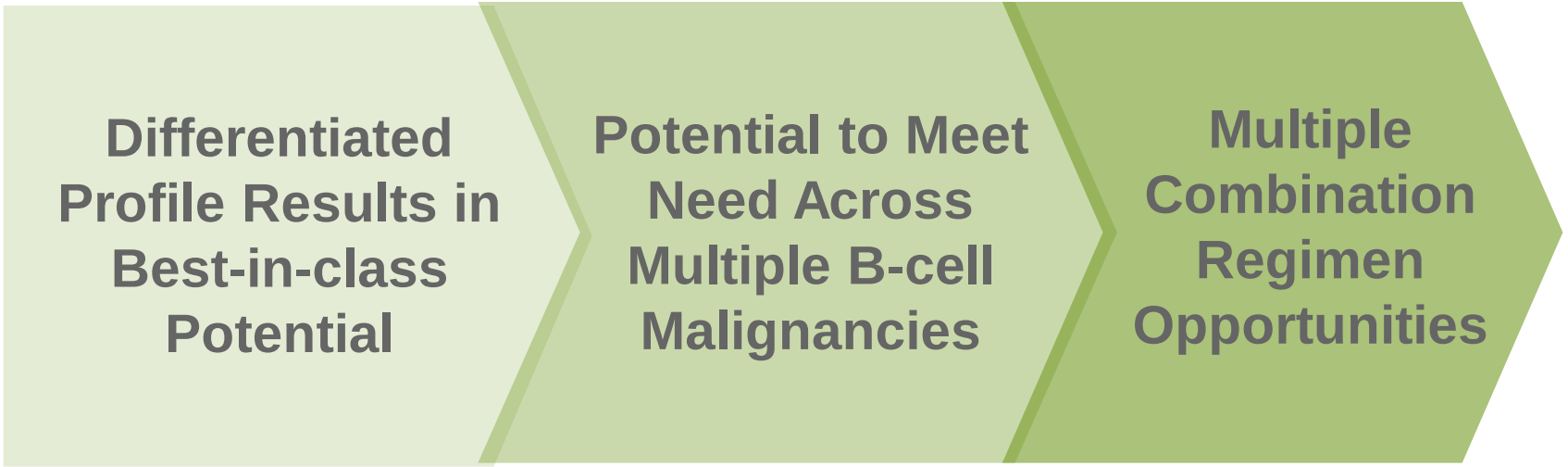
Expanding Zandelisib Development Activities to Explore Full Potential

- TIDAL study arm evaluating zandelisib monotherapy as ≥3rd line therapy in marginal zone lymphoma (MZL)
- Phase 3 study evaluating zandelisib + rituximab as ≥2nd line therapy in R/R FL and MZL
- Expanding evaluation of combination with zanubrutinib into disease specific B-cell malignancy cohorts
- Japan registrational Phase 2 study evaluating zandelisib monotherapy in R/R indolent B-cell lymphoma
- Selective IIT's (e.g., zandelisib + R-CHOP as 1st line therapy in DLBCL at the Cleveland Clinic)

Exploration of other indications and combinations are also part of the extended development plan with Kyowa Kirin

Zandelisib
Conclusion

Zandelisib: Regaining the Promise of PI3Kδ



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