BLU-782

A highly selective ALK2 inhibitor, designed specifically to target the cause of fibrodysplasia ossificans progressiva

Andrew Garner, Ph.D.

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Disclosures

I am an employee and stockholder of Blueprint Medicines Corporation (Blueprint Medicines)

I will discuss the preclinical characterization of the investigational agent BLU-782, which is being developed by Blueprint Medicines

Forward-looking statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “target” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

In this presentation, forward-looking statements include, without limitation, statements about plans and timelines for the development of BLU-782 and the ability of Blueprint Medicines Corporation (the “Company”) to implement those preclinical and clinical development plans; the potential benefits of BLU-782 in treating patients with fibrodysplasia ossificans progressiva; plans and timelines for regulatory submissions, filings or discussions; and the Company’s strategy, business plans and focus. The Company has based these forward-looking statements on management’s current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks, uncertainties and other important factors, many of which are beyond the Company’s control and may cause actual results, performance or achievements to differ materially from those expressed or implied by any forward-looking statements. These risks and uncertainties include, without limitation, risks and uncertainties related to the delay of any current or planned clinical trials or the development of the Company's drug candidates, including avapritinib, BLU-554, BLU-667 and BLU-782; the Company's advancement of multiple early-stage efforts; the Company's ability to successfully demonstrate the efficacy and safety of its drug candidates; the preclinical and clinical results for the Company's drug candidates, which may not support further development of such drug candidates; actions or decisions of regulatory agencies or authorities, which may affect the initiation, timing and progress of clinical trials; the Company’s ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing; the Company's ability to develop and commercialize companion diagnostic tests for its current and future drug candidates, including companion diagnostic tests for BLU-554 for FGFR4-driven hepatocellular carcinoma, avapritinib for PDGFRα D842V-driven gastrointestinal stromal tumors and BLU-667 for RET-driven non-small cell lung cancer; and the success of the Company’s current and future collaborations, including its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. and its collaboration with CStone Pharmaceuticals.

These and other risks and uncertainties are described in greater detail under “Risk Factors” in the Company’s Quarterly Report on Form 10-Q for the quarter ended June 30, 2018, as filed with the Securities and Exchange Commission (“SEC”) on August 1, 2018, and any other filings the Company has made or may make with the SEC in the future. The Company cannot guarantee future results, outcomes, levels of activity, performance, developments, or achievements, and there can be no assurance that the Company’s expectations, intentions, anticipations, beliefs, or projections will result or be achieved or accomplished. The forward-looking statements in this presentation are made only as of the date hereof, and except as required by law, the Company undertakes no obligation to update any forward-looking statements contained in this presentation as a result of new information, future events or otherwise.

Acknowledgements

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Blueprint Medicines thanks the International Fibrodysplasia Ossificans Progressiva Association for providing advisory support

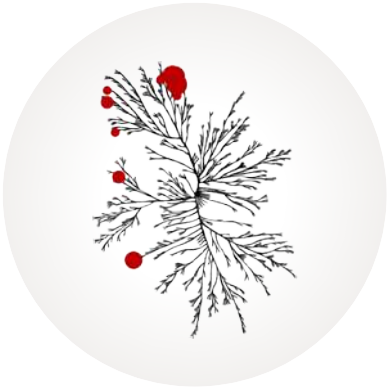
Blueprint Medicines is pioneering a new way of discovering and developing kinase medicines

Highly selective kinase medicines offer potential for improved potency, less off-target activity and increased probability of clinical success

NON-SELECTIVE

SUNITINIB

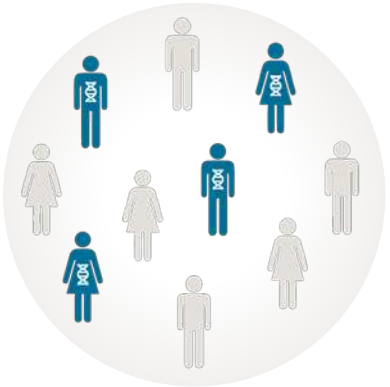
SELECTIVE



AVAPRITINIB

GENOMIC DRIVER

SELECTED PATIENT POPULATION



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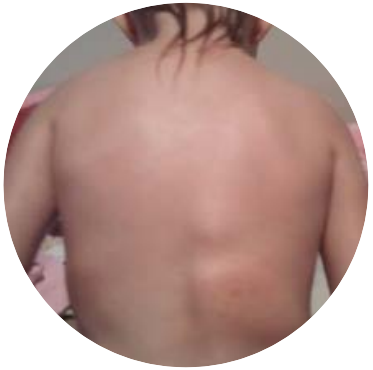
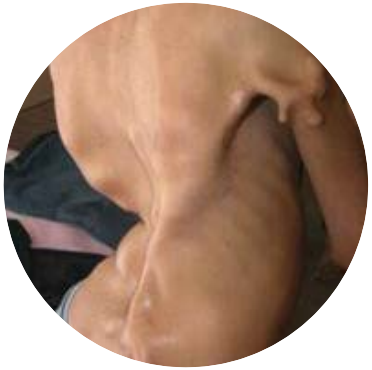
Fibrodysplasia ossificans progressiva (FOP) is caused by mutant ALK2

MALFORMED TOES



TUMOR-LIKE SWELLINGS



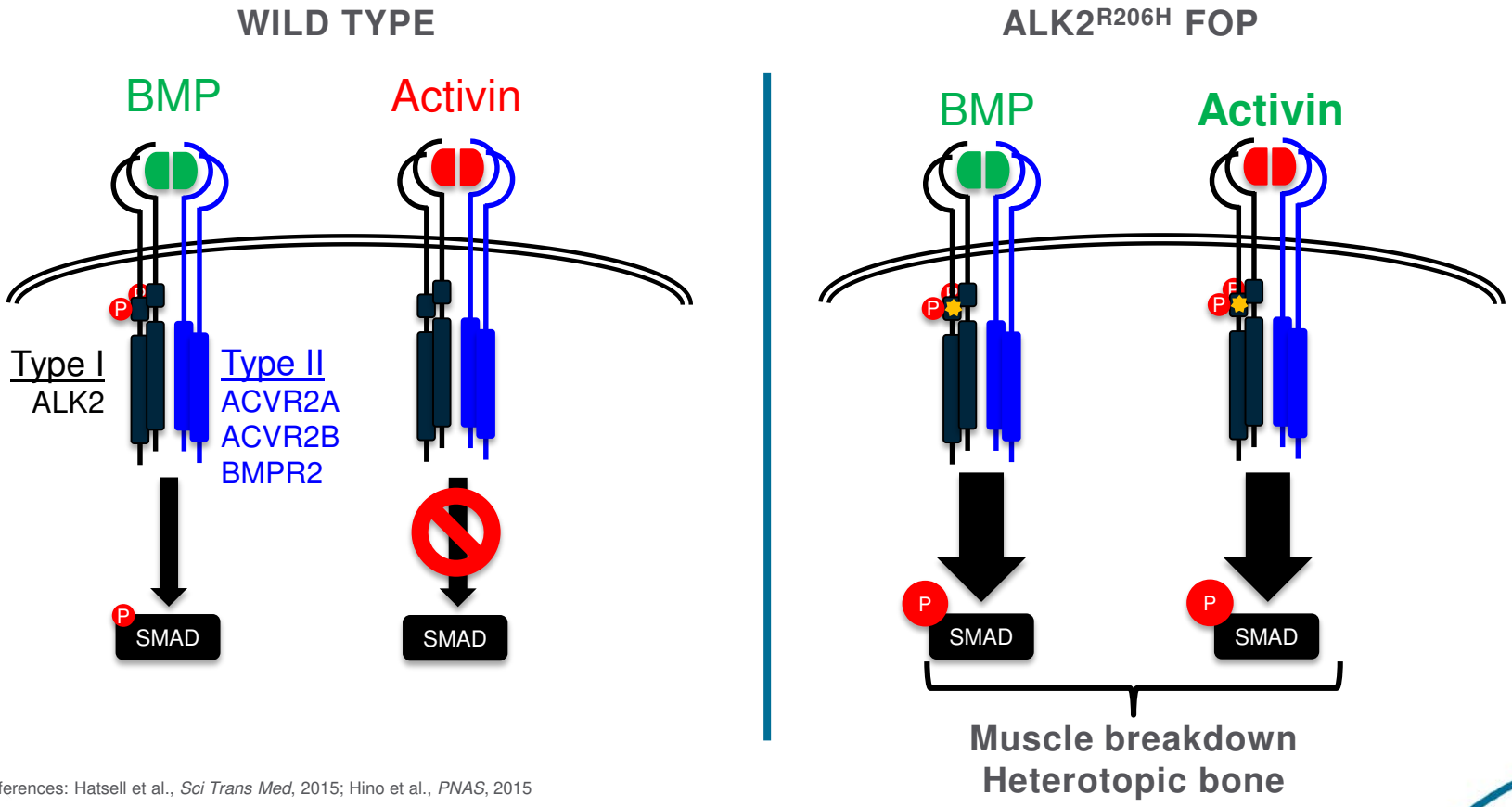
EXTRASKELETAL BONE

PROGRESSIVE INCAPACITATION

- $ALK2^{R206H}$ mutations are found in 100% of FOP patients
  - 85% – 97% are $ALK2^{R206H}$
- $ALK2^{R206H}$ mice recapitulate all the key features of FOP
- Selective ALK2 inhibition targets the underlying cause of FOP

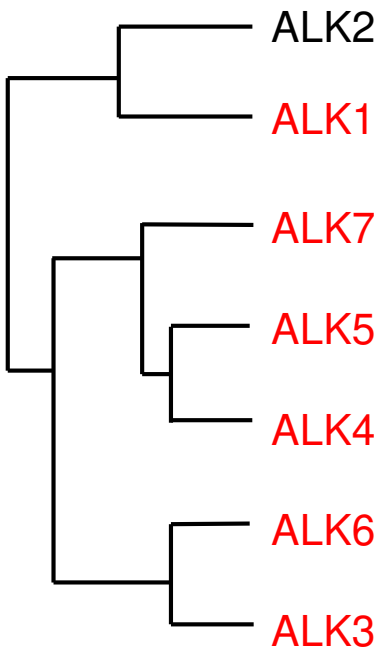
References: Kaplan et al., *Hum Mutat*, 2009; Zhang et al., *Bone*, 2013; Shore et al., *Nat Gen*, 2006; Chakkalakal et al., *JBMR*, 2012

ALK2^{R206H} causes FOP by changing the response to ligands



References: Hatsell et al., *Sci Trans Med*, 2015; Hino et al., *PNAS*, 2015

Selective ALK2 inhibition is important for chronic dosing



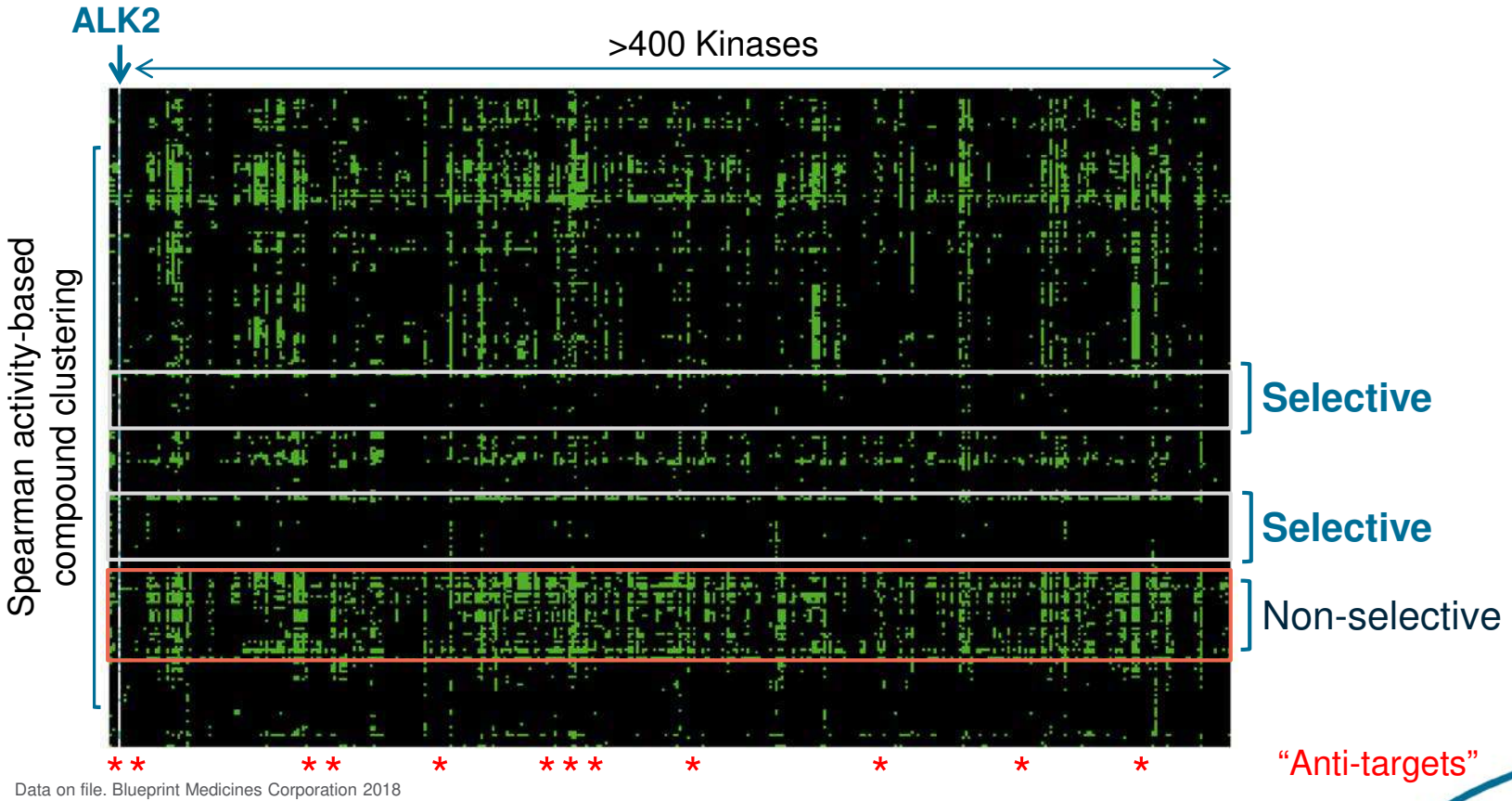
BMP Pathway ALKs: ALK1 / 3 / 6

- ALK1 regulates blood vessels
- ALK3 regulates iron storage
- ALK6 regulates embryonic digit growth

TGFβ Pathway ALKs: ALK4 / 5 / 7

- TGFβ modulates the immune response; ALK4, 5, and 7 inhibition could cause systemic inflammation
- ALK5 inhibition can result in heart valve lesions

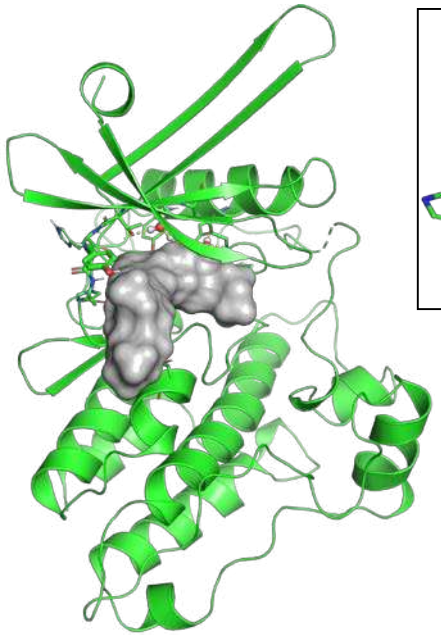
Blueprint's kinase library yielded multiple selective ALK2 start points

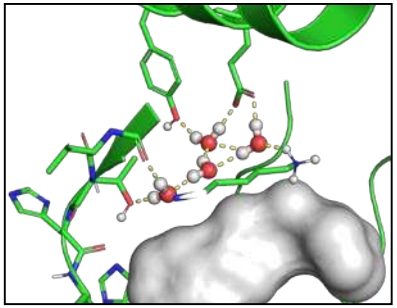


Data on file. Blueprint Medicines Corporation 2018

Structure-based drug design yielded BLU-782, a highly selective ALK2 inhibitor

BLU-782 CRYSTAL STRUCTURE

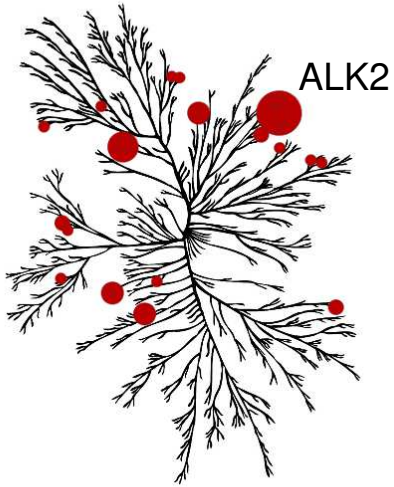




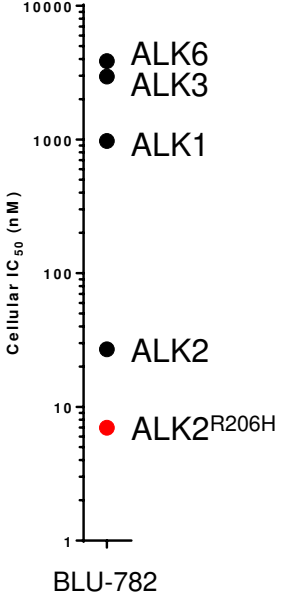
BLU-782 binding preserves a unique ALK2 water network

BLU-782 SELECTIVITY

Biochemical



Cellular



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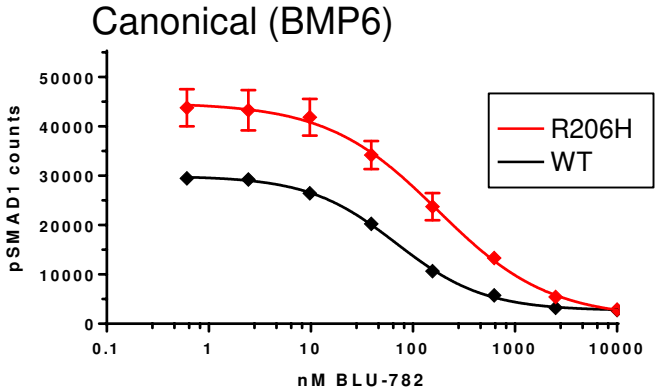
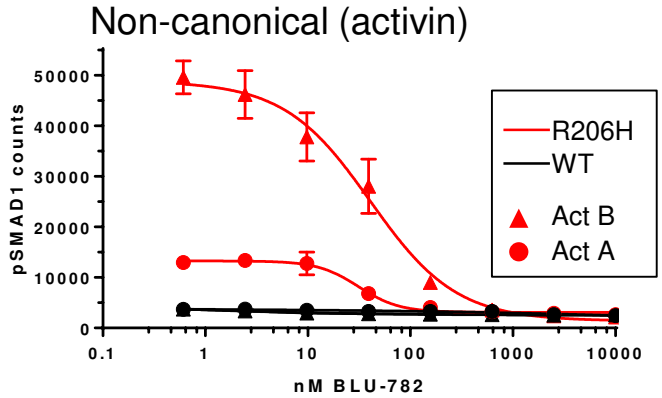
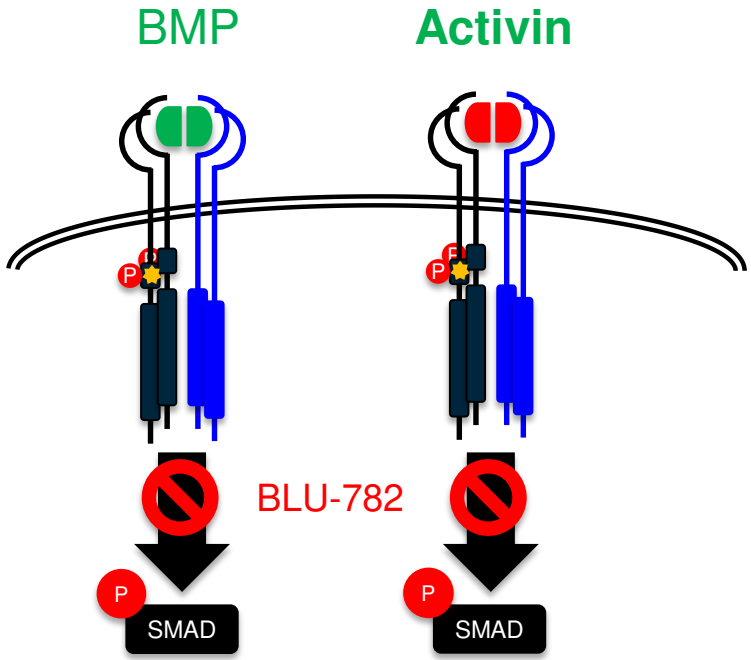
BLU-782 potently inhibits ALK2^{R206H} irrespective of the activating ligand

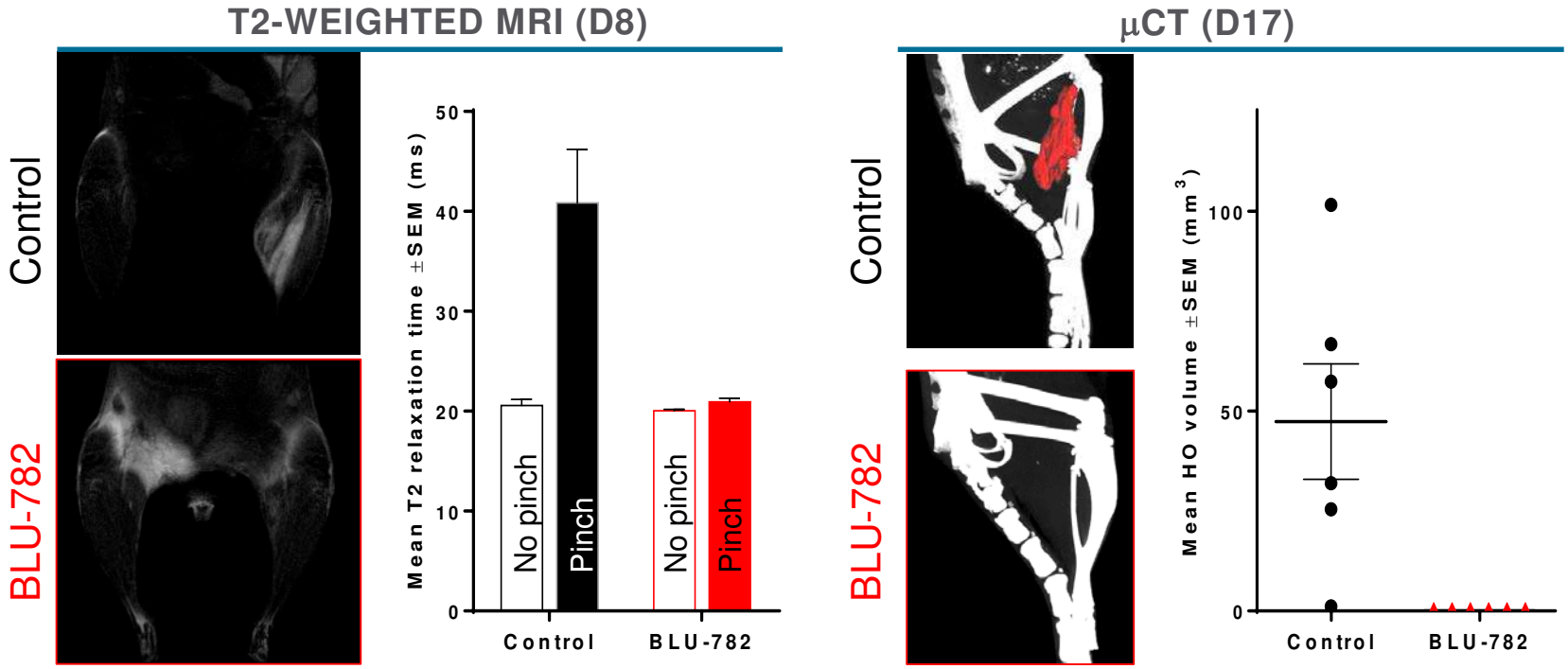






Data on file. Blueprint Medicines Corporation 2018

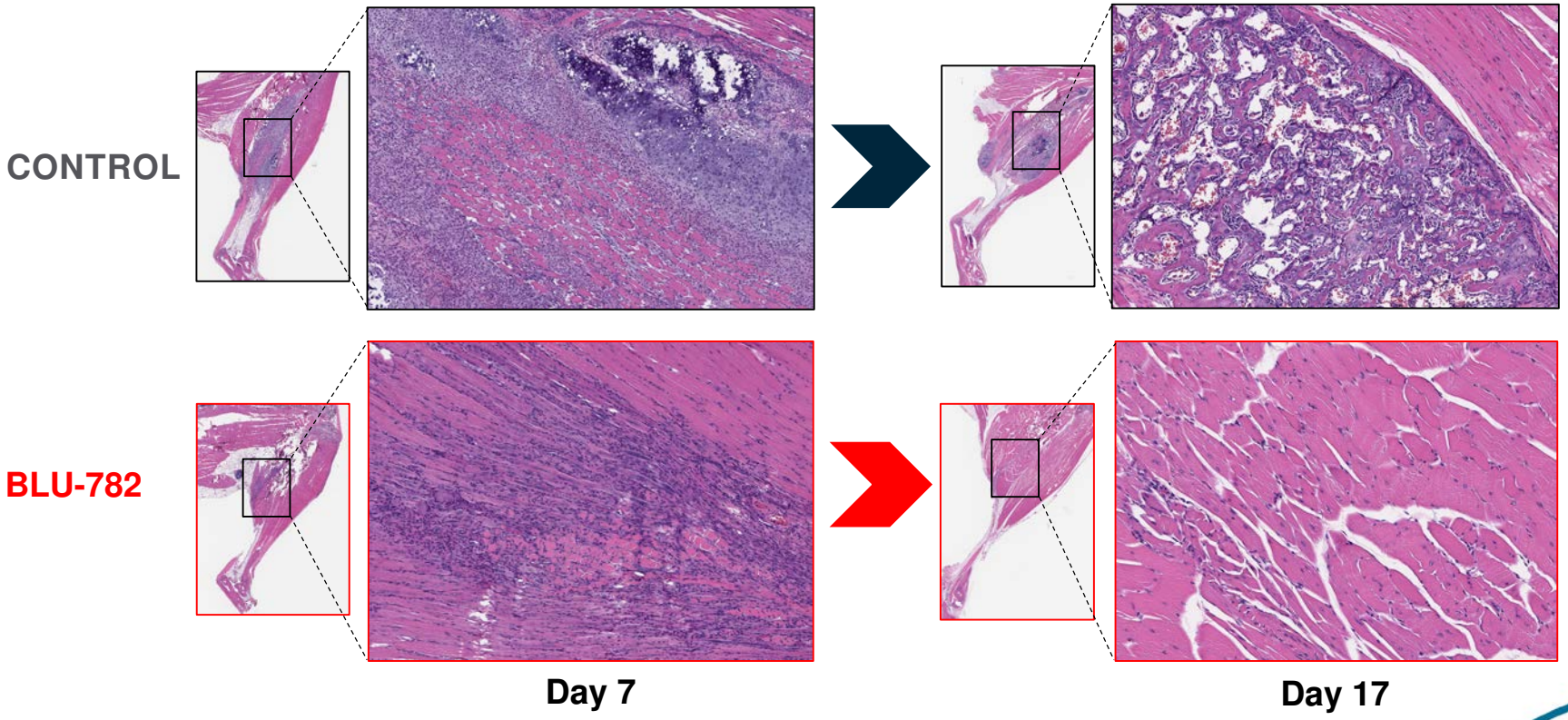
BLU-782 selectively targets the root cause of FOP



BLU-782 prevents injury-induced heterotopic ossification (HO) in ALK2^{R206H} mice

Data on file. Blueprint Medicines Corporation 2018

BLU-782 restores the normal tissue response to muscle injury in ALK2^{R206H} mice



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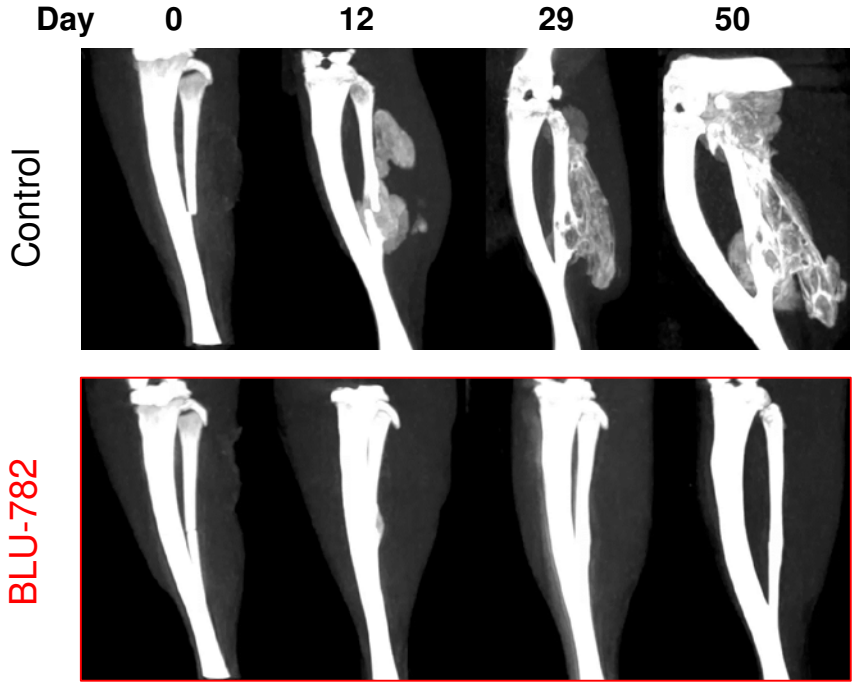
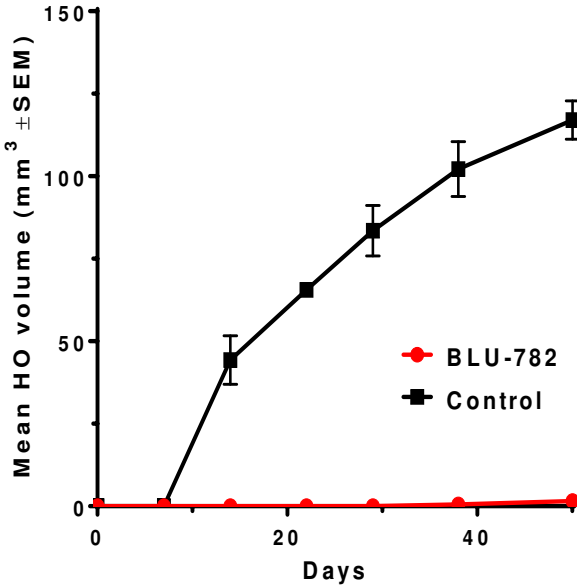
BLU-782 inhibits surgery-induced HO in ALK2^{R206H} mice





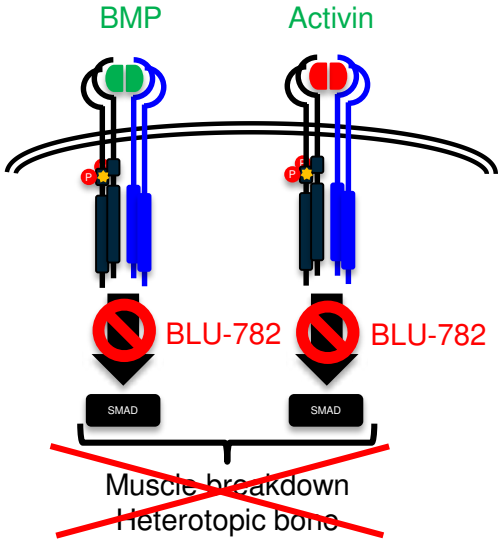
- BLU-782 prevents HO in a fibular osteotomy model in ALK2^{R206H} mice
- BLU-782 does not impact fracture repair or surgical wound closure

Data on file. Blueprint Medicines Corporation 2018

BLU-782- an ALK2 kinase inhibitor specifically tailored for FOP

BLU-782 IS HIGHLY SELECTIVE

BLU-782 TARGETS THE ROOT CAUSE OF FOP



- Plan to file an Investigational New Drug (IND) application for BLU-782 by end of 2018
- Subject to approval of IND application by the FDA, plan to initiate Phase 1 healthy volunteer study in Q1 2019

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