Krystal Biotech

Investor Factsheet | Q1 2020

Medicines for skin diseases and conditions – a gene therapy company

Krystal Biotech, Inc. is a clinical-stage gene therapy company dedicated to developing and commercializing topical and intradermal novel treatments for patients suffering from rare dermatological diseases. Krystal's platform is a patented, fully-integrated gene therapy platform consisting of an engineered viral vector and skin-optimized gene transfer technology to develop treatments for monogenic dermatological diseases with no current effective treatments. Krystal is also expanding the use of its pioneering technology beyond severe monogenic diseases to target and treat other skin conditions.

Investment Highlights

- Pipeline of first-in-class gene therapy candidates for a variety of skin conditions
- Established a patented, fully-integrated HSV-1-based gene therapy platform and a pipeline of clinical and non-clinical effectors to target skin diseases and conditions.
  - > Zero royalty burden
- Use of platform has a number of distinct advantages over other viral gene therapy vectors:
  - > Products may be applied topically in a gel-formulation or injected intradermally directly to the affected skin
  - > HSV-1 has a significant payload capacity allowing for delivery of multiple genes and/or large genes
  - > HSV-1 transduces dividing and non-dividing cells, increasing efficiency of therapeutic gene transfer
  - > HSV-1 is an episomal virus that does not insert itself into, or otherwise disrupt, the human genome. This allows for a ready-to-use chronic application of treatment unlike other customized gene therapy products.
  - > HSV-1 stability significantly minimizes supply chain and logistics issue when compared to other gene therapy treatments
  - > Platform-based products are non-replicating and are diluted by cell divisions, allowing for transient transgene expression
  - > HSV-1 has natural tropism for skin cells leading to high transduction efficiency
  - > Engineering of vector potentially allows for safe repeated administration (re-dosing) of products
  - > Strong patent and IP portfolio protecting STAR-D and STAR-D-based products
- Beremagene geperpavec (B-VEC, previously KB103), the most advanced product candidate, is in development for dystrophic epidermolysis bullosa (DEB), an incurable skin blistering condition caused by a lack of collagen 7 in the skin
  - > Clinical proof-of-concept for STAR-D platform and for B-VEC demonstrated by GEM-Phase I/II clinical trial in adult and pediatric patients with DEB
  - > Top-line data from B-VEC GEM-Phase II clinical trial announced 6/24/19
    - > Final Phase I/II data announced 10/29/19
- Construction of "Ancoris", the first in-house Good Manufacturing Practice (GMP) facility in Pittsburgh PA is complete. Broke ground on a second GMP facility, ASTRA, in Q4 2019.
- Insider ownership (management, employees, directors): Approximately 32% of fully diluted shares outstanding (as of 12/31/19)

Fast Facts

Ticker (Exchange)	KRYS (NASDAQ)
Stock Price (final 5-day moving average)	$60.04
Market Cap	~$1 Bn
Outstanding Shares	17.3 MM
52-Week Range	$18.50 – $66.50
Avg. Daily Volume (90-Day Window)	~154,000
Headquarters	Pittsburgh, PA
Fiscal Year End	December 31
Cash, Cash Equivalents, and Short-Term Investments Position	$193.7 MM
Insider ownership (management, employees, directors)	32% of fully diluted shares outstanding

All figures as of 12/31/2019

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Current Pipeline Opportunities & Development Status

Product	Indication	Discovery	Preclinical	Phase I/II	Phase III	Marketed
B-VEC†¤·Δ‡§	Dystrophic EB					
KB105†¤·‡	TGM1-deficient ARCI					
KB301	Aesthetic Skin Conditions			IND to be filed 2H 2020		
KB104	Netherton Syndrome			IND to be filed 2H 2020		
KB5XX	Chronic Skin Diseases					

†: FDA Orphan Drug Designation;
¤: FDA Rare Pediatric Disease Designation;
·: Fast-track Designation;
Δ: FDA RMAT designation;
‡: EMA Orphan Drug Designation;
§: EMA PRIME Designation.

Lead Therapeutic Candidate: B-VEC

B-VEC is a replication-defective, non-integrating viral vector that has been engineered employing Krystal's fully-integrated gene therapy platform to deliver functional human *COL7A1* genes directly to DEB patients' dividing and non-dividing skin cells. The pivotal Phase III clinical trial of B-VEC is expected to initiate in 1H2020.

- Data from final update of combined phase I/II study in adult and pediatric patients treated with B-VEC showed:
  - 9 out of 10 wounds treated with B-VEC closed completely (100%) following initial administrations of B-VEC
  - The average time to 100% wound closure on the 9 B-VEC treated wounds was 17.4 days (median 14 days)
  - The average duration of wound closure on the 9 B-VEC treated wounds at last measured timepoint was 113 days (median 110 days)
  - The wound that did not close was re-administered B-VEC and closed completely within 7 days following re-administration
    - The wound was originally reported to be open for over 4 years
    - The wound remained closed for over 100 days (and ongoing)
  - Safety data showed that B-VEC was well tolerated, even after repeat administration. No serious adverse events, and no product-related adverse events, were reported. No immune response or blistering was observed around the sites of administration following first and repeat doses. Blood and urine samples collected throughout the study revealed: no viral shedding; no adverse events associated with routine labs (chemistry and hematology); and no antibodies to COL7 were detected

Epidermolysis Bullosa Market Opportunity

- DEB affects ~7 people per 1 million worldwide, 52,000+ cases total (Kho *et al.* Arch Dermatol. 2010 146(6):635-40; Orphanet Report Series Rare Diseases Collection 2018)
- There are no approved treatments for DEB
- Current treatment for DEB is limited to palliative care estimated to cost between $200k – 400k annually

Recent Developments

October 29, 2019

The final update of the Phase I/II clinical trial data for B-VEC is released. Safety data from all of the patients in the combined Phase I/II study demonstrated that B-VEC was well tolerated following initial and repeat dosing. 90% (9 of 10) of wounds closed completely (100% closure) following initial administrations of B-VEC. The average time to 100% wound closure on the nine B-VEC administered wounds was 17.4 days (median 14 days); the average duration of wound closure on these nine wounds at the last measured timepoint was 113 days (median 110 days). One chronic wound, reported open for over four years, closed completely seven days after re-administration of B-VEC. The wound remained closed for over 100 days following the second administration.

October 10, 2019

Krystal announces that the EMA Committee for Orphan Medical Products (COMP) issued a positive opinion on Krystal's application for orphan designation of KB105 for the treatment of transglutaminase-1 (TGM1) deficient autosomal recessive congenital ichthyosis (ARCI).

September 4, 2019

Krystal announces commencement of the GEM-3 study, a phase I/II study of Krystal's second clinical product KB105 for the treatment of transglutaminase 1 (TGM1)-deficient autosomal recessive congenital ichthyosis.

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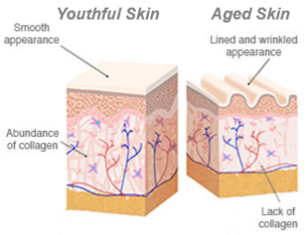
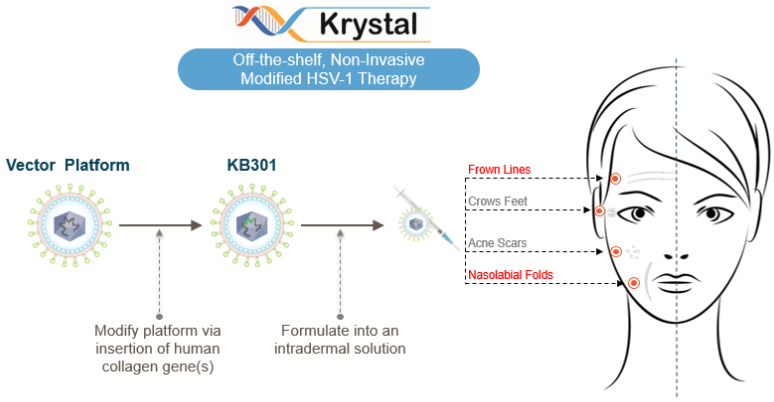
Future Opportunities

Application of fully-integrated vector platform to treat aesthetic defects

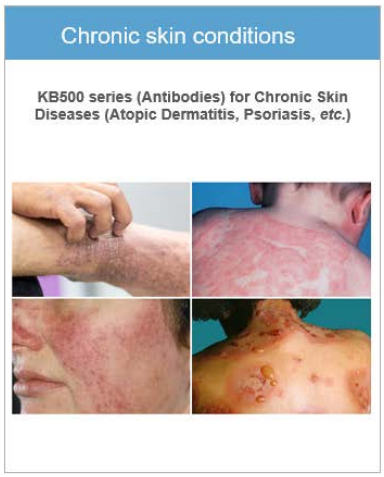


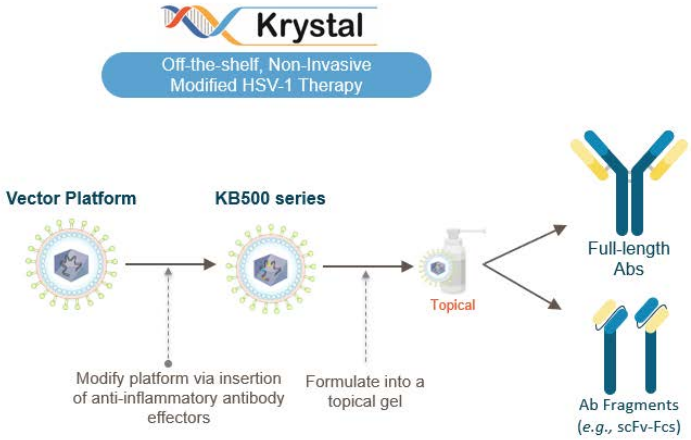
The characteristic features of skin aging are largely due to aberrant collagen homeostasis, resulting in a net collagen deficiency

Fromowitz, J. "Update on Aging Skin"; Florida Society of Dermatology



Application of fully-integrated vector platform to treat complex, chronic skin conditions





Upcoming Milestones

- Commence pivotal phase III trial for B-VEC (DEB) in 1H 2020
- Announce interim clinical readouts for KB105 (ARCI) in 1H 2020
- File IND for KB301 (aesthetics) in 2H 2020
- File IND for KB104 (Netherton Syndrome) in 2H 2020
- Build-out of second GMP manufacturing facility, ASTRA (12-15 months)

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