Krystal Biotech (KRYS) Review: Its Beauty is More Than Skin-Deep

Why We Like Krystal Biotech as a Core Holding

By Hugo Calvin, Lucent Ion LLC

October 15, 2025

Market data:

- Market capitalization (as of 10/14/25): $5.4 billion
- Net cash (debt) (as of end-Q2 2025): $820.8 million
- Enterprise value (EV): $4.6 billion

Summary: Krystal Biotech (KRYS) is a mid-cap, commercial stage biotechnology company focused on the development of genetic medicines for treatment of diseases of unmet medical need. It has one FDA approved product, Vyjuvek (B-VEC), for treatment for dystrophic epidermolysis bullosa (DEB), a rare genetic skin disorder. We think Vyjuvek has a remarkable product profile that will make it the dominant therapy in DEB for years to come and has potential to reach $1+ billion in global revenues. Vyjuvek is in the mid-stages of its U.S. launch and is set to launch internationally.

KRYS fits into our investing theme of owning high quality companies with best-in-class products that can dominate a market. With only one marketed product, KRYS is profitable and cash-flow positive, which mitigates dilution concerns and helps fund a rich pipeline of novel candidates that leverages its vector platform. While not without its controversies and we expect Vyjuvek choppiness in the quarters to come, we think KRYS is a solid name to own over the long-term.

We have a long position in KRYS stock with a price target (PT) of $245. Key tenets of our thesis is below:

- **Vyjuvek has a strong clinical profile in a market with few options**: Vyjuvek (B-VEC) treats the root cause of DEB by restoring collagen type VII, leading to meaningful wound healing – 67% of wounds healed at 6 months in the GEM-1/-2 clinical trials vs. 22% with placebo. Prior to recently approved therapies, treatment of DEB was largely limited to the management of symptoms and secondary complications. Vyjuvek is safe and well-tolerated.

- **We also like Vyjuvek's product profile among the genetic medicine class, differing from 1-time therapies**: Vyjuvek has several attractive product attributes that we think will drive commercial success: Vyjuvek has great gross margins (low-90%'s), it is off-the-shelf (not autologous), non-invasive (easy to administer as a topical gel at home), and redosable (allows for recurring revenues). It does not suffer from the same challenges of 1-time therapies of other genetic medicines, many of which are systemic therapies requiring very high doses, high upfront costs, and have long-term unknown safety risks.

- **We expect Vyjuvek to be the dominant therapy in DEB for years to come:** ABEO's Zevaskyn in recessive DEB (RDEB) is recently approved and notable competitor for large, severe wounds, but we think its launch will be gradual and should not deter Vyjuvek's growth. We think there is a scenario where both products are *complementary* in the market. Longer term, we also think Vyjuvek could have longevity beyond its patent life given the challenges of bringing a generic genetic medicine to market.

- **Our constructive outlook requires continued execution from KRYS management**: Our $1+ billion revenue estimate for Vyjuvek assumes the following: 1) KRYS will find ~1,500 DEB patients in the U.S.

eligible for Vyujvek treatment by 2030 (~50% of their targeted 3,000 estimated total U.S. DEB patients), 2) successful international expansion in EU and Japan, and 3) KB803 (ophthalmic version of B-VEC) success for DEB corneal abrasions. These assumptions are not without risk and requires continued execution from management.

- **Rich pipeline offers upside, but we want to see additional data:** We like that KRYS is advancing a pipeline that leverages its HSV-vector platform. We are keenly interested in KB801 for neurotrophic keratitis and KB707 for non-small cell lung cancer (NSCLC) where early data is promising, but we await further data to validate. Either of these assets could mean $1+ billion additional revenue opportunity, if successful. KRYS' Jeune Aesthetics subsidiary is another call option on the aesthetics market. We have modest expectations for their lung platform in cystic fibrosis (CF) and AATD lung disease for now.

- **We like KRYS' capital structure & disciplined spending:** With respect to KRYS as a business, we like that KRYS has a strong balance sheet & durable cash flows. As of 2Q25, KRYS has had 8 consecutive quarters of positive earnings-per-share (EPS) and are cash flow positive. With $821 million in net cash, KRYS is in a solid cash position. KRYS also has a track record of disciplined spending, with high operating margins (~41% in 2Q25) relative to its peers (~10-15%).[1]

Our Take on KRYS Valuation

Year-to-date (YTD), KRYS has been largely in-line with the XBI, both gaining +17-20%. At its current EV of ~$4.6 billion (as of 10/14/25), we recognize that KRYS is not cheap solely on its Vyjuvek business. Our $245 PT is DCF-based and assumes optimistic (but reasonable) assumptions about Vyjuvek's launch and the pipeline. On an EV/sales (2026) basis, KRYS trades at ~8.1x, which is below its peer average[2] of ~11.3x and far below other genetic medicines names, such as CRISPR Therapeutics (CRSP) which trades at ~36x. We think it is reasonable to believe KRYS' multiple can at least move to its peer average, which would imply an EV of ~$6.4 billion (or ~$238/share based on market cap).

As part of our investment philosophy, we like to own high quality companies with solid assets that can own a market, and hence our long position in KRYS.[3] We recognize that the stock has run up recently, but it's been largely in-line with the XBI. If we see weakness in the stock, potentially at a volatile earnings report (Q3 revenues already expected to be down sequentially) or data updates from its lung platform by year-end, we may add to our position provided our fundamental thesis on KRYS remains intact.

Upside to our $245 PT may come from KRYS' pipeline assets, or from a potential acquistion. We've mentioned KB801 for neurotrophic keratitis and KB707 for NSCLC are $1+ billion potential revenue opportunities, if successful - we model $500 million peak revenues for either one of these assets at 50% risk-discount. The Jeune's Aesthetics subsidiary is another call option, if successful.

If our thesis is wrong, our downside PT is $85. This would imply an EV of ~$1.8 billion and makes some punishing assumptions to the Vyjuvek launch and the pipeline. While we do not expect it to reach these levels, one must always be prepared for such an outcome.

[1] Average of select group of genetic medicine companies
[2] See Valuation & Financials section for a table of peers used the calculation of EV/sales (2026)
[3] As of the date of this publication, our average cost basis is $146.86

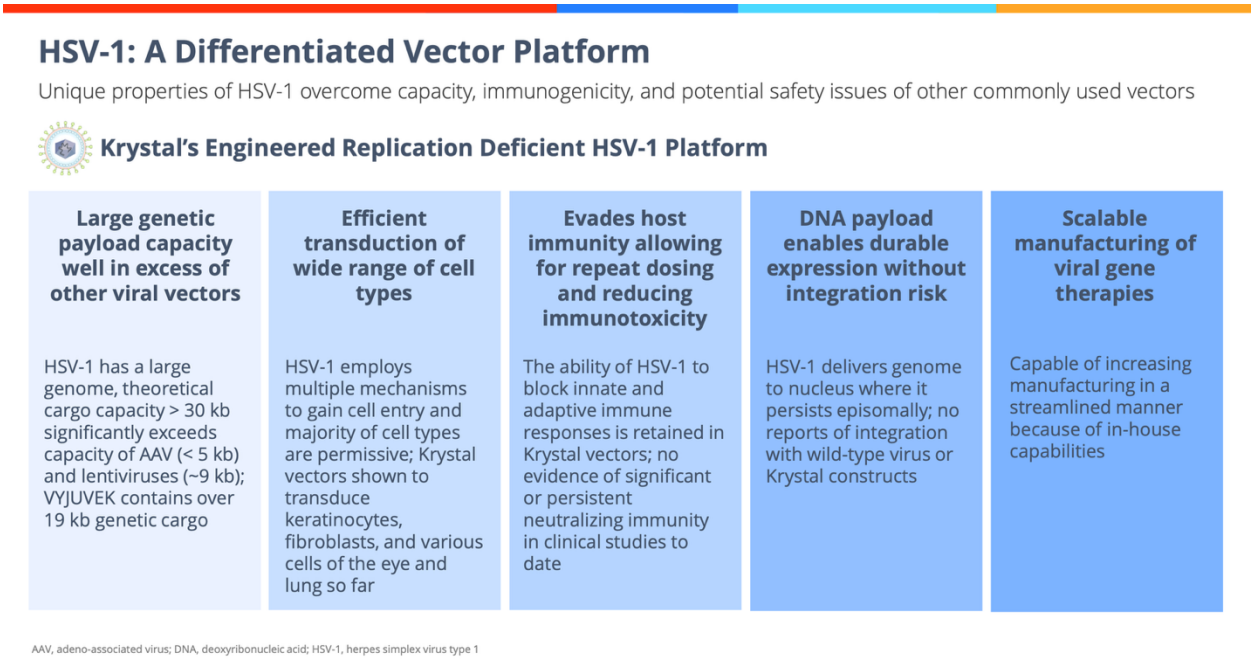
Executive Summary

Overview of Krystal Biotech

Krystal Biotech is a Pittsburgh-based commercial-stage biotechnology company focused on the development of genetic medicines for treatment of diseases of unmet medical need. They leverage their proprietary gene delivery platform based on engineered herpes simplex virus-1 (HSV) to develop their therapeutic products and pipeline candidates that can deliver transgenes to target cells to treat diseases in dermatology, ophthalmology, pulmonology, oncology, and others. They have one FDA approved product, Vyjuvek for treatment of dystrophic epidermolysis bullosa (DEB) in the mid-stages of launch. While KRYS' focus is on product candidates for diseases of unmet medical need, they've also incorporated Jeune Aesthetics, Inc., a wholly owned subsidiary, in 2019 leveraging the same technology platform to pursue candidates for aesthetic skin conditions.

Many gene therapy companies use the adeno-associated virus (AAV) or lentiviruses as their vector to deliver their respective therapeutic payload. For AAV, this includes many marketed gene therapies today such as BMRN's Roctavian for severe hemophilia A and SRPT's Elevidys for Duchenne Muscular Dystrophy (DMD). For lentiviruses, this includes bluebird bio's (now Genetix Biotherapeutics) Zynteglo for beta-thalassemia and Skysona for cerebral adrenoleukodystrophy (CALD). KRYS has dedicated its focus on the *herpes simplex virus-1 (HSV-1)* as its vector for gene delivery. A full comparison of each of these vectors is beyond the scope of this report, but KRYS outlines the key advantages of HSV-1 (Figure 1) and they have employed the vector successfully in Vyjuvek. Others HSV-1 vector-based products include Amgen's (AMGN) Imlygic (acquired from BioVex Group, Inc. In 2011) and Replimune's (REPL) RP1 in clinical development, both for treatment of melanoma.

Figure 1. Summary of Key Advantages of KRYS' HSV-1-based Vector Platform



Source: Krystalbio.com

Overview of DEB

What is dystrophic epidermolysis bullosa (DEB)?

Dystrophic epidermolysis bullosa (DEB) is a rare, genetic skin disorder caused by caused by mutations of the *COL7A1* gene which is a key structural protein to the skin's basement membrane zone, leading to defective anchoring fibrils that secure the epidermis to the dermal layer. This lack of functional anchoring fibrils leads to fragile skin and painful blistering upon minor trauma. Blistering can occur from birth and early infancy, and lead to inflammation, chronic wounds, infection, and scarring. At times, scarring can lead to deformities (pseudosyndactyly). The fragility of the skin of DEB children is often likened to the delicate nature of a butterfly's wings, and hence the children are at times referred to as "Butterfly Children."[4]

[4] ebresearch.org

Figure 2. Wounds of a dystrophic epidermolysis bullosa (DEB) patient.

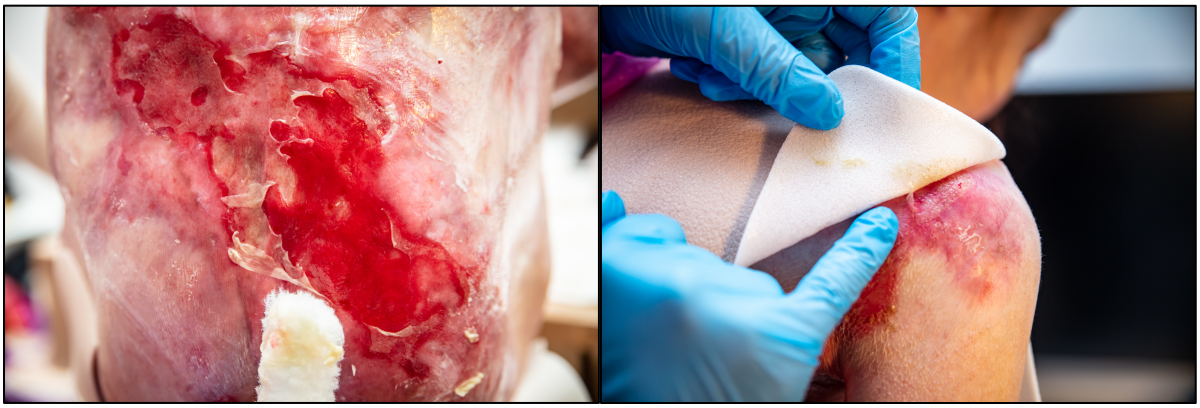


Figure 3. Wrapping of the wounds of the foot of a DEB patient. Extreme scarring can lead to deformities in the hands and feet (pseudosyndactyly).

DEB falls under the broader category of epidermolysis bullosa (EB) and is very rare. The incidence of DEB is ~6.65 per 1 million live births, and the prevalence is ~3.26 per 1 million people,[5] but estimates can vary widely in the literature. The prevalence rate of ~3.26 per 1 million people implies a little under 1,200 patients from the current U.S. population size, which corresponds well to KRYS' estimate of identified DEB patients in the U.S. determined by claims and field force data.[6] KRYS believes there may be as many as 3,000 patients in the U.S. (more on this later).

[5] Fine, J.-D. et al. *JAMA Dermatol*. 2016, 152:11, 1231-1238

[6] KRYS corporate deck (July)

There are 2 types of DEB:

- **Recessive DEB (RDEB):** RDEB is generally more severe due to null variants or out-of-frame insertions/deletions leading to little to no functional protein. Blistering can occur throughout the body, including the mucosal areas. RDEB patients typically have higher risk of developing aggressive squamous cell carcinoma (SCC), which can become metastatic and fatal. RDEB is considered rarer than DDEB, likely in the 1:1 to 1:2 ratio range depending on region, due to its autosomal recessive inheritance. The average life expectancy for an RDEB patient is age thirty.[7]

- **Dominant DEB (DDEB)**. DDEB is considered milder, and symptoms may be limited to high-friction areas, such as the hands, feet, knees, and elbows. DDEB typically involves heterozygous missense mutations exerting a dominant-negative effect (mutant protein interferes with collagen assembly, leading to reduced function of the anchoring fibrils), hence the milder phenotype. DDEB makes up the balance of the DEB population and is considered more common than RDEB.

Management of DEB

There is no cure for DEB. Prior to more recently approved therapies, treatment of DEB was largely limited to the management of symptoms and secondary complications. This includes trauma prevention, wound care, treatment of infections, managing the itch and pain, wrapping of hands and feet, and early detection and treatment of squamous cell carcinoma (SCC).[8] More recently FDA approved options for DEB include KRYS' Vyjuvek, ABEO's Zevaskyn (specific to RDEB), and Chiesi's Filsuvez.

What is Vyjuvek (B-VEC)?

Vyjuvek (beremagene geperpavec, or B-VEC is an FDA approved genetic therapy for treatment of wounds from both the recessive and dominant forms of dystrophic epidermolysis bullosa (DEB). It uses a replication-defective herpes simplex virus (HSV-1) vector to deliver the *COL7A1* gene directly to skin cells in DEB wounds, restoring the production of type VII collagen and anchoring fibrils, thereby helping to secure the epidermis to the dermal layer of DEB patients. Vyjuvek was approved in May 2023 based on supportive data from GEM-1/-2 and GEM-3 clinical studies, with additional safety data from an open-label extension (OLE) study in younger patients.

A high-level comparison of the FDA approved treatments for DEB is summarized below.

[7] ebresearch.org

[8] Tang, et al. *Orphanet J of Rare Disease* 2021, 16:175

Table 1. Comparisons between FDA-approved treatments for DEB (adapted from Grok):

Parameter	Vyjuvek (Krystal Biotech)	Zevaskyn (Abeona Therapeutics)	Filsuvez (Chiesi Farmaceutici)
Therapy Type	Topical, redosable gene therapy (HSV-1 vector-based)	Autologous cell-based gene therapy (ex vivo, retroviral vector)	Topical gel (plant-based, birch triterpenes)
FDA Approval Date	May 2023	April 2025	December 2023
Indication	Wounds in patients ≥6 months with recessive or dominant DEB (*COL7A1* mutations)	Wounds in adult and pediatric patients with recessive DEB (RDEB)	Partial-thickness wounds in patients ≥6 months with junctional or dystrophic EB
Mechanism of Action	Delivers two functional *COL7A1* gene copies via HSV-1 vector to produce type VII collagen	Uses patient's skin cells engineered ex vivo to express functional *COL7A1*, applied as sheets	Promotes wound healing via birch triterpenes; exact mechanism unclear
Administration	Topical gel, applied weekly by healthcare professional (clinic or home)	Surgical application of gene-corrected skin sheets (single application)	Topical gel, applied to wounds
Clinical Trial Data	**GEM-3 (Phase 3)**: 67% of wounds completely healed at 6 months vs. 22% placebo ($p<0.05$). Secondary endpoint: 71% complete wound healing at 3 months. Pain reduction observed	**VIITAL (Phase 3)**: 81% of wounds showed ≥50% healing at 6 months vs. 16% control. 16% complete healing vs. 0% control. Pain reduction by >3 points (Wong-Baker FACES scale) vs. <1 point control	**EASE (Phase 3)**: Increased probability of wound closure compared to placebo (specific healing rates not detailed in sources). Anti-inflammatory and antimicrobial properties noted

Note: The clinical data in this table are not from head-to-head clinical trials and cross-trial comparisons should be approached with caution.

Source: Vyjuvek, Zevaskyn, and Filsuvez prescribing information

Table 1 (continued). Comparisons between FDA-approved treatments for DEB (adapted from Grok):

Parameter	Vyjuvek (Krystal Biotech)	Zevaskyn (Abeona Therapeutics)	Filsuvez (Chiesi Farmaceutici)
Safety Profile	Well-tolerated; no serious treatment-related adverse events reported. Modified HSV-1 does not replicate in normal cells	Well-tolerated; procedural pain and itching in <5% of patients. Potential risk of infection from human/animal materials; long-term cancer monitoring recommended	Generally safe; specific adverse events not detailed in sources. No gene therapy-related risks
Cost	~$631,000 per year (weekly dosing)	$3.1 million for up to 12 sheets (single application)	Not specified in available data
Key Advantages	Non-invasive, redosable, suitable for smaller/recurring wounds, home administration possible	Single application, effective for large chronic wounds, long-term healing (years)	Non-gene therapy, potentially simpler to administer, approved for both JEB and DEB
Key Limitations	Requires weekly application, high lifetime cost for chronic use	Surgical procedure, limited to RDEB, high upfront cost, cancer risk monitoring	Mechanism less targeted, limited data on long-term efficacy
Availability	Available in the US since Q3 2023; recent approvals in EU & Japan	Available in the US from Q3 2025 via Qualified Treatment Centers	Available in the US since Q1 2024; EU approval since June 2022

Note: The clinical data in this table are not from head-to-head clinical trials and cross-trial comparisons should be approached with caution.
Source: Vyjuvek, Zevaskyn, and Filsuvez prescribing information

Why We Like Vyjuvek as a Treatment for DEB

Vyjuvek has several aspects of its clinical & product profile that we think will help take it to $1+ billion annually in global revenue:

- *Vyjuvek has a strong clinical profile and addresses the underlying pathophysiology of disease*: Prior to Vyjuvek, treatment of DEB was largely limited to supportive care, managing the symptoms and secondary complications. Vyjuvek works by helping the cells produce the key missing structural protein, collagen type VII, thereby addressing the underlying pathophysiology of disease. Clinical data from the pivotal trials is strong, in our view – in GEM-3 clinical trial, 67% of wounds achieving complete healing at 6 months vs. 22% in placebo (a high bar) is very clinically meaningful for these patients. Vyjuvek is safe and well-tolerated.

- *Its gross margins are excellent:* In 2Q25, KRYS reported gross margins of ~93% for Vyjuvek (~94% in 1Q25), which we think are excellent for a genetic medicine – close to small molecule margins. This partially stems from its local administration to the DEB wound, unlike other gene therapies like BMRN's Roctavian and SRPT's Elevidys which are systemic requiring ultra-high doses (>1E13-14 vg/kg). Vyjuvek is a topical therapy administered directly to the local DEB wound once a week until closure.

- *It is non-invasive and re-dosable:* Vyjuvek treatments can lead to complete & durable wound closures[9]. However, the half-life of collagen type VII may be as short as ~30 days[10] to a few months. Therefore, even if closure was achieved from initial treatment, as the patient resumes their daily activities the wound may reopen or the patient may suffer from new wounds elsewhere, necessitating ongoing applications. Thus, from a *commercial* standpoint, unlike other gene therapies that are 1-time treatments, Vyjuvek can be a recurring revenue stream.

- *It is an off-the-shelf product:* Vyjuvek is simple to administer relative to many other cell and gene therapies - it is applied topically to the wound via a gel. It requires no other regimens with treatment, like lymphodepleting or corticosteroid prophylactic regimens required by other cell and gene therapies, some of which require hospital administration. The recent Vyjuvek approval in Japan in July goes further and allows for administration at home by the patients or their family members. The U.S. label was revised shortly after in September that also allows for application by patients and caregivers, allowing for full flexibility when it comes to applying the therapy.

- *It has no black box warning, REMS, or post-marketing requirements*. Vyjuvek has no black box warning or REMS, meaning fewer impediments to market uptake. No post-marketing requirements means no long-term drag on R&D expenses.

- *Vyjuvek should have market durability*: We think it is unlikely as a genetic medicine that Vyjuvek will face generic competition when its patents expire in 2036.[11] We think this is unlike small molecules, where generics generally enter a market once the drug's main patent expires and its revenues can drop by >90%. Furthermore, aside from recently approved ABEO's Zevaskyn (more discussion on that below), we don't see any meaningful competitors in clinical development that would disrupt its market share. In our view, from a KRYS valuation perspective, this justifies including a terminal value.

We Think Vyjuvek is Unique in the Class of Genetic Medicines that have Faced Significant Commercialization Challenges: From a market perspective, given the attributes above, we believe Vyjuvek is unique in its class of genetic medicines that have suffered commercialization challenges. We highlight two examples: 1) in August 2024 BioMarin announced a focused strategy for Roctavian, a gene therapy for the treatment of severe hemophilia A, where it noted that it would focus its commercialization efforts in the U.S., Germany, and Italy, where the therapy is approved and reimbursed. Despite BMRN's efforts since then, Roctavian sales were still only $9 million in 2Q25.[12] 2) VRTX/CRSP's Casgevy, a genetic medicine leveraging CRISPR technology, was FDA approved in December 2023 for treatment of sickle cell disease, and later for treatment in beta-thalassemia. Despite being nearly two years on the market, Casgevy sales were $30 million in 2Q25 and only $10 million for FY 2024.[13]

Many of these genetic medicines offer significant therapeutic value to patients – but that is not the issue. Many of them require immunosuppressive regimens, have complex logistics, are costly (in the millions per treatment), administered in-hospital, and/or approved in markets with an already established standard of care.

---

[9] Marinkovich, M. P. et al. *Am. J. Clinical Dermatology* 2025, 26, 623-635

[10] Kühl, T. et al. *J. Invest. Dermatol*. 2016, 136(6), 1116-1123

[11] KRYS 10-K filing (2024)

[12] BMRN 2Q25 press release (8/4/25)

[13] VRTX 2Q25 presentation

Vyjuvek has Potential to Expand into DEB with Ocular Manifestations: Vyjuvek is topically administered directly to the DEB wounds on the skin, and therefore there are opportunities to address areas of the body also impacted by the disease, such as mucosal areas: the eye, oropharynx, esophagus, and rectum. KRYS is investigating KB803, a redosable, ophthalmic administered version of B-VEC designed to address the DEB complications in the eye, such as corneal abrasions. There are no therapies approved to address ocular involvement – standard of care is supportive wound care to prevent scarring that can ultimately lead to blindness. There is mechanistic rationale for investigating B-VEC for corneal abrasions, given structural similarities between the skin and the cornea that rely on collagen type VII to anchor the epithelium of the eye.

Supportive data comes from one case study in a 13-year-old male DEB patient complicated by recurrent cicatrizing conjunctivitis, investigating ophthalmic administration of B-VEC on a compassionate-use basis.[14] This patient had multiple symblepharon lysis surgeries in the left eye, and the condition of his right eye was deteriorating. This patient was treated in the right eye with KB803 following symblepharon lysis surgery. This patient experienced complete healing of the epithelium 8 months after the surgery and regular administration of KB803. *Importantly, KB803 led to marked improvement in vision acuity, from hand motion before surgery to 20/25 vision without correction at 8 months after surgery*. This is a remarkable improvement given previously before treatment he was deemed legally blind.

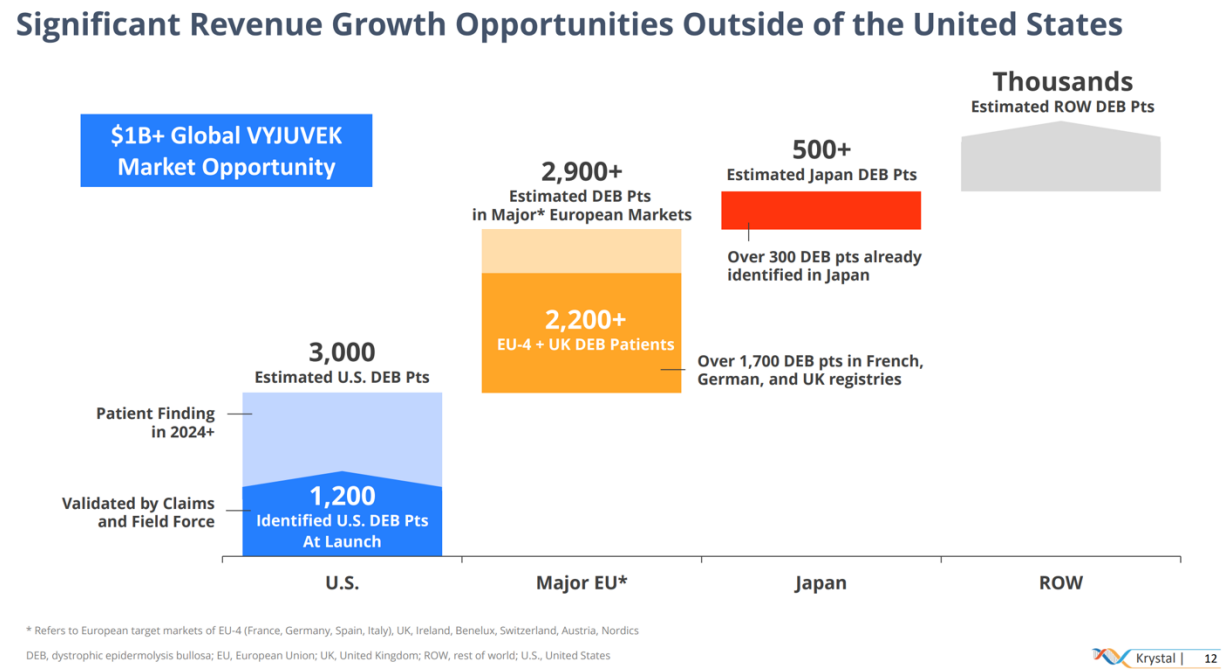
We note that this is a study with only an *n* of 1. We typically like to see more confirmation of clinical impact in a greater number of patients. There are other limitations to the study, including not having an untreated control. We still have many questions. But in this case, the mechanistic rationale is strong, and the vision improvement experienced by this patient is so stark, that we understand KRYS' decision to move quickly into a pivotal trial.

KRYS announced that the first patient has been dosed with KB803 in the Phase 3 IOLITE pivotal study in June 2025. They have not specifically guided to topline data but given that the first patient was dosed in 2Q25 and the trial size is ~15-30 patients, we would anticipate enrollment to complete soon with data sometime in ~mid-2026 on a 24-week primary endpoint. KRYS estimates over 50% of patients with RDEB suffer from ocular complications. We assume KB803 can be approved in 2027, and we estimate incremental global peak KB803 revenue of ~$50 million (with 50% risk-discount). We will adjust our estimates when more information about KB803 about its clinical & product becomes available.

We Think $1+ Billion in Global Revenue Potential for Vyjuvek is Achievable: To summarize, we agree with KRYS in that Vyjuvek has potential to earn $1+ billion annually in global revenue. We think Vyjuvek has the attributes that make it poised to be the leading global go-to treatment option for patients with DEB. We'd argue KRYS is still in the relatively early stages of the Vyjuvek launch in the U.S., and with the recent approvals in Europe (April 2025) and Japan (July 2025), international expansion is underway. KRYS' prevalence estimates for DEB are shown in Figure 4, and they believe the true prevalence in each of the geographies may be greater than currently estimates. Lastly, we are optimistic on its opportunity for expansion into DEB with ocular complications that can leverage its existing sales teams, the physicians and patients.

[14] Vetencourt, A. T. et al. *N Engl J Med*, 2024, 390, 530-535

Figure 4. DEB prevalence estimates from KRYS presentation.



Source: Krystalbio.com

Where We See Risk to Our Thesis

Vyjuvek's march towards $1+ billion annually in global revenue is not without risk. We outline the key risks below:

DEB is Ultra-Rare, and its True Prevalence Seems Unknown: DEB is a *very* rare genetic disorder. The prevalence of DEB is estimated to be 3.26 per 1 million people,[15] which from the current U.S. population size corresponds to a little under 1,200 patients. KRYS also estimates ~1,200 cases in the U.S., as identified by claims and field force data. Internationally, KRYS estimates ~2,200 cases in Europe and ~300 patients in Japan - so, ~3,700 total patients worldwide. So, this is a limited total addressable market (TAM), indeed. As we've said, we prefer therapies that can dominate a market, even if small, rather than those trying to weave themselves into a crowded one.

KRYS believes there could be unidentified DEB patients - the total TAM therefore could be larger than currently estimated. So instead of ~3,700 total DEB patients worldwide there could be as many as ~6,400+, and even "thousands" more from other countries (~9,000 globally, per KRYS presentation). So, what is the true DEB prevalence? Stating the obvious, this impacts Vyjuvek's TAM, and hence KRYS' overall valuation.

Some literature suggest that this could indeed be the case. One group of researchers estimates upwards of 3,850 in the U.S. using a genetic modeling approach to estimate allele frequency,[16] and this is in-line with KRYS estimate of ~3,000 patients. Another group looked at the epidemiology of EB in the Netherlands extracted from

[15] Fine, J.-D. et al. *JAMA Dermatol*. 2016, 152:11, 1231-1238

[16] Eichstadt, S. et al. *Clinical, Cosmetic and Investigational Dermatology* 2019, 12, 933-942

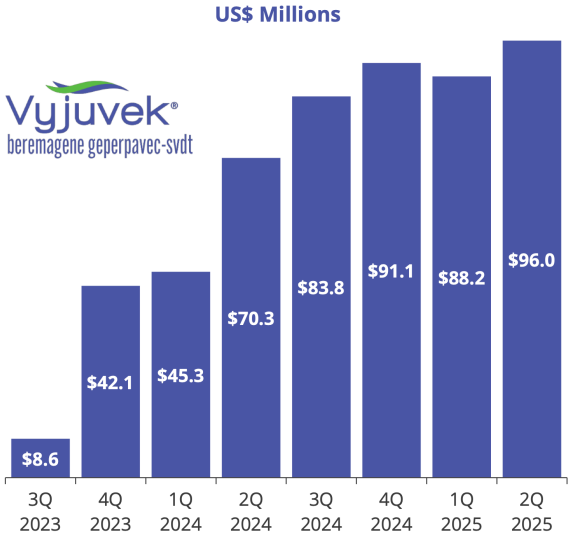
the Dutch EB Registry, and noted that the epidemiological outcomes of EB in the Netherlands are higher than in other countries, which could be attributed to a high detection rate in a well-organized set-up.[17] The authors note this could imply broadly that EB is more common than previously estimated.

KRYS has noted they intend to find these patients. *The key risk here is that these excess DEB patients beyond the registries may not be found – which could limit the TAM*. Our model conservatively assumes they find only half of their target patients, peaking at ~1,500 total DEB patients (and thereafter growing with population). This is only ~25% above the 1,200 number, so we don't think this is a big stretch – but it does depend on KRYS finding these patients. We assume peak penetration of ~70% by 2032 and onward, modestly higher than their current share (KRYS set a goal reaching ~60% share at 2 years following approval).

As the Vyjuvek Launch Matures, its Ramp Could Get Lumpy: KRYS already noted that Q3 Vyjuvek revenues will be lower than Q2, marking a sequential decline, with a return to growth in Q4 as their salesforce expansion efforts begin to take effect. Compliance, which currently stands at 82% as of end-2Q25 and already expected to trend down over the next few quarters, could moderate further in the coming years as the patient mix of severe DEB patients incorporates more mild-to-moderate ones. So, there may understandably be fears that Vyjuvek's growth curve is already flattening (Figure 5). We think KRYS management is still getting a feel for their patients' behavior patterns as they navigate this novel market.

From our perspective, drug launches rarely grow in a straight line, even successful ones. The quarter-to-quarter volatility is furthermore exacerbated by the fact that DEB is a *very small* market, so any minute changes to the treated pool or patient behavior can wildly swing Vyjuvek uptake in any given quarter. Taking a longer-term view, so long as Vyjuvek's product profile remains (with no surprises, such as a treatment-related patient death or long-term safety event) and no major shifts in market dynamics, we are comfortable holding KRYS through volatility and give the management team the chance to execute.

Figure 5. Vyjuvek quarterly U.S. sales since launch.



Source: Krystalbio.com

[17] Baardman, R. et al. *JEADV*, 2021, 35, 995-1006

Competitive Impact from ABEO's Zevaskyn Deserve Watching, But We Think its Launch Will Take Time: ABEO's Zevaskyn (prademagene zamikeracel) was recently FDA approved in April 2025 for RDEB. It is a 1-time surgical application of gene corrected-skin sheets based on supportive data from the Phase III VIITAL program (Table 2). The first patient is expected to be treated with commercial Zevaskyn in 3Q25.[18] We think having another treatment option is a big win for RDEB patients.

The Zevaskyn launch deserves watching given its potential impact on KRYS' Vyjuvek's market trajectory. Firstly, there may not be huge overlap between Vyjuvek (approved for RDEB and DDEB) and Zevaskyn (approved for RDEB only) early in its launch. Secondly, we think the Zevaskyn's launch will be gradual. As an autologous therapy, Zevaskyn requires complex administration, including biopsy sample procurement, manufacturing of the skin sheets requiring genetic modification, surgical procedure, and hospital stay and discharge. Manufacturing time for the Zevaskyn skin sheets is ~25 days, but the total turnaround time from biopsy to treatment and ultimately payer reimbursement we believe could be several months. Furthermore, the cost per application of Zevaskyn (of up to 12 sheets) is not cheap at $3.1 million (WAC price). ABEO has noted on their conference call that they initially expect to treat ~4 patients / month, ramping up to ~6 patients / month by ~YE 2025 / early 2026 and potentially up to ~10 patients per month by mid-2026.

Even within RDEB, there is an argument that Vyjuvek and Zevaskyn could be *complementary* in the market. Zevaskyn could be reserved for large, chronic wounds of RDEB (such as large wounds >20 cm^2 and chronic wounds open >6 months, as in the Phase 3 VIITAL trial), while Vyjuvek could be used for all other mild and moderate cases in RDEB and DDEB. This would be a decent outcome for both products. But even in this scenario, we still lean in favor of Vyjuvek.

Lastly, ABEO's Zevaskyn uses a retroviral vector to insert the functional *COL7A1* gene into the genomic DNA of autologous keratinocytes and fibroblasts *ex vivo* and does so at semi-random sites. Therefore, there is theoretical risk of insertional mutagenesis, such as within an oncogene or tumor suppressor gene. While ABEO has mitigated this risk with extensive quality control and treated patients are being monitored in long-term follow up, the risk of secondary malignancy is not zero. We prefer to err on the side of KRYS' Vyjuvek, which does not rely on genomic integration to deliver its payload.

Chiesi's Filsuvez is FDA approved for treatment of DEB but its mechanism is unclear and its clinical benefit not as robust as Vyjuvek or Zevaskyn, and so we believe its market impact will be limited.

Pipeline Review

Pipeline Offers Optionality & Upside, But We Currently Ascribe Minimal Value: Among KRYS' pipeline portfolio products, we are keenly interested in KB801 for neurotrophic keratitis and KB707 for non-small cell lung cancer (NSCLC). We have modest expectations for KRYS' lung platform overall, but we are hopeful. We are also intrigued by KB304 for wrinkles of the décolleté (through the Jeune Aesthetics subsidiary). We may publish deep dives on select candidates as we get closer to the data catalysts.

In the meantime, we provide our high-level overview of their pipeline (note our views may change with time):

[18] ABEO 2Q25 earnings conference call (8/14/25)

Table 2. Overview of KRYS' pipeline (adapted from Grok, with our commentary on the right):

Therapeutic Area	Candidate (payload)	Indication	Development Stage	Key Progress and Timelines	High-level Commentary
Dermatology	KB105 (*TGM1*)	Lamellar ichthyosis	Phase 1/2 (JADE-1 trial)	KRYS expects to initiate Phase 2 portion in pediatric patients in 2026	KRYS is leveraging the success of Vyjuvek in KB105 using its HSV-based platform to deliver the TGM1 payload for a different genetic skin disease Preclinical data in mice has been encouraging with TGM1 protein expression observed in TGM1-deficient human keratinocytes from KB105 treatment* but we await further clinical data
Respiratory	KB407 (*CFTR*)	Cystic fibrosis (CF)	Phase 1 (CORAL-1 trial)	Enrolled 4 patients in Cohort 3 (dose escalation); **interim molecular data readout expected by YE 2025**	Vertex's (VRTX) CFTR modulators have established $ppFEV_1$ as the gold standard for approval in cystic fibrosis. We remain optimistic but acknowledge that it may be challenging to demonstrate $ppFEV_1$ benefit given other genetic medicine experiences in the field Delays in interim data readout (originally mid-2025) give us pause
Respiratory	KB408 (*SERPINA1*)	Alpha-1 antitrypsin deficiency (AATD) lung disease	Phase 1 (SERPENTINE-1 trial)	Amended protocol for repeat dosing (Cohort 2B); first patient dosed August 2025 **Molecular data update potentially in 2025**	We are encouraged by the data from patient 7 from Cohort 2 without augmentation therapy with AAT levels in the lung ELF of 729 nM (from 85 nM at baseline) with >50% reduction in unbound neutrophil elastase (NE) after a single KB408 dose AAT level of 729 nM in the lung ELF is within KRYS' target range of 5-10% of systemic levels. However, AAT levels in the ELF considered protective is ≥1 µM, so currently it falls short after a single dose Potential re-dosing of KB408 could give it the opportunity to build on efficacy, and potentially bring the AAT level in the ELF over the ≥1 µM threshold to be protective We await further data in a greater number of patients to understand what these AAT and NE levels mean clinically
Ophthalmology	KB803 (*COL7A1*)	Corneal abrasions in DEB patients	Phase 3 (IOLITE trial)	First patient dosed June 2025; ongoing enrollment in double-blind, placebo-controlled study with crossover Natural history run-in study also active	*(See our prior commentary on KB803)*
Ophthalmology	KB801 (*NGF*)	Neurotrophic keratitis (NK)	Phase 2 (EMERALD-1 trial)	First patient dosed July 2025; ongoing enrollment in randomized, placebo-controlled study Preclinical data (nerve growth factor production) presented at ARVO 2025.	In July, KRYS reviewed early preclinical data in mice supporting its therapeutic potential in NK KRYS noted that compliance from FDA-approved Oxervate (dosed 6x daily for 8 weeks) is one of the biggest issues for NK
Oncology	KB707 (*IL-2 + IL-12*), inhaled	Solid tumors of the lung (e.g., NSCLC)	Phase 1/2 (KYANITE-1 trial)	ORR 36% in heavily pre-treated NSCLC cohort (ASCO 2025 data); median duration/PFS not reached; well-tolerated (no Grade 4/5 AEs). Outpatient suitable	We think the ASCO results are respectable, and we like that KB707 is amenable to outpatient treatment, but we await longer follow up to see if ORR holds and what the DOR will be Typical bogey for a late-stage oncology drug for physicians is ORR 20%+ and DOR 6+ months We would like to see ORR 30%+ maintained (with hopefully a CR) and 6+ months in median durability of response
Oncology	KB707 (*IL-2 + IL-12*), intra-tumoral	Injectable solid tumors	Phase 1/2 (OPAL-1 trial)	Dose escalation and expansion ongoing	In August, KRYS announced it would pause enrollment on OPAL-1 amid regulatory uncertainties (given the REPL experience with RP1 in melanoma),** and that they would prioritize development inhaled KB707 in NSCLC **We think this is the right move until the regulatory dust settles**
Aesthetics	KB304 (*COL3 + elastin*), via subsidiary Jeune Aesthetics	Moderate-to-severe wrinkles of the décolleté	Phase 1 (PEARL-2)	Positive interim safety/efficacy data announced July 2025; significant aesthetic improvements observed **Full data expected later in 2025. Potential Phase 2 start in H1 2026, pending FDA feedback**	*(See our commentary below on Jeune Aesthetics subsidiary)*

*Freedman, J. C. et al. *J. Investig. Dermatol*. 2021, 141, 874-882.

**KRYS press release (8/21/25)

Abbreviations: ORR = objective response rate; CR = complete response; DOR = duration of response

Jeune Aesthetics Subsidiary – A Call Option on the Aesthetics Market

Jeune Aesthetics is a wholly owned, clinical-stage aesthetics subsidiary of KRYS that was incorporated in 2019 and focused on the development of candidates for aesthetic skin conditions. Their lead candidate is KB304 that leverages the same gene delivery platform from KRYS to deliver Type III collagen (COL3) and elastin to the skin via intradermal injection, restoring youthfulness and resilience. We like that KB304 offers a fundamentally different approach of restoring key skin proteins than neurotoxins, fillers, and energy-based devices – but this is no guarantee of success. Jeune's initial target indication for development is wrinkles of the décolleté (upper chest), where the wrinkles are difficult to address and have limited options.

In July, Jeune Aesthetics shared encouraging initial KB304 data from the Phase 1 PEARL-2 clinical trial, with KB304 demonstrating statistically significant aesthetic improvements over placebo using the Global Aesthetic Improvement Scale (GAIS), as assessed by both investigators and the subjects. KB304 appeared to be safe and well-tolerated. We won't review the data in detail but can be viewed in their press release.[19] We'll work a deeper dive as the key data catalyst approaches.

We don't include KB304 in our KRYS valuation, but we like the optionality of the Aesthetic's program that leverages the success of KRYS' gene delivery platform to the skin for a totally different skin market. If one or more of its assets can be clinically successful, we see Jeune Aesthetics as an easy fit for the likes of ABBV's Allergan Aesthetics subsidiary.

KRYS estimates 9.9 million cosmetic neurotoxin injections and 6.3 million cosmetic filler injections in the U.S. KRYS believes the global skin rejuvenation market will grow to $44.5 billion by 2030 (from $24.6 billion in 2023). We thought it was especially interesting that Jeune cited increasing demand for skin rejuvenation product due to GLP-1 accelerated skin aging, which has seen rapid uptake for obesity in recent years. Jeune cites collagen and elastin damage due to the significant weight loss from GLP-1 drugs.

There are key differences between the aesthetics market and Vyjuvek's market – DEB is ultra-rare with severe unmet medical need, whereas the aesthetics market is extremely large and includes nearly every adult, and there is no real medical need (except for our vanity). From that perspective, we believe there are several outstanding questions that need to be answered before we can include it in our valuation. Will Jeune's proposed photonumeric scale be accepted by the FDA? Can KB304 be priced appropriately for this market that's acceptable to consumers (likely to be cash-based rather than reimbursed by the healthcare system)? Will the Jeune products have an acceptable *safety* profile for this market (bar for safety is much higher than DEB)? Finally, will customers accept an *HSV-based* genetic medicine as a beauty product?

KB304 and remainder of Jeune's pipeline is still in its early stages and the road ahead for Jeune is a long one, but it's also exciting and potentially opens a significant market opportunity for them, if successful. KRYS expects Jeune Aesthetics to be a separate subsidiary sometime in ~H2 2026.

Valuation & Financials

KRYS' capital structure & spending discipline are also appealing to us. Overall, we simply like the way KRYS management runs its company. We summarize below:

[19] KRYS press release (7/24/25)

- **KRYS is profitable & cash flow positive:** KRYS is profitable on net income (on both GAAP & non-GAAP basis). KRYS has had 8 consecutive quarters of positive EPS. KRYS is also cash-flow positive. Vyjuvek in DEB should provide long & durable cash flows.

- **Solid cash position:** As of end-2Q25, KRYS had cash of $821 million, which puts them in a solid cash position. We do not expect them to raise capital in the near-term. KRYS has no long-term debt.

- **KRYS has demonstrated disciplined spending:** KRYS runs their business with high operating margins (~41% in 2Q25) relative to its peers (~10-15%). On top of the excellent gross margins with Vyjuvek (low 90%'s), KRYS' overall expense spending is low.

- **Insider ownership of KRYS is high at >10%:** Major individual insiders include founder executives Suma Krishnan (President, R&D, Director) and Krish S. Krishnan (President, CEO, Director), at 1.53 million and 1.46 million shares respectively. We like to see high insider ownership as it means to us that incentives for its management team are aligned with shareholders.

Summary:

- **We own a long position in KRYS with a 12-month price target (PT) of $245**. Our thesis is predicated on:
    - 1) Continued (but potentially lumpy) growth of Vyjuvek in the DEB market. We estimate global peak sales estimates of $1.3 billion by 2036
        - We expect continued Vyjuvek penetration into both RDEB and DDEB markets, with successful global expansion into EU and Japan markets
        - Assume U.S. market of ~1,500 total DEB potential patient population by 2030, 50% of the total estimated ~3,000
        - We expect overall compliance to find its footing at ~75%
        - Overall peak market penetration of ~70% by 2032, and considers potential competition
        - We assume no Vyjuvek-generic competition at the time of patent expiry (end-2036). Instead, we apply a –1.0% terminal growth rate to its terminal value (TV)
        - Assume potential expansion of KB803 into DEB with ocular complications. Modestly assume ~$50 million in global peak sales (with 50% risk discount). This will be adjusted as more information becomes available
    - 2) At this time, we include modest value for KRYS' pipeline, modeling $500 million in peak sales (with 50% risk-discount) in one of these assets
        - We are most interested in KB801 for neurotrophic keratitis and KB707 for non-small cell lung cancer (NSCLC)
            - We await further clinical data to better validate these assets

- DCF Parameters:
    - Our DCF-based price target (PT) is $245, on the global opportunity of Vyjuvek for DEB, including KB803 expansion for corneal abrasions
        - Discount rate: 11%
        - Terminal value (TV), assuming –1.0% growth
        - Shares outstanding (YE 2025 estimate): 30.3 million
    - We do not expect KRYS to need an equity financing currently

Below is a table of how we compare KRYS to its genetic medicine peers on an EV/Sales (2026) basis:

Figure 6. Peer table of genetic medicine companies.

Company	Ticker	Stage of Company	EV/Sales (2026)
Krystal Biotech	KRYS	Commercial	8.1
CRISPR Therapeutics	CRSP	Commercial	35.7
BioMarin	BMRN	Commercial	2.7
Sarepta Therapeutics	SRPT	Commercial	1.7
Alnylam Pharmaceuticals	ALNY	Commercial	12.3
PTC Therapeutics	PTCT	Commercial	6.7
Ionis Pharmaceuticals	IONS	Commercial	12.1
Average:			*11.3*

EV based on 10/14/25 closing prices

Note: Some genetic medicine companies such as NTLA, BEAM, WVE and PRME are precommercial and not expected to earn revenues from FDA approved products in 2026. These companies are therefore not included in this analysis.

Source: EV/sales (2026) metric is based on 2026 sales estimates from Godel

Risks

- **Commercial Risks**: Vyjuvek is FDA approved and marketed for treatment of DEB. However, the true DEB prevalence beyond the 1,200 identified U.S. patients remains uncertain and there is risk that KRYS will not be able to find all their estimated ~3,000 U.S. patients. Similar risk applies to the international markets, such as Europe and Japan. Therefore, Vyjuvek may not be able to achieve our sales estimates as we have modeled in the U.S. or globally. Secondly, the patient mix for Vyjuvek is moving more towards milder and moderate DEB patients, who do not suffer from the same severe wounds. Overall compliance may fall below our long-term estimate, impacting Vyjuvek peak sales.

- **Data & Regulatory Risks**: Negative clinical trial results in efficacy and safety for Vyjuvek in DEB corneal abrasions and any of KRYS' pipeline products are potential risks to our thesis. Even if favorable, there are no guarantees that they will be granted regulatory approval. The data in our tables are not based on head-to-head clinical trials, and any cross-trial comparisons should be made with caution.

- **Manufacturing risks**: Manufacturing of gene therapies is complex. While KRYS has established its manufacturing for Vyjuvek for DEB, there may be additional considerations or complexities for its other products as it expands to other indications. Jeune Aesthetics subsidiary is pursuing much larger markets in aesthetics and carries unique risks when it scales, assuming their clinical trials are successful and are approved.

- **Competitive Risk**: Vyjuvek may not reach our sales estimates in DEB given competition, both on the market and in clinical development, continues to advance. Our model also assumes that generic competition for Vyjuvek at the end of its patent life will be challenging. But if a regulatory framework for generic entry for gene therapies is established by that time, the market entry of a generic-Vyjuvek would be a material risk to our thesis.

Disclaimers:

The information provided by Lucent Ion LLC ("the Company") is for informational and educational purposes only and does not constitute personalized investment advice, financial advice, legal advice, or tax advice. The Company is a publisher of financial research and commentary and is not registered as an investment adviser with the U.S. Securities and Exchange Commission (SEC) or with any state securities regulatory authority.

All content, including but not limited to research reports, newsletters, articles, opinions, and analyses, is of a general and impersonal nature and does not take into account the specific investment objectives, financial situation, or needs of any individual.

No information contained in the Company's publications or communications should be construed as:

- A recommendation to buy, sell, or hold any security or financial instrument;
- An offer to buy or sell securities;
- Investment, legal, or tax advice tailored to any individual.

Investing involves risk, including the potential loss of principal. Past performance is not indicative of future results. You should consult with a qualified investment adviser, tax professional, or attorney before making any investment decisions.

The Company, its owners, employees, and affiliates may hold positions in securities mentioned in its publications, but will disclose any material conflicts of interest where required.

By using our services, you agree that the Company will not be held liable for any decisions or actions you take based on the information provided.

Disclosures:

As of the date of this publication, Lucent Ion LLC and/or its principals have beneficial positions in the following companies:

- Krystal Biotech (KRYS): long
- Sarepta Therapeutics (SRPT): long
- All other companies mentioned in this report: none
    - This includes, but not limited to: ABEO, VRTX, CRSP, BMRN, ALNY, PTCT, IONS, ABBV, REPL, Chiesi, Genetix (bluebird bio)

The Company does not receive direct compensation from the companies listed above for this research. Our views are our own, based on publicly available information, and are provided for informational purposes only.

As a matter of policy:

- We do not trade in securities within 24 hours before or 48 hours after publishing research on those securities
- We may buy or sell securities mentioned in our research at any time after this cooling-off period, without notice
- Trading decisions are made independently of our publications