

CRISPR Therapeutics AG

NASDAQ: CRSP · Genome editing · Domicile Switzerland (Zug) · Large capitalization biotechnology

SHORT INTEREST	SHORT SHARES	DAYS TO COVER
19.47% of float	18.74M	12.77

Short interest as of the 29 August 2026 settlement. FINRA publishes short interest twice a month, about seven business days after each settlement date, so this figure is not a daily number.

FRAMEWORK VIEW: CONSTRUCTIVE

Horizon 24 to 48 months. Setup: a crowded short base into a validated catalyst path and an active acquisition thesis.

Initiated 5 Sep 2026 at **Constructive**. Current view as of 5 Sep 2026: **Constructive**, unchanged.

POSITION DISCLOSURE

No position. Neither Contra Research Group nor its personnel held a position in CRSP at the time of writing or hold one now.

If we open a position in CRSP it will be disclosed here as a dated update. See how we trade what we cover.

KEY DATA				
MARKET CAPITALIZATION		\$5.39B	SHORT INTEREST, % FLOAT	19.47%
CASH AND INVESTMENTS		\$2.36B	DAYS TO COVER	12.77
SHORT INTEREST, SHARES		18.74M	PUBLIC FLOAT	96.3M
52 WEEK RANGE		44.1 to 78.5	CONSENSUS TARGET	\$87
CASGEVY REVENUE, Q2		\$76M	INSTITUTIONAL OWNERSHIP	~80%
Sources: company filings, consensus, market data as of 4 September 2026, exchange short interest settlement 29 August 2026. Last traded price omitted by request. Casgevy figure is Vertex reported product revenue recognized under the collaboration.				

01 Investment Case

We initiate coverage of CRISPR Therapeutics with a Constructive framework stance. The equity carries the only approved CRISPR medicine, the largest treasury in the subsector, and a wholly owned in vivo pipeline that cleared its central safety question on 28 August. Against that, roughly one fifth of the float is sold short. A validated near term catalyst path sitting on a crowded short base and an active acquisition thesis defines an asymmetry the current quotation does not reflect.

The balance sheet is the first support. Cash and investments of \$2.36B as of 30 June 2026 fund the wholly owned programs into the end of the decade without equity issuance. No peer in the pure play editing group holds comparable resources, and most have already restructured or cut headcount. The second support is in vivo readout. At ESC on 28 August, CTX310 editing of ANGPTL3 produced mean knockdown of 79%, an LDL reduction of 53% and a triglyceride reduction of 48%, durable to one year, with no Grade 3 or higher hepatic enzyme elevation and no treatment related serious adverse events across 15 dosed patients. That profile separates CRSP from the hepatic toxicity that forced Intellia to halt its Phase 3 program, which we address in Section 06.

Positioning is the third. Short interest of 18.7M shares equals 19.5% of float at a 12.8 day cover ratio. The capital funding that short rested on slow Casgevy revenue conversion and on the assumption that the in vivo pipeline carried Intellia style liver risk. The August data removes the second leg of that argument while the short position remains outstanding. We value CRSP as two assets the market prices as one: a 40% economic interest in a commercialized gene therapy, and a wholly owned in vivo and cell therapy pipeline that CTX310 has begun to validate. The catalyst calendar, the treasury and the short structure point the same direction for the first time since the Casgevy launch. Our stance is to accumulate into the H2 CTX310 Phase 1b readout.

02 Positioning and Ownership

The short base is the single most actionable feature of the capital structure. At 19.5% of float and a 12.8 day cover ratio, CRSP screens among the most heavily shorted large capitalization genomic names, requiring roughly thirteen sessions of average volume to unwind. Into a defined catalyst path and an open acquisition thesis, that is the asymmetry we underwrite: limited incremental bear catalysts against multiple identified upside events. Institutional ownership sits near 80% across approximately 500 filers, but holders reduced positions by roughly 16M shares in the most recent quarter, consistent with the drift off the 52 week high. Ownership concentrates in thematic and quantitative hands rather than dedicated biotechnology specialists, which raises the reflexivity of the short structure.

SELECTED 13F HOLDERS, MOST RECENT FILINGS

HOLDER	SHARES	STAKE	CHARACTER
ARK Investment Mgmt	10.5M	10.8%	Largest holder, thematic, high turnover
BlackRock	7.5M	6.5%	Index core
Orbis / Allan Gray	6.0M	6.2%	Contrarian value, low turnover
Capital International	5.9M	6.1%	Reduced approximately 81%
State Street	3.8M	3.9%	Index
T. Rowe Price	3.2M	3.4%	Active fundamental

The most recent 13F cycle shows a split among the bulge bracket desks that is worth noting. Morgan Stanley and Bank of America added materially, while UBS and Goldman Sachs trimmed. Index managers continued to accumulate, and Rockefeller Capital reversed to a buyer. The table below lists the largest position changes for the quarter ended 30 June 2026.

LARGEST POSITION CHANGES, QUARTER ENDED 30 JUNE 2026

INSTITUTION	ACTION	SHARES HELD	CHANGE, SH	CHANGE, %
Morgan Stanley	Added	879,949	+209,989	+31.7%
Bank of America	Added	1,155,105	+171,505	+17.5%
State Street	Added	4,321,666	+355,074	+8.5%
Rockefeller Capital	Added	101,649	+38,063	+38.6%
Vanguard (Cap. Mgmt)	Added	1,181,847	+39,247	+3.4%
Dimensional Fund Adv.	Reduced	275,375	-221,153	-44.3%
UBS Group	Reduced	1,317,499	-441,837	-25.3%
Goldman Sachs	Reduced	272,372	-139,236	-34.2%
Affinity Asset Advisors	Reduced	100,000	-50,000	-33.3%
Algert Global	Reduced	65,880	-31,065	-32.0%

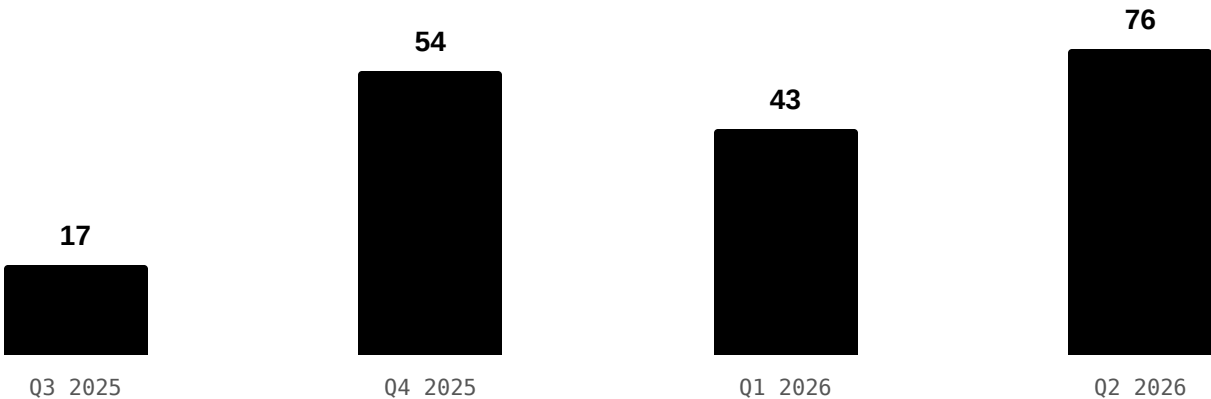
Figures are individual 13F filer entities and are reported on a settlement and filing lag. A single manager may file under multiple entities.

03 **Casgevy, the Annuity**

Casgevy (exagamglogene autotemcel) is the first approved CRISPR medicine, cleared for transfusion dependent beta thalassemia and severe sickle cell disease. Commercialization and manufacturing sit with Vertex under a 60/40 economic split in Vertex's favor. CRSP recognizes its 40% share through collaboration accounting rather than as direct product revenue, which is why the reported top line understates the underlying commercial value.

METRIC	VALUE	INTERPRETATION
List price	\$2 . 2M	Single administration, autologous
Q2 2026 revenue	\$76M	Up 151% year over year, 78% quarter over quarter
Approved markets	39	North America, Europe, Gulf states
CRSP economics	40%	Vertex leads, CRSP shares profit and cost
Consensus peak	~\$3 . 6B	Slow conversion, long duration annuity

EXHIBIT 1. CASGEVY NET PRODUCT REVENUE, \$M PER QUARTER (COLLABORATION TOTAL)



FY2025 total \$116M. Q2 2026 up 151% year over year and 78% quarter over quarter. Source: Vertex and CRISPR Therapeutics filings.

The revenue conversion is deliberately slow. Each patient requires stem cell collection, a multi month manufacturing cycle, and myeloablative conditioning before infusion, and payer

authorization runs 3 to 12 months. The binding constraint on the ramp is authorized treatment center capacity, not demand. The quarterly path is lumpy, as Exhibit 1 shows, with a soft third quarter of 2025 and a strong recovery into 2026. We model Casgevy as a long duration annuity that compounds through the decade, not on a conventional launch curve.

04 Pipeline and Catalysts

The wholly owned pipeline is where 100% of the economics accrue to CRSP and where the re rating sits. The in vivo liver franchise is the near term value driver following the CTX310 validation.

PROGRAM	TARGET AND INDICATION	STAGE	NEXT CATALYST	EST. ENTRY
CTX310	ANGPTL3, cardiovascular	Phase 1b	1b update H2 2026	2029 to 2031
CTX320	Lp(a), cardiovascular	Phase 1	Update 2026	2030+
CTX340	AGT, refractory hypertension	Phase 1	Enrollment 2026	Early 2030s
CTX460	SERPINA1, AAT deficiency	Phase 1	Dosing mid 2026	Early 2030s
CTX112	CD19 CAR T, autoimmune and oncology	Phase 1/2	Reads H2 2026	2029 to 2032
CTX211 / 213	Beta cell, type 1 diabetes	Preclinical	Development updates	Mid 2030s

The next binary is the CTX310 Phase 1b update in H2 2026, in severe hypertriglyceridemia patients at the fixed flat dose equivalent to 0.8 mg/kg. A confirmatory efficacy and safety profile converts the cardiovascular franchise from optionality into a modelable asset, and is the specific event we expect to pressure the short base. On the strength of the ESC data, individual sell side targets have begun to move higher, with Chardan raising to \$112, while the twenty two analyst consensus still sits near \$88.

05 CTX310 Competitive Positioning

CRSP is not first in lipid lowering. Repeat dose siRNA and antibody therapies are already approved or in Phase 3. The differentiated claim is dosing: a single administration that durably removes a cardiovascular risk factor, against a chronic injection. The question that sets the ceiling for the in vivo cardiovascular franchise is whether a one time edit displaces a well tolerated repeat dose drug, and in which patients.

THE LIPID LOWERING COMPETITIVE SET

ASSET	COMPANY	TARGET	MODALITY	DOSING	STAGE
CTX310	CRISPR (CRSP)	ANGPTL3	CRISPR knockout, in vivo	Single dose	Phase 1b
CTX320	CRISPR (CRSP)	Lp(a)	CRISPR knockout, in vivo	Single dose	Phase 1
VERVE 102	Eli Lilly (LLY)	PCSK9	Base editing, in vivo	Single dose	Phase 1b
VERVE 201	Eli Lilly (LLY)	ANGPTL3	Base editing, in vivo	Single dose	Phase 1
Zodasiran	Arrowhead (ARWR)	ANGPTL3	siRNA	Repeat, subcutaneous	Phase 3
Evkeeza	Regeneron (REGN)	ANGPTL3	Monoclonal antibody	Repeat, intravenous	Approved
Olpasiran	Amgen (AMGN)	Lp(a)	siRNA	Repeat	Phase 3
Pelacarsen	Novartis (NVS)	Lp(a)	Antisense	Repeat	Phase 3
Lepodisiran	Eli Lilly (LLY)	Lp(a)	siRNA	Repeat	Phase 3

The one time editing race

The direct rival is Eli Lilly. Through its 2025 acquisition of Verve, Lilly holds the leading one time base editing programs in cardiovascular disease. VERVE 102, a PCSK9 base editor, has shown a single dose reducing PCSK9 by up to 88% and LDL by up to 62% with durable effect, and VERVE 201 targets ANGPTL3, the same target as CTX310. Lilly therefore competes on the one time editing thesis directly, and also fields a repeat dose Lp(a) siRNA, lepodisiran, against CTX320. A global pharmaceutical company with deep cardiovascular commercial infrastructure building the entire genetic medicine stack is the single most serious competitive threat to CRSP's cardiovascular franchise.

Durability against convenience

Against the siRNA and antibody incumbents the axis is durability against reversibility. A single administration edit offers permanent target knockdown and solves adherence, which matters most in the severe and refractory segments: homozygous familial hypercholesterolemia, severe hypertriglyceridemia, and statin intolerant high risk patients. A repeat dose siRNA given a few times a year is reversible, titratable, and already de risked in Phase 3, which favors it in the broad moderate risk population where a permanent edit is a harder sell. We expect the market to split along that line. That split, rather than any single trial, sets the realistic commercial ceiling for CTX310 and CTX320, and it is a central input to the pipeline value in Section 08.

06

The Intellia Read Across

The valuation of every in vivo liver editing program depends on one question: is lipid nanoparticle delivery of Cas9 to the liver safe at therapeutic doses. Intellia's data raised doubt. CRSP's data answered it in the affirmative for its own construct.

Intellia, the warning

A patient dosed in September 2025 developed a Grade 4 hepatic injury requiring hospitalization. Intellia halted its Phase 3 MAGNITUDE and MAGNITUDE 2 trials for ATTR amyloidosis (nex z) in late October 2025, with more than 450 of 650 patients already dosed. A patient death was subsequently reported in the program. The FDA released two trials from hold in July 2026. The episode framed the bear narrative for the entire in vivo Cas9 modality.

CTX310, the answer

At ESC on 28 August 2026, across 15 dosed patients with one year follow up: ANGPTL3 fell 79% (maximum 89%), LDL fell 53% and triglycerides fell 48%, durable through one year. There was no dose limiting toxicity, no treatment related serious adverse event, and no Grade 3 or higher liver enzyme elevation. A single transient aminotransferase elevation resolved without sequelae. Deep durable efficacy with a clean hepatic profile at the precise endpoint where Intellia failed.

The read across does not render Cas9 in liver universally safe. Target, guide RNA and dose differ by program, and a single serious event in a CRSP trial would reprice the equity. What the data does is detach CRSP from the sector's dominant bear thesis and move CTX310 from lottery ticket to credible clinical asset. We regard it as the central swing factor for the equity over the next twelve months.

07

Strategic Acquisition Scenario

A Vertex acquisition of CRSP is a precedented and financeable catalyst. Vertex already paid CRSP \$900M upfront plus \$200M in milestones to move Casgevy economics from 50/50 to 60/40. The mechanism by which Vertex writes CRSP a check to consolidate the asset is already established, and the equity previously spiked on takeover speculation in March 2026.

VERTEX CAPACITY AND PRECEDENT

ITEM	FIGURE	RELEVANCE
Vertex cash and investments	\$13.6B	Q2 2026, ample versus CRSP \$5.4B capitalization
Crinetics acquisition	\$8.8B net	Closing Q3 2026 at a 102% premium

ITEM	FIGURE	RELEVANCE
Alpine Immune, 2024	\$4.9B	Prior large premium acquisition
Casgevy amendment paid	\$1.1B	Direct precedent for buying CRSP economics

TWO STRUCTURES AND THE SHAREHOLDER CONSEQUENCE

SCENARIO	MECHANISM	OUTCOME FOR CRSP	EQUITY IMPACT
A. Stake buyout	Vertex purchases the residual 40% Casgevy interest for a lump sum	Remains independent, treasury swells, funds pipeline with no dilution	Most constructive for a holder
B. Full acquisition	Vertex acquires the company for cash at a premium	Ceases as a standalone; becomes the Vertex genetic medicine unit	Premium captured, then upside capped

ILLUSTRATIVE TAKEOUT MATH, NOT A PRICE TARGET

PREMIUM	IMPLIED EQUITY VALUE	IMPLIED PER SHARE	FINANCEABILITY
+50%	~\$8.1B	~\$84	Cash plus modest debt
+75%	~\$9.4B	~\$98	Term loan required
+100%	~\$10.8B	~\$112	Stretch post Crinetics, precedented

The timing tension is the point to monitor. Vertex is incentivized to move before the pipeline re rates the equity, while every clean readout raises the acquisition price. The Crinetics outlay plus a \$4.5B term loan constrains Vertex's near term firepower, which likely pushes any CRSP action into 2027 or later. The CTX310 print therefore makes CRSP simultaneously more valuable to Vertex and more expensive to acquire. We would treat the takeout as optionality rather than the thesis: an inevitable buyout view can become a value trap, and if no transaction materializes while the pipeline disappoints, the residual is a Casgevy stub.

08 Valuation: Sum of the Parts

The clearest way to see the mispricing is to value the components separately. Net cash of \$2.4B plus a conservative figure for the 40% Casgevy interest already approximates the entire \$5.4B market capitalization. On that arithmetic the market pays close to nothing for the wholly owned in vivo and cell therapy pipeline. Our base case sum of the parts is approximately \$9B, and the gap to the current quotation is almost entirely the pipeline the tape is not paying for.

ILLUSTRATIVE SUM OF THE PARTS, \$B AND PER SHARE ON 96.7M SHARES

COMPONENT	METHOD	BEAR	BASE	BULL
Net cash and investments	Balance sheet	2.4	2.4	2.4
Casgevy, 40% interest	Risk adjusted NPV, approved	2.5	3.0	4.0
In vivo cardiovascular	Probability weighted, Phase 1	0.3	2.0	4.5
CAR T autoimmune, CTX112	Probability weighted	0.2	1.0	2.0
AATD, diabetes, platform	Option value	0.1	0.6	1.5
Equity value	Sum	5.5	9.0	14.4
Per share	96.7M shares	57	93	149

The bear column is the one to sit with. At roughly \$57 per share it is close to the current quotation, and it is built from net cash plus a modest Casgevy value plus almost nothing for the pipeline. At the current price the market is close to that bear case, which means an investor is receiving the in vivo and cell therapy pipeline as a free option. The base case near \$93 requires only that the pipeline is worth a probability weighted fraction of large markets, consistent with the CTX310 data in Section 01 and the competitive framing in Section 05. This complements the acquisition math in Section 07: a strategic acquirer would underwrite the same pipeline value that the public market presently declines to pay for.

Illustrative scenario framework, not a price target. Casgevy is valued on the risk adjusted net present value of CRSP's 40% profit share against a consensus peak near \$3.6B. Pipeline components are probability weighted at their clinical stage. Inputs are analytical assumptions set out to be challenged, not asserted as forecasts.

09 Governance and the Acquisition Network

The board is not a passive scientific advisory panel. It concentrates three overlapping networks in one room: institutional venture capital, Wall Street finance, and large pharmaceutical research leadership. The composition tells you who is present when a sale is negotiated and which acquirers sit one relationship away from the boardroom.

BOARD NETWORK, SELECTED DIRECTORS

DIRECTOR	PRIMARY AFFILIATION	NETWORK	NOTABLE EXITS AND SEATS
Samarth Kulkarni	CEO and Chairman, CRSP	Ex McKinsey biopharma	Runs the company

DIRECTOR	PRIMARY AFFILIATION	NETWORK	NOTABLE EXITS AND SEATS
Ali Behbahani	Partner, Co Head Healthcare, NEA	VC and Wall Street	Arcellx to Gilead \$7.8B; chairs Nkarta
Simeon George	CEO and Managing Partner, SR One	VC and Wall Street	Principia to Sanofi \$3.68B; Turning Point to BMS \$4.1B
Katherine High	CEO RhyGaze; ex President AskBio (Bayer)	Gene therapy founder	Spark to Roche \$4.3B; developed Luxturna, first FDA gene therapy
Douglas Treco	Lead Independent Director; CEO Inozyme	Serial founder	Ra Pharmaceuticals to UCB \$2.5B; TransKaryotic to Shire
Christian Rommel	EVP, Global Head of R and D, Bayer Pharma	Large pharma R and D	Boards of AskBio and BlueRock (Bayer), Vividion
Maria Fardis	CEO Lassen; Venture Partner, Frazier	VC and oncology operator	Ex CEO Iovance; ex Pharmacyclics, Gilead
John T. Greene	CFO, Discover Financial Services	Wall Street (HSBC, GE)	Bioverativ to Sanofi \$11.6B
Sandy Mahatme	Ex CFO Sarepta; ex Celgene finance	Capital markets	Flexion to Pacira; Celgene to BMS during tenure

The deal record

Directors have collectively carried companies into more than **\$34B of trade sales to large pharmaceutical acquirers** across at least six transactions: Bioverativ to Sanofi, Arcellx to Gilead, Spark to Roche, Turning Point to Bristol Myers Squibb, Principia to Sanofi, and Ra Pharmaceuticals to UCB. This is the composition a company assembles when a strategic sale sits inside the intended range of outcomes, and the specific personnel who know how to run and time one. It reinforces the acquisition scenario in Section 07.

The Bayer cluster and acquirer breadth

The acquirer analysis should not stop at Vertex. Christian Rommel is Bayer's sitting Global Head of Research and Development. Katherine High ran therapeutics at AskBio, Bayer's gene therapy subsidiary, and Rommel also sits on the board of BlueRock, Bayer's cell therapy arm. Bayer therefore holds two direct lines of sight into CRSP strategy. High also developed Luxturna, the first FDA approved gene therapy, and cofounded Spark. This is foundational gene therapy credibility, not decoration, and it widens the set of credible strategic acquirers.

Political exposure

We screened director federal contributions in FEC records directly. CEO Kulkarni gives bipartisanly and pragmatically, with nine itemized contributions to Congressional health and commerce committee members of both parties. Democratic recipients include Moulton, Auchincloss, DeGette, Neal and Pallone; Republican recipients include Bilirakis, Burgess, McMorris Rodgers and Tim Scott. Behbahani and Mahatme show no itemized federal giving, and George shows at most a single Democratic platform contribution. No director we screened has contributed to a Trump aligned committee. The pattern is committee relationship giving aimed at the members who govern FDA and drug policy, not ideological alignment.

10 The Bottleneck and Where to Allocate

If gene editing is a durable theme rather than a single stock bet, position sizing should follow the choke points, not the therapeutic sponsors. The modality has five structural constraints. The entities that own each constraint convert editing volume into revenue regardless of which sponsor wins a given indication. This is the picks and shovels layer, and it is where we would anchor client capital.

THE FIVE STRUCTURAL CONSTRAINTS

CONSTRAINT	WHAT IT GATES	SEVERITY
Delivery	Reaching tissues beyond the liver. Liver via lipid nanoparticle is solved; extrahepatic delivery is not. Gates the addressable market past liver and blood indications.	CRITICAL
Safety ceiling	Off target edits, chromosomal translocations, hepatic toxicity. FDA April 2026 guidance mandates deep next generation sequencing screens.	CRITICAL
Reagents and manufacturing	Cas9 mRNA and protein, guide RNA, plasmid DNA, capping and nucleotides, consumed at GMP grade by every program.	HIGH
Reimbursement and capacity	Single administration therapies above \$2M strain payer models and treatment center throughput.	HIGH
Foundational IP	PTAB reaffirmed Broad Institute priority for Cas9 in eukaryotic cells, March 2026. Licensees may owe royalties by lineage.	STRUCTURAL

ALLOCATION MAP: BOTTLENECK OWNERS, LISTED VEHICLES

CHOKE POINT	INVESTABLE OWNER	TICKER	CONTRA STANCE
Delivery	Ainylam Pharmaceuticals	ALNY	Core. Delivery IP leader and commercial proof of in vivo genetic medicine

CHOKE POINT	INVESTABLE OWNER	TICKER	CONTRA STANCE
Delivery	Arcturus Therapeutics	ARCT	Higher beta LNP pure play; binary, size accordingly
Delivery	Ionis Pharmaceuticals	IONS	Conjugate delivery and antisense platform toll
Reagents and mfg	Danaher (Aldevron)	DHR	Core. Quality compounder; supplies Cas9 mRNA, guide RNA, plasmid
Reagents and mfg	Thermo Fisher Scientific	TMO	Diversified CDMO and tools; lower beta exposure
Reagents and mfg	Maravai LifeSciences	MRVI	Pure play mRNA inputs; higher beta, higher torque
Safety and NGS	Illumina	ILMN	Sequencing toll on every mandated off target screen
Safety and NGS	Twist Bioscience	TWST	Synthetic DNA and guide libraries
Safety testing	Charles River Labs	CRL	Direct beneficiary of the tighter 2026 safety guidance
Editing platform	CRISPR Therapeutics	CRSP	Preferred sponsor on balance sheet, product, validated in vivo
Editing platform	Intellia, Beam, Prime	NTLA BEAM PRME	Next generation optionality; earlier, cash constrained

Positioning

For durable exposure to the theme rather than a single binary, we would anchor capital in the choke point owners. The delivery and reagent layers monetize editing volume irrespective of which sponsor wins a given indication. Danaher (DHR) and Alnylam (ALNY) provide the highest quality exposure. Maravai (MRVI), Arcturus (ARCT) and Twist (TWST) provide higher beta pure play exposure to the same constraints. Charles River (CRL) monetizes the tightening regulatory safety bar. Within the therapeutic sponsors, CRSP remains our preferred holding.

The adjacent watch list is the CTX310 competitive set: Arrowhead (ARWR), Regeneron (REGN), Amgen (AMGN) and Eli Lilly (LLY, via Verve base editing). The competitive question for CTX310 is the durability of a single dose edit against repeat dose siRNA, which sets the commercial ceiling for the cardiovascular franchise.

11 Risk Assessment

RISK	SEVERITY	ASSESSMENT
Safety event, CRSP in vivo trial	EXISTENTIAL	The Intellia read across is the sharpest risk. A single Grade 4 hepatic event or death in any CRSP in vivo program reprices the equity and possibly the sector. Controlled by the FDA via clinical hold.
Vertex dependency	EXISTENTIAL	The only current revenue is 40% of one Vertex controlled drug. Deprioritization, renegotiation, or a competing Vertex therapy leaves CRSP limited recourse.
Commercial ceiling	HIGH	If treatment center capacity and payer friction hold Casgevy well below the \$3.6B peak, the annuity thesis weakens and the owned pipeline must carry the valuation.
Squeeze cuts both ways	HIGH	A 19.5% short is a setup, not a guarantee. Absent positive catalysts the same crowd can press the position lower, and thematic ownership amplifies drawdowns.
IP levy and regulatory cost	MEDIUM	The Broad priority ruling may impose royalty tolls; the 2026 off target guidance raises preclinical cost and lengthens timelines across the field.
Political and ethical	TAIL	CRSP operates only in somatic editing, broadly accepted. Sector reputational risk from germline editing and shifting science funding priorities remains a low probability overhang.

12 Sovereign, Geographic and Regulatory Footprint

The government layer is not an equity stake. It is three things that matter more: who approves the product, who pays for it, and who funds the underlying science. Casgevy carries approvals in 39 markets, each a separate regulatory clearance that is difficult to replicate and that functions as a market by market moat. At a list price above \$2M, the effective buyers are national single payer health systems, which makes reimbursement policy the true demand driver.

JURISDICTIONS ENGAGED

JURISDICTION	ROLE	DETAIL
Switzerland	Domicile	Zug incorporation; corporate and IP base; Charpentier founding lineage
United States	Operations, regulation, science	Boston operations; FDA approvals; NIH Somatic Cell Genome Editing program, roughly \$190M research base

JURISDICTION	ROLE	DETAIL
United Kingdom	First approval	MHRA cleared Casgevy first globally; pediatric submission for ages 5 to 11
EU and Germany	Approval and reimbursement	EMA approval; Germany reimburses ages 12 and above
Saudi Arabia	Approval and access	SFDA approval; pediatric submission; sovereign health system as buyer
Bahrain	First Middle East administration	Vertex accredited center of excellence, positioned to treat patients globally
China	Restriction and risk	FDA move, June 2025, to limit routing of US patient cells to China on security grounds

The current FDA posture is active and bifurcated. Under Commissioner Makary the agency introduced a plausible mechanism pathway in November 2025 to accelerate bespoke editing therapies for ultra rare disease, following the Baby KJ personalized CRISPR case, while also issuing stricter off target safety guidance in 2026 and restricting cell routing to China. For CRSP the China restriction is a mild positive, since Casgevy manufacturing sits in the United States and allied jurisdictions under Vertex. The offsetting policy risks are federal science budget pressure on the NIH research base and drug pricing policy that could compress single administration economics. The Gulf states are a genuine growth vector rather than a token market, given high sickle cell and thalassemia prevalence and sovereign payers willing to fund access.

13 The Long View: Industrializing Genetic Cures

Position sizing over two to four years rests on the pipeline and the takeout. The reason to own a genome editing franchise over ten years is larger. Casgevy is the first commercial proof that a single administration can functionally cure a genetic disease instead of managing it for life. If editing becomes standard of care across even a fraction of the roughly 7,000 known monogenic disorders, the modality shifts from niche therapy to the industrialization of genetic cures, and the addressable market is measured in the hundreds of billions.

The line between cure and enhancement is already blurring

CTX310 durably lowers ANGPTL3, LDL and triglycerides from a single dose. Delivered to a healthy person, that same edit is preventive enhancement rather than treatment. Individuals born with natural ANGPTL3 or PCSK9 loss of function carry lifelong protection against cardiovascular disease. CRSP is, in effect, demonstrating durable single gene metabolic enhancement and correctly calling it therapy, because the trials enroll patients. That is the first

commercial foothold of a much larger idea: editing the genome to remove disease risk a person was born with.

The realistic frontier is the disease free human, not the superhuman

The science does not support a near term path to engineered strength or cognition. Those traits are polygenic, somatic editing reaches only a subset of tissues (today mainly liver and blood), and heritable germline editing is banned across essentially every jurisdiction after the He Jiankui episode. The credible frontier is the durable correction of known pathogenic variants. That is precisely where CRSP operates, and it is the more valuable frontier in any case, since the population for genetic disease correction dwarfs any market for enhancement.

Why this is a national security theme, not only a biotechnology vertical

States are treating capability in genetic medicine as strategic infrastructure. US intelligence has publicly stated that China pursued biologically enhanced military personnel; DARPA funds the defensive counterpart through its Safe Genes program; and the FDA now restricts routing American patient cells through China. That framing supports durable sovereign and defense linked demand for the underlying toolchain, which reinforces the bottleneck allocation in Section 10. Ownership of delivery, manufacturing and validation capacity is being treated by governments as a national asset.

The conclusion for a long horizon allocator is that genetic cures are moving from one off miracles toward an industrial process, and that in an industrial process the value accrues to whoever owns the constraints: delivery, manufacturing and the tools that validate safety. CRSP is the highest quality sponsor and the clearest single takeout candidate. The bottleneck owners in Section 08 are the instrument for holding the theme itself over a ten year horizon.

14 Analyst Agenda

Open workstreams that most move the valuation, to be resolved in subsequent notes.

- 01 Sum of the parts.** Separate the Casgevy annuity from the risk adjusted NPV of CTX310 and the CAR T autoimmune franchise to quantify the mispricing directly.
 - 02 Vertex acquisition model.** Build the explicit case, both stake buyout and full takeout, with financing and accretion analysis.
 - 03 Cardiovascular competition.** Map CTX310 and CTX320 against Arrowhead, Regeneron, Amgen and Verve on the durability against repeat dose axis.
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- 04

Autoimmune CAR T. Position CTX112 against Cabaletta and Kyverna on the allogeneic against autologous question.
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- 05

Vertex diabetes overlap. Assess the collision between CRSP islet replacement and Vertex zimislecel.
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- 06

Casgevy contribution margin. Track manufacturing cost per patient toward the point where the collaboration turns earnings positive.
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- 07

IP exposure. Quantify royalty liability from the Broad priority ruling given CRSP's Charpentier lineage licenses.
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- 08

Bottleneck baskets. Construct sized delivery and reagent baskets (ALNY, DHR, MRVI, ILMN, CRL) as the durable theme vehicle.
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References and Disclosures

CTX310 Phase 1a data, ESC 2026	FDA 2026 off target guidance
CRSP Q2 2026 results	FDA restriction on China gene editing trials
CRSP short interest and float statistics	FEC individual contributions, director screen
CRSP institutional ownership and 13F activity	CRSP board of directors
Intellia Phase 3 hepatic hold	US intelligence on China military enhancement
Vertex and CRISPR collaboration amendment	Eli Lilly to acquire Verve Therapeutics
Vertex acquires Crinetics, 102% premium	VERVE 102 single dose PCSK9 and LDL data
Vertex Q2 2026, \$13.6B cash	Arrowhead zodasiran Phase 3 YOSEMITE
PTAB Broad priority ruling	Lp(a) therapies from Novartis, Amgen, Lilly

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