Filed by BioCryst Pharmaceuticals, Inc. pursuant to Rule 425
Under the Securities Act of 1933
And Deemed Filed Pursuant to Rule 14a-12
Under the Securities Exchange Act of 1934
Subject Company: BioCryst Pharmaceuticals, Inc.
Commission File No. of Subject Company: 000-23186

# Combining Capabilities to Serve More Patients with Rare Diseases

## Additional Information and Where to Find It

***Additional Information and Where to Find It***

In connection with the proposed mergers, Nautilus Holdco, Inc. ("Holdco") has filed with the U.S. Securities and Exchange Commission (the "SEC"), and the SEC has declared effective on May 23, 2018, a Post-Effective Amendment to the Registration Statement on Form S-4 (as may be amended from time to time, the "Registration Statement") that includes the joint proxy statement of BioCryst Pharmaceuticals, Inc. ("BioCryst") and Idera Pharmaceuticals, Inc. ("Idera") and that also constitutes a prospectus of Holdco. BioCryst, Idera and Holdco may also file other documents with the SEC regarding the proposed transaction. This document is not a substitute for the definitive joint proxy statement/prospectus or Registration Statement or any other document that may be filed by each of BioCryst and Idera with the SEC. BEFORE MAKING ANY VOTING DECISION, IDERA'S AND BIOCRYST'S RESPECTIVE STOCKHOLDERS ARE URGED TO READ THE JOINT PROXY STATEMENT/PROSPECTUS IN ITS ENTIRETY AND ANY OTHER DOCUMENTS FILED BY EACH OF IDERA AND BIOCRYST WITH THE SEC IN CONNECTION WITH THE PROPOSED TRANSACTION OR INCORPORATED BY REFERENCE THEREIN BECAUSE THEY CONTAIN IMPORTANT INFORMATION ABOUT THE PROPOSED TRANSACTION AND THE PARTIES TO THE PROPOSED TRANSACTION. Investors and stockholders may obtain free copies of these materials and other documents filed with the SEC (when available) by BioCryst, Idera and Holdco through the website maintained by the SEC at www.sec.gov. Idera and BioCryst make available free of charge at www.iderapharma.com and www.biocryst.com, respectively (in the "Investors" section), copies of materials they file with, or furnish to, the SEC.

***Participants in the Solicitation***

This document does not constitute a solicitation of proxy, an offer to purchase or a solicitation of an offer to sell any securities. Idera, BioCryst and their respective directors, executive officers and certain employees and other persons may be deemed to be participants in the solicitation of proxies from the stockholders of Idera and BioCryst in connection with the proposed mergers. Security holders may obtain information regarding the names, affiliations and interests of Idera's directors and officers in Idera's Annual Report on Form 10-K for the fiscal year ended December 31, 2017, which was filed with the SEC on March 7, 2018 and its definitive proxy statement for the 2018 annual meeting of stockholders, which was filed with the SEC on May 22, 2018. Security holders may obtain information regarding the names, affiliations and interests of BioCryst's directors and officers in BioCryst's Annual Report on Form 10-K for the fiscal year ended December 31, 2017, and any amendments thereto, which was filed with the SEC on March 12, 2018 and its definitive proxy statement for the 2018 annual meeting of stockholders, which was filed with the SEC on May 10, 2018. Additional information about the interests of BioCryst's directors and officers and Idera's directors and officers in the proposed mergers can be found in the above-referenced Registration Statement. These documents may be obtained free of charge from the SEC's website at www.sec.gov, Idera's website at www.iderapharma.com and BioCryst's website at www.biocryst.com.

# Forward-Looking Statements

These materials contain forward-looking statements within the meaning of the federal securities laws, including Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements involve known and unknown risks, uncertainties and other factors which may cause actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties, and important factors that could cause actual events or results to differ materially from Idera's or BioCryst's plans, estimates or expectations. Given these uncertainties, you should not place undue reliance on these forward-looking statements. With respect to the transactions contemplated by the merger agreement between Idera and BioCryst, these factors could include, but are not limited to: (i) Idera or BioCryst may be unable to obtain stockholder approval as required for the mergers; (ii) conditions to the closing of the mergers may not be satisfied; (iii) the mergers may involve unexpected costs, liabilities or delays; (iv) the effect of the announcement of the mergers on the ability of Idera or BioCryst to retain and hire key personnel and maintain relationships with patients, doctors and others with whom Idera or BioCryst does business, or on Idera's or BioCryst's operating results and business generally; (v) Idera's or BioCryst's respective businesses may suffer as a result of uncertainty surrounding the mergers and disruption of management's attention due to the mergers; (vi) the outcome of any legal proceedings related to the mergers; (vii) Idera or BioCryst may be adversely affected by other economic, business, and/or competitive factors; (viii) the occurrence of any event, change or other circumstances that could give rise to the termination of the merger agreement; (ix) risks that the mergers disrupt current plans and operations and the potential difficulties in employee retention as a result of the mergers; (x) the risk that Idera or BioCryst may be unable to obtain governmental and regulatory approvals required for the transactions, or that required governmental and regulatory approvals may delay the transactions or result in the imposition of conditions that could reduce the anticipated benefits from the transactions contemplated by the merger agreement or cause the parties to abandon the transactions contemplated by the merger agreement; (xi) risks that the anticipated benefits of the mergers or other commercial opportunities may otherwise not be fully realized or may take longer to realize than expected; (xii) the impact of legislative, regulatory, competitive and technological changes; (xiii) risks relating to the value of the new holding company shares to be issued in the mergers; (xiv) expectations for future clinical trials, the timing and potential outcomes of clinical studies and interactions with regulatory authorities; (xv) the risk that the credit ratings of the combined company or its subsidiaries may be different from what the companies expect; (xvi) economic and foreign exchange rate volatility; (xvii) the continued strength of the medical and pharmaceutical markets; (xviii) the timing, success and market reception for Idera's and BioCryst's products; (xix) the possibility of new technologies outdating Idera's or BioCryst's products; (xx) continued support of Idera's or BioCryst's products by influential medical professionals; (xxi) reliance on and integration of information technology systems; (xxii) the risks associated with assumptions the parties make in connection with the parties' critical accounting estimates and legal proceedings; (xxiii) the potential of international unrest, economic downturn or effects of currencies, tax assessments, tax adjustments, anticipated tax rates, raw material costs or availability, benefit or retirement plan costs, or other regulatory compliance costs; and (xxiv) other risks to the consummation of the mergers, including the risk that the mergers will not be consummated within the expected time period or at all. These risks, as well as other risks associated with the proposed mergers, are more fully discussed in the joint proxy statement/prospectus included in the Registration Statement filed with the SEC in connection with the proposed mergers.

While the list of factors presented here is, and the list of factors presented in the Registration Statement are, considered representative, no such list should be considered a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward looking statements. Consequences of material differences in results as compared with those anticipated in the forward-looking statements could include, among other things, business disruption, operational problems, financial loss, legal liability to third parties and similar risks, any of which could have a material adverse effect on BioCryst's or Idera's consolidated financial condition, results of operations, credit rating or liquidity. Readers are urged to consider these factors carefully in evaluating these forward-looking statements, and not to place undue reliance on any forward-looking statements. Readers should also carefully review the risk factors described in other documents that Idera and BioCryst file from time to time with the SEC. The forward-looking statements in this document speak only as of the date of this document. Except as required by law, Idera and BioCryst assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.



# Combination Creates Substantial Value

| | |
|---|---|
| **Maximizing Value and Market Potential** | ◆ Creates a unique player in rare diseases, with scale and strengthened competitive position |
| **Robust, Rare Disease Focused Pipeline** | ◆ More opportunities for success through diversified late-stage pipeline, variety of early-stage programs and supporting assets |
| **Synergistic Discovery Engines** | ◆ Synergistic discovery engines with enhanced development opportunities, including through joint small molecule and oligo treatments |
| **Proven Clinical and Commercial Track Record** | ◆ Complementary leadership with best-in-class people, facilities and commercial know-how in rare diseases |
| **Increased Financial Strength** | ◆ Increased financial strength and flexibility through significant cost synergies and opportunities to generate non-dilutive capital |

***New Data Presented on Tilsotolimod at ASCO 2018***

***Complementary Assets and Platforms Enhance Market Opportunities and Accelerate Value Creation***

# Combination Highlights

| | |
|---|---|
| **Terms** | • Stock for stock transaction<br>• Each share of BioCryst to be converted into 0.50 shares of new company stock<br>• Each share of Idera to be converted into 0.20 shares of new company stock |
| **Ownership at Closing** | • BioCryst stockholders to own 51.6% of new company and Idera stockholders to own 48.4%, on a fully diluted basis |
| **Cash Position** | • ~$204 million net cash balance*<br>• Opportunities for non-dilutive capital |
| **Board of Directors** | • Robert A. Ingram (Chairman)<br>• Vincent Milano<br>• Jon Stonehouse<br>• James Geraghty<br>• Mark Goldberg, M.D.<br>• Maxine Gowen, Ph.D.<br>• Nancy Hutson, Ph.D.<br>• Kenneth B. Lee, Jr. |
| **Company Name, CEO, Headquarters, and Research Center** | • Valenscion Incorporated<br>• Vincent Milano, Chief Executive Officer<br>• Headquarters: Exton, PA<br>• Research Center: Birmingham, AL |
| **Closing Conditions** | • Subject to approval of BioCryst and Idera stockholders<br>• Subject to other customary closing conditions |
| **Voting Agreement** | • A significant stockholder of each company has agreed to enter into a voting and support agreement and has agreed to vote in favor of the transaction. This stockholder owns ~18% of outstanding Idera shares and ~14% of outstanding BioCryst shares. |
| **Transaction Close** | • Expected in third quarter 2018 |

* Unaudited pro-forma cash balance as of March 31, 2018



# Creating a Leader in Innovative Rare Disease Therapies

| biocryst |
|---|
| Developing Oral Therapies for Life Threatening Rare Diseases |
| Small Molecule Rare Disease Discovery Engine |
| 2 Late-Stage Programs |
| Lead Candidate: **BCX7353** Prophylactic HAE |

| idera |
|---|
| Rare Disease Company with Strong Immuno-Oncology Assets |
| Oligo Rare Disease Discovery Engine |
| Recent Positive Data on Key Late-Stage Program |
| Lead Candidate: **Tilsotolimod** PD-1 Refractory Melanoma |

***Strengthened Scale and Competitive Position***

# Robust Rare-Disease Focused Pipeline

Idera BioCryst

| | Lead optimization | Pre-clinical | Ph 1 | Ph 2 | Ph 3 | Filed | Approved |
|---|---|---|---|---|---|---|---|
| **STRATEGY: Discover and develop novel therapies for life-threatening, rare diseases** | | | | | | | |
| Tilsotolimod – PD-1 Refractory Melanoma in combination with ipilimumab | | | | Orphan-Designation | | | |
| BCX7353 – HAE Prophylaxis (Capsule) | | | | Orphan-Designation | | | |
| BCX7353 – HAE Acute (Liquid) | | | | | | | |
| Tilsotolimod – Solid Tumor Monotherapy | | | | | | | |
| Second generation kallikrein inhibitors (HAE & Other Indications) | | | | | | | |
| BCX9250 – Fibrodysplasia Ossificans BCX9499 – Progressiva (FOP) | | | | | | | |
| Other rare diseases | | | | | | | |
| **SUPPORTING ASSETS: Externally funded, potential for significant capital infusions** | | | | | | | |
| RAPIVAB® (peramivir injection) | | | | licensed to Seqirus, Shionogi and Green Cross | | | |
| IMO-9200 – Autoimmune Disease | | | | licensed to Vivelix | | | |
| Galidesivir (broad spectrum antiviral) I.M. | | | | | | | |
| 3GA Candidate – Renal Target | | | | licensed to GSK | | | |



# Tilsotolimod Data from ILLUMINATE-204 Trial

*Trial Objectives*

## Primary Objective

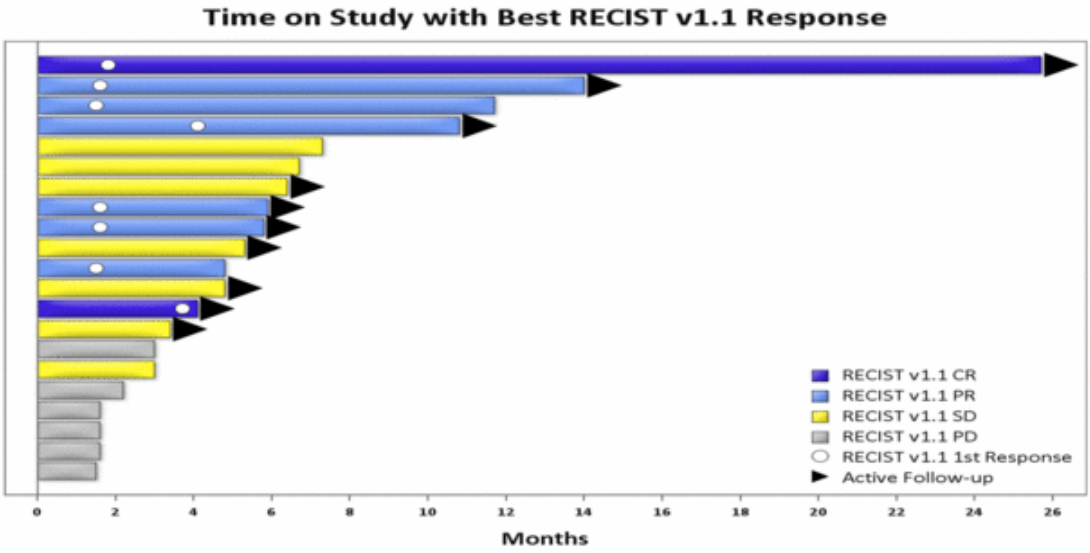
**Assess preliminary clinical activity of tilsotolimod in combination with ipilimumab at the respective recommended Phase 2 dose (RP2D) in patients with metastatic melanoma that is not responsive to PD-1 inhibitor therapy, using Response Evaluation Criteria in Solid Tumors (RECIST v1.1) with a target of ORR of 35%**

## Secondary Objective

**Further assess the safety and tolerability of tilsotolimod in combination with ipilimumab**

# Tilsotolimod Data from ILLUMINATE-204 Trial

## *38.1% Response Rate / 71.4% Disease Control Rate*

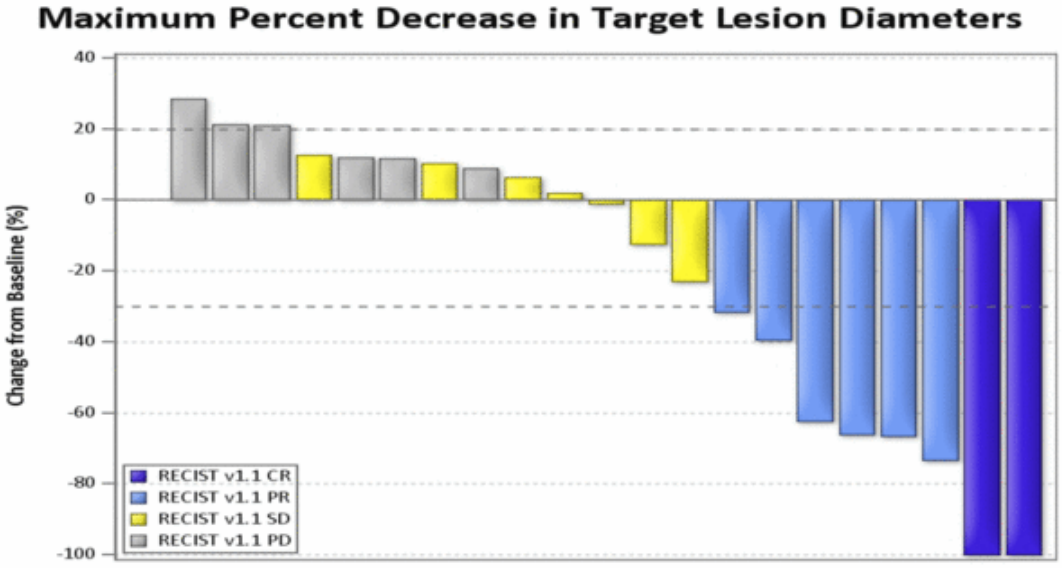



Data cut-off date: 09MAY2018



# Tilsotolimod Data from ILLUMINATE-204 Trial

## *38.1% Response Rate / 71.4% Disease Control Rate*




Data cut-off date: 09MAY2018

# Tilsotolimod Data from ILLUMINATE-204 Trial
## *Results Reinforce Clinical Attractiveness of Treatment*

- Tilsotolimod + ipilimumab revives the immune response in anti-PD-1-resistant tumors resulting in altering the tumor microenvironment and conversion of cold (noninflamed) to hot (inflamed) tumors
- This combination treatment has produced durable responses and demonstrates substantial disease control rate in this clinically challenging population, including subjects with Stage IV M1c disease and BRAF mutations
- The combination regimen is generally well tolerated and no synergistic toxicity was observed
  - The toxicity profile was consistent with ipilimumab alone
  - Six subjects (23%) had immune-related toxicities
- The current data led to an ongoing global randomized Phase 3 study comparing tilsotolimod plus ipilimumab to ipilimumab alone in the anti-PD-1 refractory melanoma population



# Tilsotolimod Data from ILLUMINATE-204 Trial
## *Phase 3 Asset with Real Utility in I/O Toolkit*

- Tilsotolimod data continues to be very clinically meaningful even after doubling the number of patients
- Response rate of 38.1% in Idera's trial is approximately triple that of response rates of ipilimumab alone
- Tilsotolimod is the most advanced and has the best objective response rate, controllable disease rate and durability of response for all of the TLR9's in PD-1 refractory melanoma
- Trial results create a treatment profile that is more attractive than BioCryst used in market research and to forecast the value
- Significantly larger data set and robust result demonstrate less risk and support value proposition of combined company

# Tilsotolimod Data from ILLUMINATE-204 Trial

## *Results Reinforce Clinical Attractiveness of Treatment*

Unresectable or metastatic melanoma w/ confirmed radiologic progression on or after a PD-1 inhibitor:

- ≥21d from most recent aPD-1 and no intervening systemic Tx
- No prior ipi (except adjuvant)
- Ocular melanoma excluded

**N~300**

Ipilimumab 3 mg/kg Q3wks for 4 doses

**No Crossover**

Ipilimumab (same, beginning wk 2)
+
intratumoral tilsotolimod,
wks 1, 2, 3, 5, 8, 11, 16, 20, 24

$1^0$ endpoint family:

- OS
- ORR (RECIST v1.1)



# Merger Upside: Maximizing Value and Market Potential

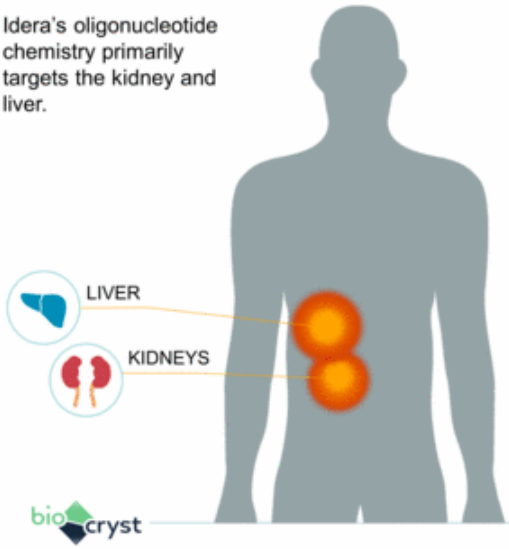
| Value Driver | | Merger Amplifier |
|---|---|---|
| Commercializing BCX7353 | → | **Idera management HAE launch experience** |
| Investing in commercial launch and ongoing pipeline development | → | **Capital from out-licensing opportunities** |
| Expanding market opportunity + diffusing risk | → | **BCX7353 and tilsotolimod Phase 3 opportunities in rare disease markets + tilsotolimod in other cancer markets** |
| Building rare disease pipeline | → | **Leveraging and combining complementary discovery engines** |

***Complementary Assets and Platforms Enhance Market Opportunities and Accelerate Value Creation***

# Synergistic Discovery Engines with Enhanced Development Opportunities

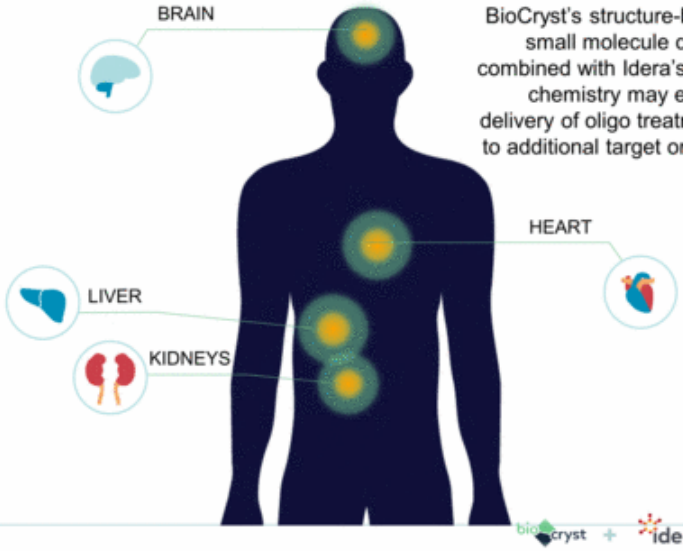
idera

Idera's oligonucleotide chemistry primarily targets the kidney and liver.




idera + bio cryst

BioCryst's structure-based small molecule design combined with Idera's oligo chemistry may enable delivery of oligo treatments to additional target organs.






# Proven Rare Disease Clinical & Commercial Track Record

CINRYZE® C1 inhibitor (human)

- 1st prophylactic treatment of HAE
- Grew to ~$400M in N.A. annual sales in 5 years

Hizentra® Immune Globulin Subcutaneous (Human) 20% Liquid

- Multiple global and U.S. rare disease launches
- Led launch for 5 global brands that drive ~70% of CSL's current revenue
- Grew U.S. Hizentra and Privigen sales to >$1B

privigen® Immune Globulin Intravenous (Human), 10% Liquid

Kcentra® Prothrombin Complex Concentrate (Human)

- >245 HAE patients dosed and studied
- CMOs clinical development/launch experience: Aranesp®, Enbrel®, Kineret®, Neulasta® and Sensipar® Taxotere® Bactroban®, Relafen®/ Reliflex® Lovenox®, Celectol®, Augmentin®, Timentin®, temocillin®.

VANCOCIN® HCl (vancomycin hydrochloride capsules, USP)

- Treatment of C. difficile-associated diarrhea (CDAD)
- Grew to ~$300M in annual sales

| Vincent Milano | Dan Soland | William Sheridan, MB BS | Joanna Horobin, MB ChB | Lynne Powell | Clayton Fletcher |
|---|---|---|---|---|---|
| Chief Executive Officer | Chief Operating Officer | Chief Medical Officer | Chief Medical Officer | Chief Commercial Officer | VP, Strategy/ Bus. Development |

# Solid Capital Position & Meaningful Operational Synergies

- ~$204 million net cash balance*
  - Capital for continued clinical development through next major milestone events and into Q3 2019
  - Capital for commercial launch planning and preparation
  - Multiple options for non-dilutive capital through renegotiating our debt, cash from in the money warrants and government stockpiling
  - Opportunities to generate larger amounts of non-dilutive capital through partnering in the near term and commercializing in the long term
- Projected $20 million in cash synergies in year two and approximately $30 million in annual pre-tax cost synergies expected in year three after closing
  - Facilities consolidation: Headquarters to Exton, PA; research center to Birmingham, AL
  - Expense consolidation over time expected to create additional cost savings and benefits

***Strong Combined Financial Profile with Opportunities to Generate Non-Dilutive Capital***

* Unaudited pro-forma cash balance as of March 31, 2018

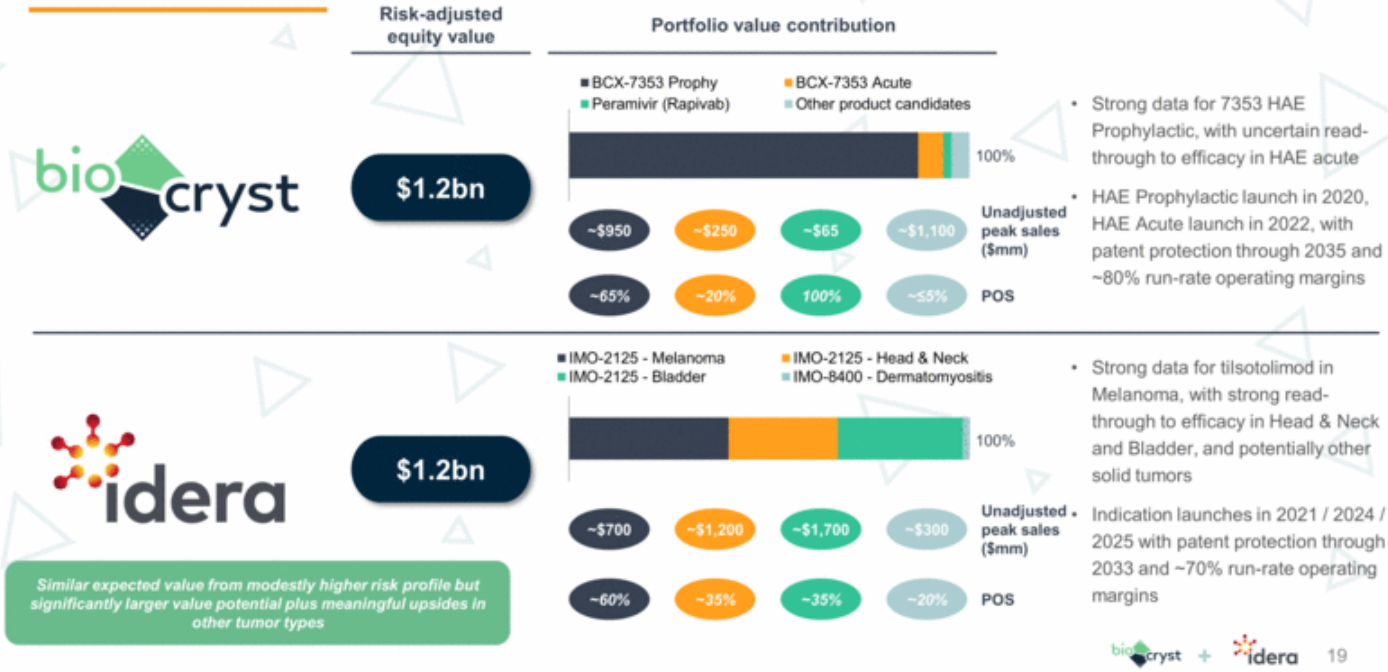


# BioCryst & Idera Boards Carefully Evaluated Strategic Options

- Engaged, well-advised Boards
  - BioCryst and Idera Boards comprised of highly experienced directors with extensive industry knowledge
  - BioCryst Board of Directors met numerous times over last two years to discuss value enhancing opportunities for BioCryst
  - Both Boards retained financial and legal advisors to assist in the evaluation
- Reviewed alternative value enhancing strategies
- BioCryst and Idera Boards engaged in discussions with numerous potential partners

***Both Boards Determined Merger Made Strategic Sense and is a Unique Opportunity to Enhance Stockholder Value***

# BioCryst + Idera: Valuation Perspectives




- Strong data for 7353 HAE Prophylactic, with uncertain read-through to efficacy in HAE acute
- HAE Prophylactic launch in 2020, HAE Acute launch in 2022, with patent protection through 2035 and ~80% run-rate operating margins

- Strong data for tilsotolimod in Melanoma, with strong read-through to efficacy in Head & Neck and Bladder, and potentially other solid tumors
- Indication launches in 2021 / 2024 / 2025 with patent protection through 2033 and ~70% run-rate operating margins

*Similar expected value from modestly higher risk profile but significantly larger value potential plus meaningful upsides in other tumor types*



# Combination Creates Substantial Value

| | |
|---|---|
| **Maximizing Value and Market Potential** | ◆ Creates a unique player in rare diseases, with scale and strengthened competitive position |
| **Robust, Rare Disease Focused Pipeline** | ◆ More opportunities for success through diversified late-stage pipeline, variety of early-stage programs and supporting assets |
| **Synergistic Discovery Engines** | ◆ Synergistic discovery engines with enhanced development opportunities, including through joint small molecule and oligo treatments |
| **Proven Clinical and Commercial Track Record** | ◆ Complementary leadership with best-in-class people, facilities and commercial know-how in rare diseases |
| **Increased Financial Strength** | ◆ Increased financial strength and flexibility through significant cost synergies and opportunities to generate non-dilutive capital |

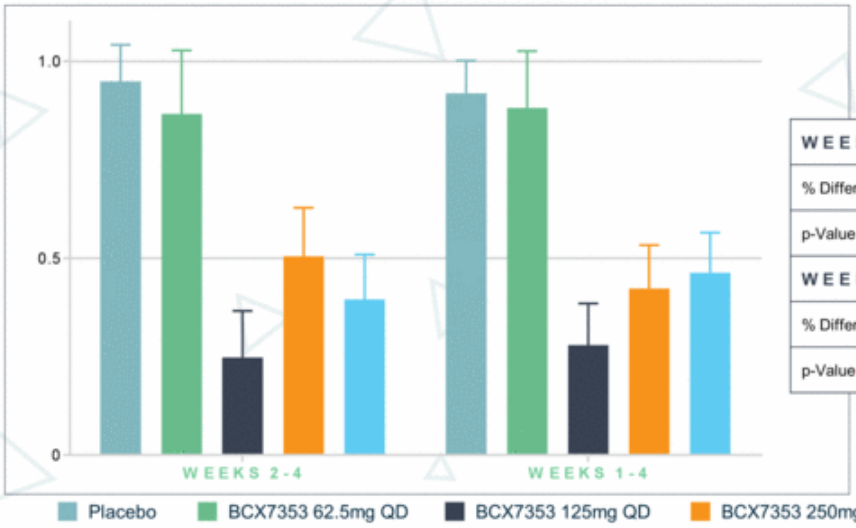
***New Data Presented on Tilsotolimod at ASCO 2018***

***Complementary Assets and Platforms Enhance Market Opportunities and Accelerate Value Creation***

# Appendix

## APeX-1: Overall Angioedema Attack Rate per Week, PP Population, Weeks 2-4 and 1-4

Attack Rate: LS Mean Attacks/Week




| | 62.5mg | 125mg | 250mg | 350mg |
|---|---|---|---|---|
| WEEKS 2-4 | | | | |
| % Difference, Active-PBO | -9% | -74% | -47% | -58% |
| p-Value | 0.657 | <0.001 | 0.005 | <0.001 |
| WEEKS 1-4 | | | | |
| % Difference, Active-PBO | -4% | -70% | -54% | -50% |
| p-Value | 0.818 | <0.001 | <0.001 | <0.001 |

# APeX-1: 125 mg Dose Provided Consistent Reductions in Attack Rate

| Analysis | n | LS mean[1] Attacks per Week | | Difference vs Placebo | Percentage Reduction vs Placebo | p-Value vs Placebo |
|---|---|---|---|---|---|---|
| | | BCX7353 125 mg | Placebo | | | |
| Confirmed attacks, Weeks 2-4 PP population | 13 | 0.248 | 0.949 | -0.700 | 74% | <0.001 |
| Confirmed attacks, Weeks 2-4 ITT population | 14 | 0.249 | 0.952 | -0.703 | 74% | <0.001 |
| Confirmed attacks, Weeks 1-4 PP population | 13 | 0.279 | 0.919 | -0.641 | 70% | <0.001 |
| Confirmed attacks, Weeks 1-4 ITT population | 14 | 0.271 | 0.913 | -0.642 | 70% | <0.001 |
| Confirmed attacks requiring treatment, Weeks 2-4 PP population | 13 | 0.222 | 0.823 | -0.601 | 73% | <0.001 |
| Confirmed attacks requiring treatment, Weeks 2-4 ITT population | 14 | 0.225 | 0.786 | -0.562 | 71% | 0.002 |
| Confirmed attacks requiring treatment, Weeks 1-4 PP population | 13 | 0.221 | 0.812 | -0.591 | 73% | <0.001 |
| Confirmed attacks requiring treatment, Weeks 1-4 ITT population | 14 | 0.218 | 0.776 | -0.558 | 72% | <0.001 |

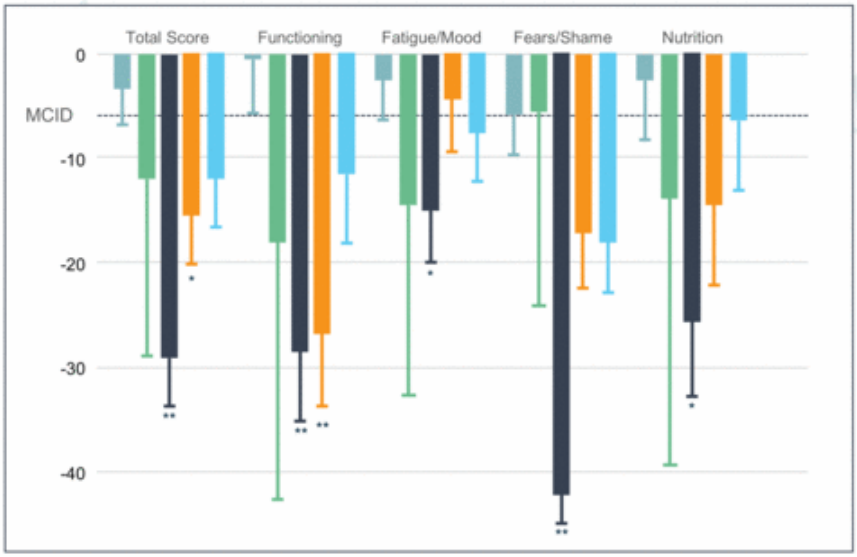
[1] Least squares mean calculated using an ANCOVA model with qualifying attack rate as covariate

Final Data



# APeX-1: Angioedema Quality of Life (AE-QoL): LS Mean Change from BL at Day 29, PP

QOL Score Improved




Difference in adjusted least square means are shown (Active treatment minus Placebo). ANCOVA Model includes terms of treatment and adjusted qualifying attack rate. Reductions (negative changes from BL) represent improvement in quality of life scores. MCID, minimum clinically important difference, -6 points (*Weller, K. 2016. Allergy 71(8): 1203-1209.*) BCX7353 dose level compared with placebo

# APeX-1: Treatment-Emergent Adverse Event Summary

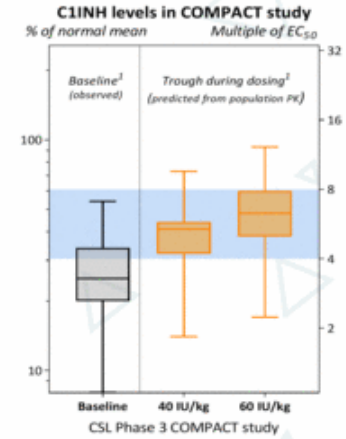
| Category | BCX7353 62.5 mg N = 7 | BCX7353 125 mg N = 14 | BCX7353 250 mg N = 14 | BCX7353 350 mg N = 18 | Placebo N = 22 |
|---|---|---|---|---|---|
| Subjects with any TEAE[1], n (%) | 4 (57) | 7 (50) | 11 (79) | 14 (78) | 15 ( 68.2) |
| Subjects with any Serious AE, n (%) | 0 | 0 | 1 (7)[2] | 0 | 0 |
| Subjects with Drug-Related Grade 3/4 AE, n (%) | 0 | 0 | 0 | 1 (6) | 0 |
| Subjects with AE Leading to D/C from Study Drug, n (%) | 0 | 0 | 0 | 3 (17) | 0 |
| Non-drug-related, n (%) | 0 | 0 | 0 | 1 (6)[3] | 0 |
| Drug-related, n (%) | 0 | 0 | 0 | 2 (11)[4,5] | 0 |

[1] TEAE- treatment-emergent adverse event.
[2] GI infection- investigator assessed as unrelated to study drug. Abdominal symptoms similar to several previous non-HAE-attack episodes occurring over past 3 years resulting in severe vomiting and diarrhea. Pt presented to ER and hospitalized for IV fluids and antiemetics as a precaution. No HAE acute attack meds given. Recovered and discharged the following day. Missed 1 day of dosing due to event.
[3] Pre-existing liver disorder (improved from baseline, but persisting). Previously reported in 1st interim analysis.
[4] n=1 Gastroenteritis with liver disorder (both assessed as related) (elevated ALT 1.9x ULN, GGT 5.4x ULN and ALP 1.6x ULN, with normal AST and bilirubin). Previously reported in 1st interim analysis.
[5] n=1 Vomiting/abdominal cramps. Previously reported in 2nd interim analysis.



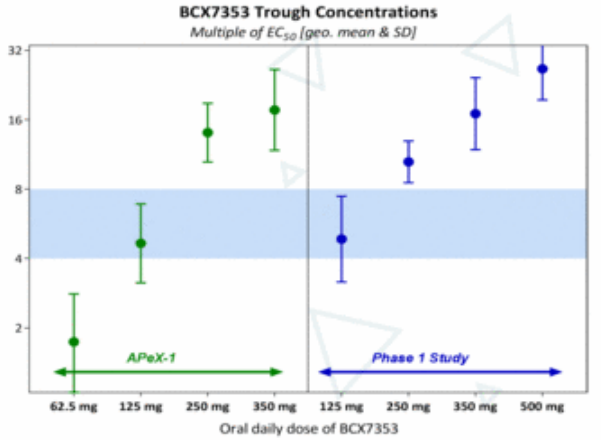
# APeX-1: Exposure Comparisons of BCX7353 and SC C1INH

**CSL-830 Phase 3 Study**




**C1INH levels at baseline and after SC dosing with CSL-830[1]**

**BCX7353 APeX-1 & Phase 1 Study**




**BCX7353 plasma concentrations at 24 hours post-dose**

[1] Longhurst, H. et al. N Engl J Med 376, 1131-1140 (2017). Box plots represent median, 25th and 75th percentiles, minimum and maximum values. CSL-830 and BCX7353 data are from distinct clinical trials and no head to head study has been conducted.

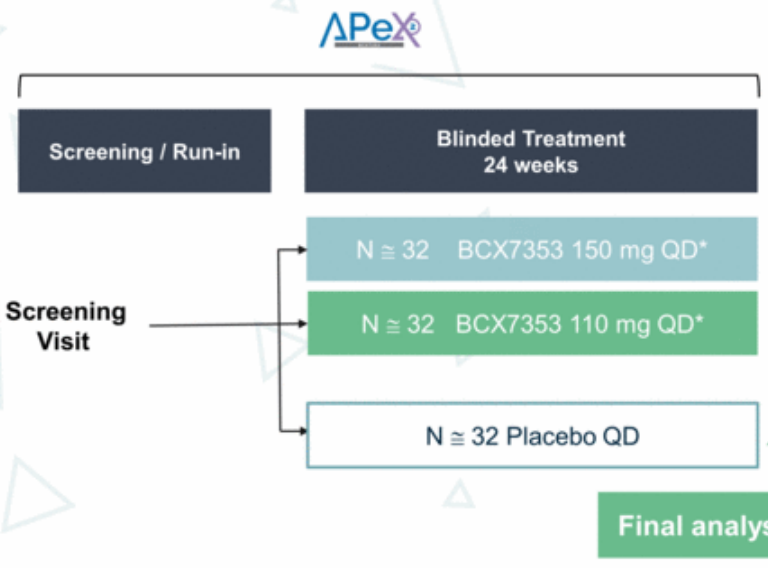
# Predictable PK Supports 175 mg as Second Dose in Phase 3

| Dose, mg QD | % > 4 x $EC_{50}$ | | % > 6 x $EC_{50}$ | | % > 8 x $EC_{50}$ | |
|---|---|---|---|---|---|---|
| | Predicted | Actual | Predicted | Actual | Predicted | Actual |
| 62.5 | -- | *0* | -- | *0* | -- | *0* |
| 125 | 70 | *64* | 38 | *43* | 17 | *0* |
| 175 | 93 | | 80 | | 58 | |
| 200 | 97 | | 88 | | 73 | |
| 225 | 98 | | 93 | | 83 | |
| 250 | 100 | *100* | 97 | *100* | 93 | *100* |

- Given the predictable PK of BCX7353, simulations are helpful in selecting an intermediate dose of BCX7353 to study that is between 125 mg and 250 mg.
- These simulations suggest a relatively small increase in dose above 125 mg should achieve a significant increase in the proportion of subjects achieving trough levels above the therapeutic target.
- These simulations suggest 175 mg dose should maintain trough drug levels > 4 x $EC_{50}$ in > 90% of patients.
- Doses ≥ 200 mg offer little additional increment in proportions achieving target level.



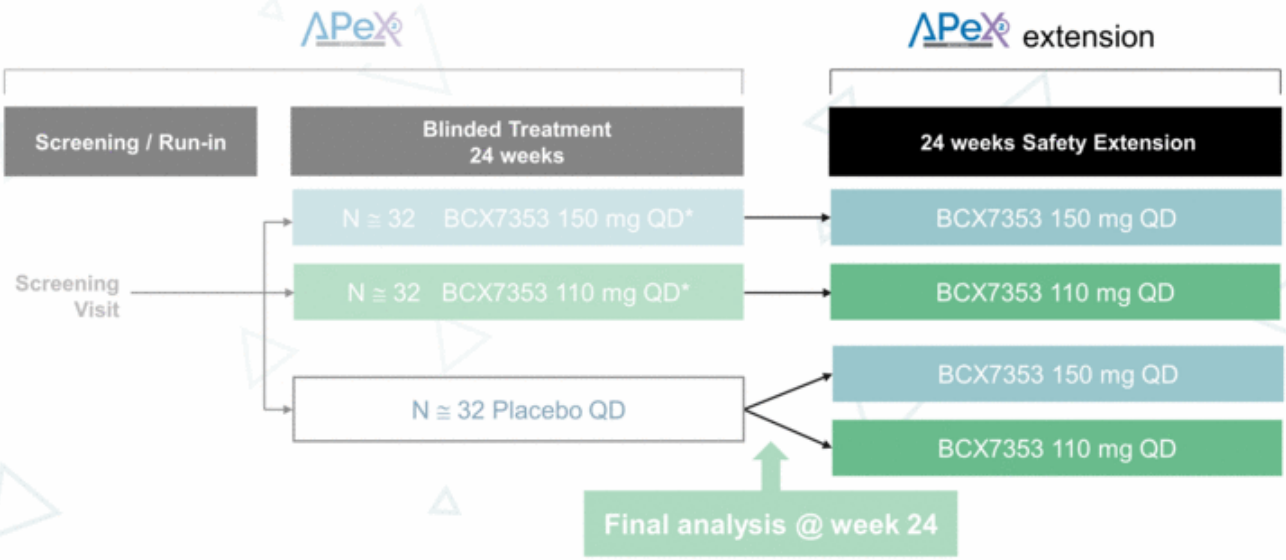
# APeX-2: Phase 3 Trial Design




- Primary endpoint at Week 24:
  - Rate of Investigator-confirmed HAE attacks through entire treatment period
- Study powered at >90% to detect a ≥50% reduction in attack rate over placebo

*Doses in Phase 2 APeX-1 were shown as the dihydrochloride salt:
150 mg = 175 mg dihydrochloride salt; 110 mg = 125 mg dihydrochloride salt

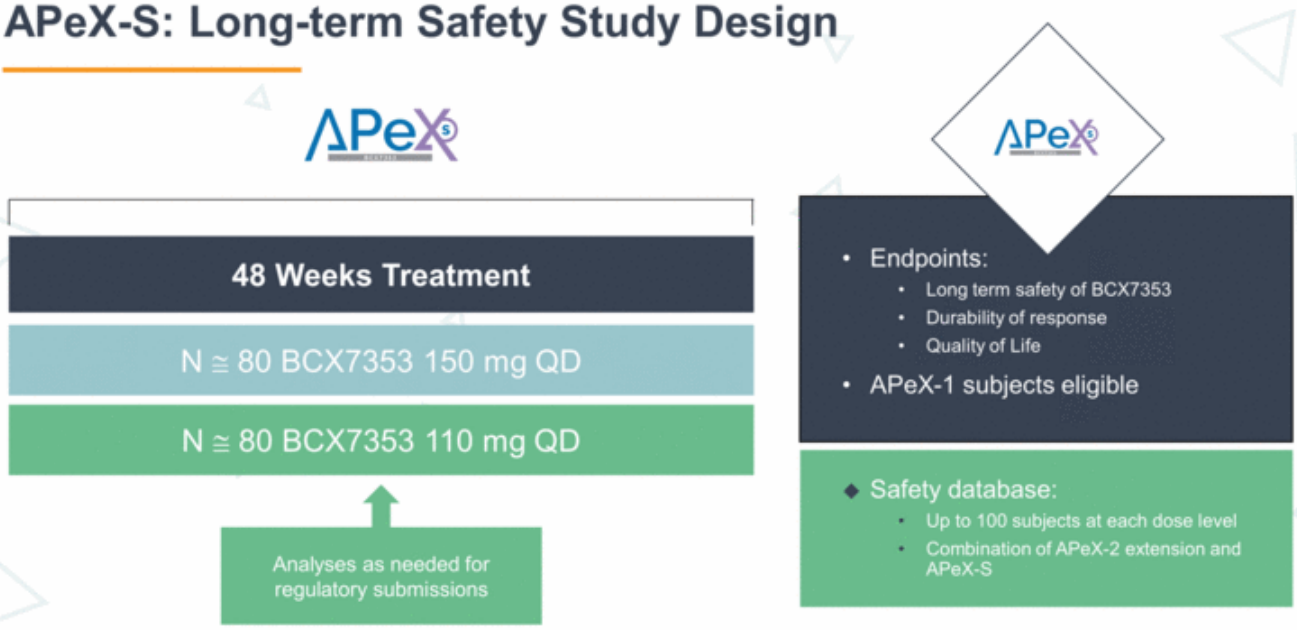
# APeX-2: Phase 3 Trial Design – Safety Extension




*Doses in Phase 2 APeX-1 were shown as the dihydrochloride salt:
150 mg = 175 mg dihydrochloride salt; 110 mg = 125 mg dihydrochloride salt



# APeX-S: Long-term Safety Study Design




*Doses in Phase 2 APeX-1 were shown as the dihydrochloride salt:
150 mg = 175 mg dihydrochloride salt; 110 mg = 125 mg dihydrochloride salt

# Phase 1/2 Study in Anti-PD-1 Refractory Melanoma

illuminate Oncology Clinical Trials 2125-204

Phase 2 Expansion with Ipilimumab Enrolling

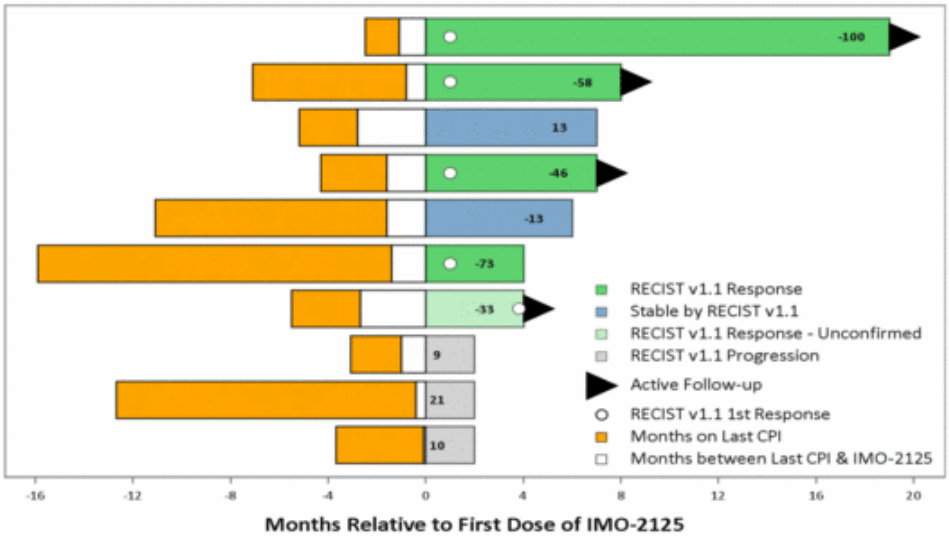
RP2D of IMO-2125 is 8mg

| | |
|---|---|
| Dose-finding: IMO-2125 + ipilimumab SAFETY ASSESSMENT COMPLETED | → Phase 2 IMO-2125 + ipilimumab OPEN |
| Dose-finding: IMO-2125 + pembrolizumab ONGOING | → Phase 2 IMO-2125 + pembrolizumab PLANNED |

Dosing:
Tilsotolimod is given as a single intratumoral agent week 1,2,3,5,8,11,15,19,23 Ipilimumab and pembrolizumab are administered per label beginning week 2
Deep injections are permitted with interventional radiology guidance
No need for infectious precautions

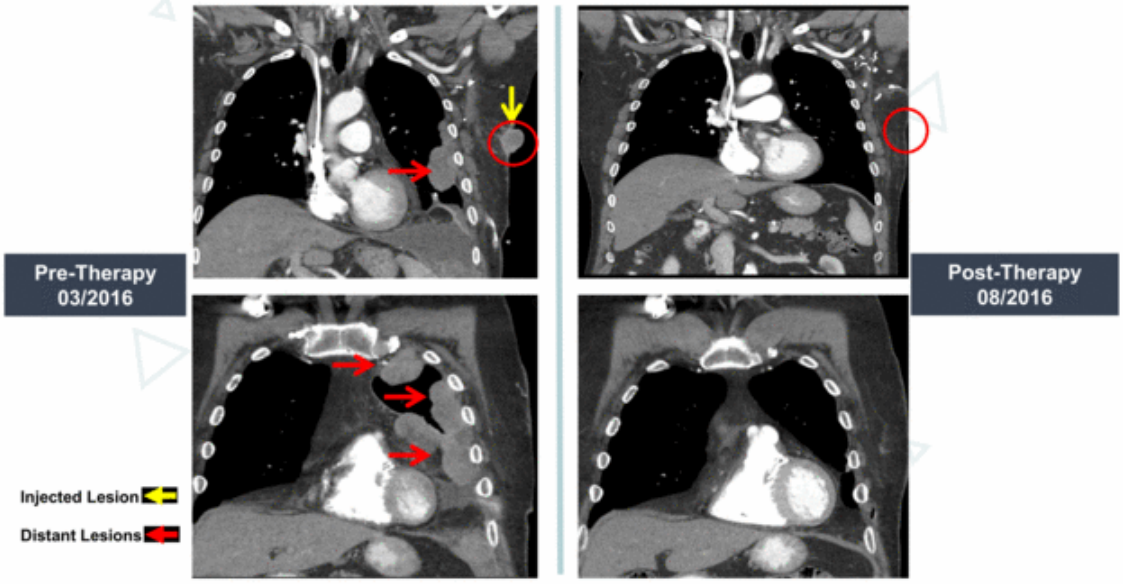


# Time on Study: Best RECIST v1.1 Response and Largest Percentage Decrease in Target Lesions (8mg subjects)




Time on study ends at RECIST v1.1 PD (including death & start of anti-cancer therapy) or withdrawal for any reason.
Subjects treated with IMO-2125 8mg + Ipilimumab with at least 1 post-baseline disease evaluation. Some CPI start and stop dates have been imputed.
Data cut-off date: 03NOV2017

# Patient 004 Remains a CR since May 2016






# Phase 1 Conclusions

- The combination of tilsotolimod with ipilimumab was tolerable at all dose levels studied
- Dendritic cell activation, detectable within 24 hours of the first tilsotolimod injection, is evidence for target acquisition at the Recommended Phase 2 Dose (8mg)
- Tilsotolimod with ipilimumab showed clinical activity at the RP2D of 8mg in anti-PD-1 refractory melanoma
  - 5 of 10 (50%) responded
  - 7 of 10 (70%) experiencing disease control
  - An additional PR of >1 year has been reported at 4mg
- Dose finding for tilsotolimod with pembrolizumab is ongoing, and one partial response (PR) has been seen

## Phase 2 Expansion Update

illuminate Oncology Clinical Trials 2125-204

- Ipilimumab Combination Phase 2 Trial Expansion – Targeting approximately 60 patients with PD-1 refractory metastatic melanoma treated with 8mg
  - 21 patients enrolled
  - 10 Centers (5 sites currently enrolling)
    - MD Anderson, Roswell Park, Vanderbilt, Huntsman, Uni. of Arizona
  - Open label design
    - Allows for periodic data updates
    - Opportunistic engagements with regulatory authorities

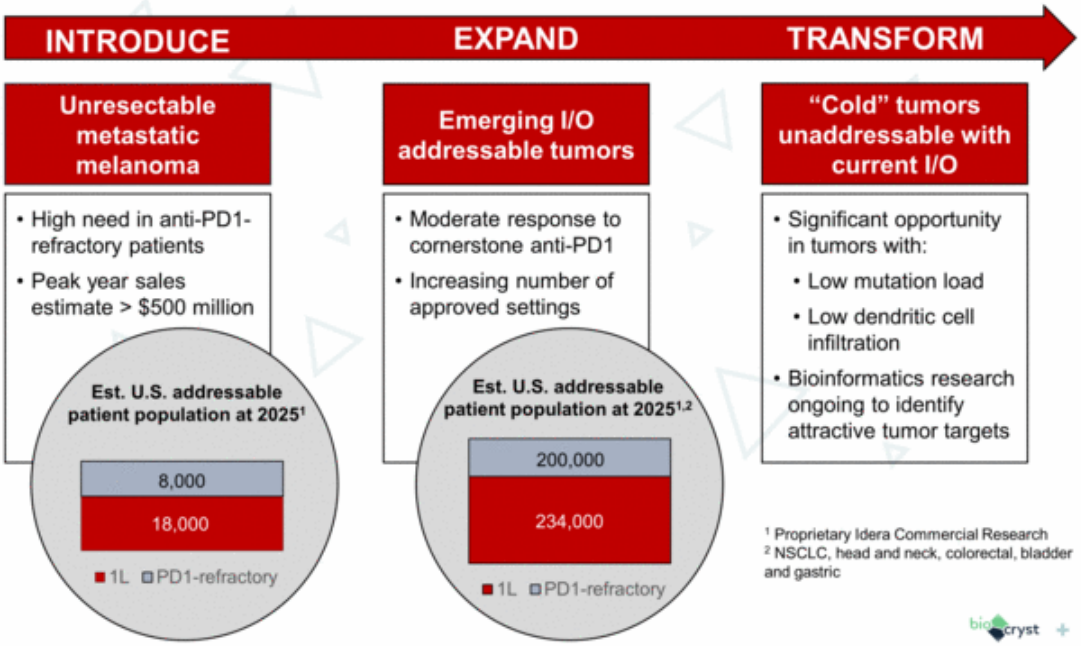


## Phase 3 Readiness (FPFV 1Q18)

illuminate IMO-2125 Clinical Trials 2125-MEL-301

- Agreement with FDA and MHRA on design and path forward for regular and accelerated approval (one study)
- Fast Track Designation Granted by U.S. FDA in Q4 2017
- Global trial (US, Can, EU, Aus)
  - ~300 patients
  - ~70 sites planned
- CMC work commenced1Q18
  - Commercial presentation of tilsotolimod will be used
- Regulatory filings underway
  - Open U.S. IND
  - CTA filings on track

# Growth/Partnering Opportunities




[1] Proprietary Idera Commercial Research
[2] NSCLC, head and neck, colorectal, bladder and gastric