

# Oncternal Shareholder Update

May 16, 2019



# Forward Looking Statements

This presentation contains forward-looking statements. These statements may discuss goals, intentions and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current beliefs of Oncternal Therapeutics, Inc. ("Oncternal"), as well as assumptions made by, and information currently available to Oncternal. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negatives of these terms or other similar expressions. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation: (i) the risk that the conditions to the closing of the merger between Oncternal and GTx, Inc. ("GTx"), are not satisfied; (ii) risks related to the ability of Oncternal and GTx to manage its operating expenses and its expenses associated with the merger pending closing; (iii) the risk that as a result of adjustments to the exchange ratio, Oncternal stockholders or GTx stockholders could own more or less of the combined company than is currently anticipated; (iv) Oncternal's plans to present data at the ASCO Annual Meeting; (v) the timing of enrollment of the Phase 1/2 clinical trial of cirmtuzumab in combination with ibrutinib; (vi) Oncternal's clinical plans for cirmtuzumab, TK-216 and its CAR-T product candidate; (vii) uncertainty regarding whether potential adverse reactions or side effects may occur in the course of developing and testing product candidates such as cirmtuzumab. All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

If any of these risks or uncertainties materialize or any of these assumptions prove incorrect, the results of Oncternal, GTx or the combined organization could differ materially from the forward-looking statements. All forward-looking statements in this presentation are current only as of the date on which the statements were made. Oncternal and GTx do not undertake any obligation to publicly update any forward-looking statement to reflect events or circumstances after the date on which any statement is made or to reflect the occurrence of unanticipated events.

# Additional Information and Where to Find It

In connection with the proposed merger between Oncternal Therapeutics, Inc. and GTx, Inc., GTx has filed with the SEC a registration statement on Form S-4 that contains a prospectus/proxy statement/information statement. The registration statement was declared effective on May 7, 2019 and the definitive proxy statement/prospectus/information statement was distributed to the stockholders of GTx and Oncternal. For a discussion of the factors that may cause Oncternal, GTx or the combined organization's actual results, performance or achievements to differ materially from any future results, performance or achievements expressed or implied in such forward-looking statements, see the section entitled "Risk Factors" of the definitive proxy statement/prospectus/information statement. Additional factors that could cause actual results to differ materially from those expressed in the forward-looking statements are discussed in reports filed with the SEC by GTx including GTx's most recent Annual Report on Form 10-K, Form 10-K/A and Current Reports on Form 8-K filed with the SEC. Investors and security holders of GTx and Oncternal are urged to read the definitive proxy statement/prospectus/information statement and other materials filed or that will be filed with the SEC before making any voting or investment decision with respect to the merger because they contain or will contain important information about Oncternal, GTx and the merger. The proxy statement/prospectus/information statement and other relevant materials (when they become available), and any other documents filed by GTx with the SEC, may be obtained free of charge at the SEC web site at [www.sec.gov](http://www.sec.gov). In addition, investors and security holders may obtain free copies of the documents filed with the SEC by GTx by directing a written request to: GTx, Inc., 17 W Pontotoc Ave., Suite 100, Memphis TN 38103, Attention: Corporate Secretary. Investors and security holders are urged to read the definitive proxy statement/prospectus/information statement and other relevant materials when they become available before making any voting or investment decision with respect to the merger.

This communication shall not constitute an offer to sell or the solicitation of an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction. No offering of securities shall be made except by means of a prospectus meeting the requirements of Section 10 of the Securities Act of 1933, as amended.

## **Participants in the Solicitation**

Oncternal and its directors and executive officers and GTx and its directors and executive officers may be deemed to be participants in the solicitation of proxies from the stockholders of GTx in connection with the proposed merger. Information regarding the special interests of these directors and executive officers in the merger is contained in the preliminary proxy statement/prospectus/information statement referred to above and in the available definitive proxy statement/prospectus/information statement. These documents are available free of charge at the SEC web site ([www.sec.gov](http://www.sec.gov)) and from the Corporate Secretary of GTx at the address above.

A decorative graphic consisting of multiple thin, light blue lines that flow and curve across the page, creating a sense of movement and depth. The lines are most dense in the upper left and lower right areas, tapering off towards the center.

# Oncternal Development Program Update



# Oncternal Pipeline

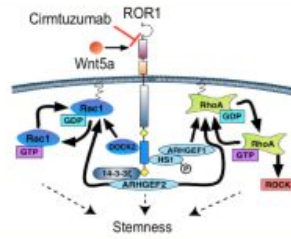
Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestone
Cirmtuzumab	CLL	Phase 2a				Report Phase 1 data mid 2019
	MCL	Phase 1b				Report Phase 1 data 2H 2019
	Breast Cancer	Phase 1b				Assess safety of Paclitaxel combination
TK216	Ewing Sarcoma	Phase 1				Initiate expansion cohort mid 2019
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	Prostate Cancer	Preclinical				Initiate IND enabling studies 1H 2020
ROR1 CAR-T	Heme Cancers	Preclinical				Select candidate construct 2H 2019
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CLL – chronic lymphocytic leukemia; MCL – mantle cell lymphoma; AML – acute myeloid leukemia

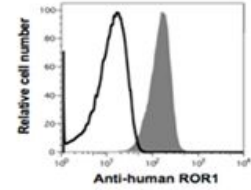
# Cirtuzumab: Potential First-in-Class ROR1 Monoclonal Antibody

## Cirtuzumab humanized ROR1 mAb

- Humanized high affinity mAb
- Blocks Wnt5a growth & invasion
- Does not recognize normal adult tissues
- High ROR1 expression on MCL and CLL
- Expression on multiple solid tumors
- Exclusive worldwide license from UCSD
- Development supported by CIRM grant

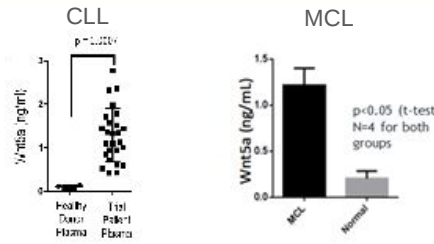


ROR1 expression MCL

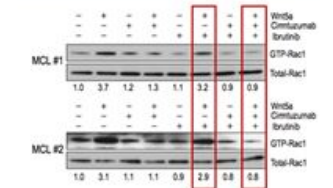


## Cirtuzumab synergism in MCL/CLL

- High Wnt5a levels in MCL and CLL patients
- Wnt5a pathway remains active in ibrutinib treated MCL and CLL
- Cirtuzumab inhibits Wnt5a signalling
- Cirtuzumab plus ibrutinib believed to exert synergistic effects in MCL and CLL<sup>1</sup>
- Cirtuzumab believed to be synergistic with venetoclax<sup>2</sup>

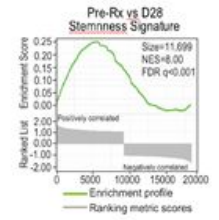
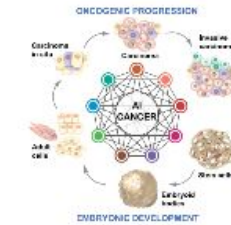
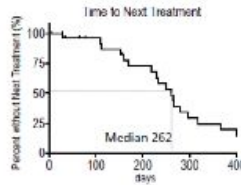


Cirtuzumab but Not ibrutinib Inhibits ROR1 Mediated Signaling Via Downstream GTP-Rac1



## Cirtuzumab CLL Phase 1

- Long half-life may support monthly dosing
- Prolonged progression-free survival with anti-CLL effects<sup>3</sup>
- Novel de-differentiating effect reversing CLL stemness signature<sup>3,4</sup>
- Phase 1/2 study now evaluating cirtuzumab plus ibrutinib



# Phase 1/2 Study of Cirmtuzumab and Ibrutinib in Patients with MCL and CLL

- Unmet medical need - Ibrutinib single agent active, but:
  - Complete responses for previously treated CLL consistently <10%<sup>1</sup>
  - Complete responses for previously treated MCL 26%<sup>2</sup>
- **Part 1** dose-finding in MCL and CLL
  - Cirmtuzumab at 2, 4, 8 and 16 mg/kg per dose
  - One month cirmtuzumab for biomarkers then combination treatment
- **Part 2** expansion cohorts in MCL and CLL
- **Part 3** randomized efficacy
  - Arm A: Cirmtuzumab + Ibrutinib combination
  - Arm B: Ibrutinib
  - Primary endpoint: complete response (CR) rate
- Data will be used to determine whether to seek regulatory approval through accelerated approval pathway
- Funding for this study is expected to include a total of \$16.1 million development milestone payments from CIRM

# Phase 1b-2 Study of Cirmtuzumab and Ibrutinib in Patients with MCL and CLL

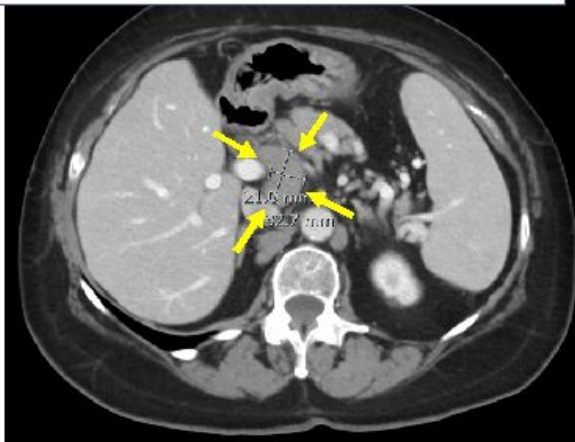
## Part 1 dose finding completed for CLL, and interim results\* include:

- 12 patients with CLL: ages 57-86, 75% previously treated
- Cirmtuzumab dosing 2-16 mg/kg monthly up to one year
- No dose limiting toxicity observed
- Cirmtuzumab well-tolerated
- Side effects typical for ibrutinib
- Overall response rate 67% after 16-48 wk
  - 1 confirmed complete response, 1 clinical complete response, 6 partial responses, 4 stable disease, no progressive disease
- Phase 2 dose recommended selected

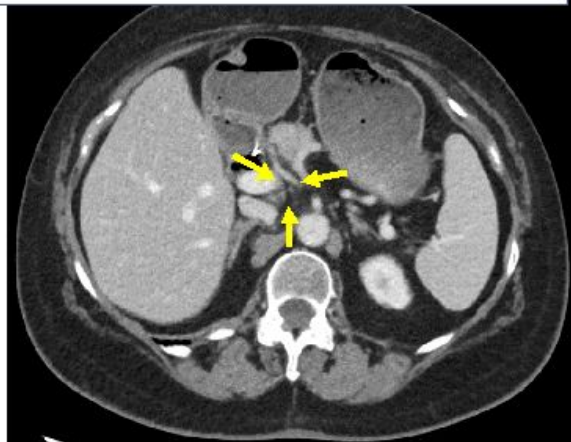


# Phase 1b/2 Clinical Trial of Cirmtuzumab + Ibrutinib CLL Patient with Confirmed Complete Response

Baseline



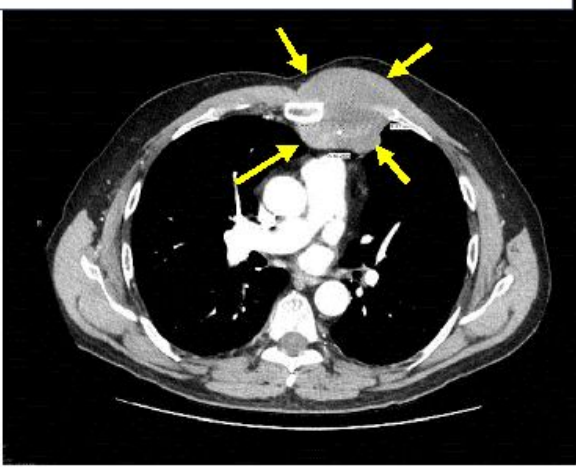
9 months cirmtuzumab + ibrutinib



- Prior treatment with chlorambucil + obinutuzumab
- Cirmtuzumab 4 mg/kg plus ibrutinib 420 mg
- Steady decrease in lymph node size to within normal limits by 9 months cirmtuzumab + ibrutinib
- Steady decrease in absolute lymphocyte count to within normal limits by 10 months cirmtuzumab + ibrutinib
- Bone marrow biopsy with no visible CLL by 10 months cirmtuzumab + ibrutinib

## Phase 1b/2 Clinical Trial of Cirmtuzumab + Ibrutinib MCL Patient with Confirmed Complete Response

Baseline



3 months cirmtuzumab + ibrutinib



- Relapsed following high dose chemotherapy and stem cell transplant
- Large chest wall lesion (9 x 6.7 cm)
- Cirmtuzumab at 2 mg/kg plus ibrutinib 560 mg
- Rapid reduction in mass, complete response durable after 6 and 9 months cirmtuzumab + ibrutinib

# TK216: Potential First-in-Class ETS Family Inhibitor

## Discovery of ETS\* family inhibitors

- First ETS family inhibitor in clinic
- Class discovered by Jeff Toretsky
- Exclusive worldwide license from Georgetown University
- Extensive and fresh IP portfolio
- ETS family oncogenes increasingly implicated in cancer

## ETS Fusion Proteins

**Ewing sarcoma:** EWS-FLI1, EWS-ERG. **AML:** ETV6-various (20+). **ALL:** ETV6-RUNX1.  
**Prostate cancer:** TMPRSS2-ERG (>50%). **Secretory breast cancer:** ETV6-NTRK3.

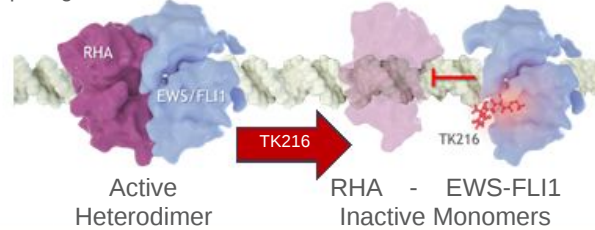
## ETS Overexpression

**AML:** FLI1, ERG, ETV5, ETS2. **Prostate cancer:** ERG, ETV1, ETV4, ETV6.  
**Lung cancer:** ETV5, ETV1, FLI1, ETS1. **Breast cancer:** ETV6, ETV4, SPIB, ETV5.

## TK216 Mechanism of Action

- Disrupts protein-protein binding between ETS protein and RNA Helicase A (RHA)
- Inhibits abnormal RNA transcription
- Inhibits abnormal RNA splicing
- Inhibits expression of other oncogenes
- Enhances tumor suppressor expression
- Apoptotic tumor cell death

Model depicting the inhibition of the interaction of EWS/FLI1 and RHA



## TK216-Vincristine Synergy

- Toretsky lab screened ETS inhibitors against 70 chemotherapeutic or targeted agents
- Unique synergy with vinca alkaloid drugs
- MOA identified: Disrupted cell division machinery
  - 'microtubule catastrophe'

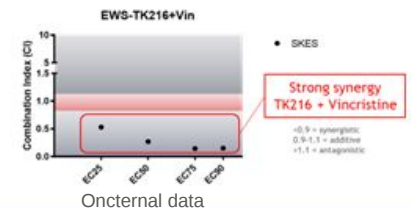
SCIENCE SIGNALING | RESEARCH ARTICLE

### PHARMACOLOGY

**Inhibition of the oncogenic fusion protein EWS-FLI1 causes G<sub>2</sub>-M cell cycle arrest and enhanced vincristine sensitivity in Ewing's sarcoma**

Stefan K. Zöllner,<sup>1,2</sup> Saravana P. Selvanathan,<sup>1</sup> Garrett T. Graham,<sup>1</sup> Ryan M. T. Commins,<sup>1</sup> Sung Hyeok Hong,<sup>1</sup> Eric Moseley,<sup>1</sup> Sydney Parks,<sup>1</sup> Jessica N. Haladyna,<sup>1</sup> Hayriye V. Erkizan,<sup>1</sup> Uta Dirksen,<sup>2</sup> Michael D. Hogarty,<sup>2</sup> Aykut Üren,<sup>2</sup> Jeffrey A. Toretsky<sup>1\*</sup>

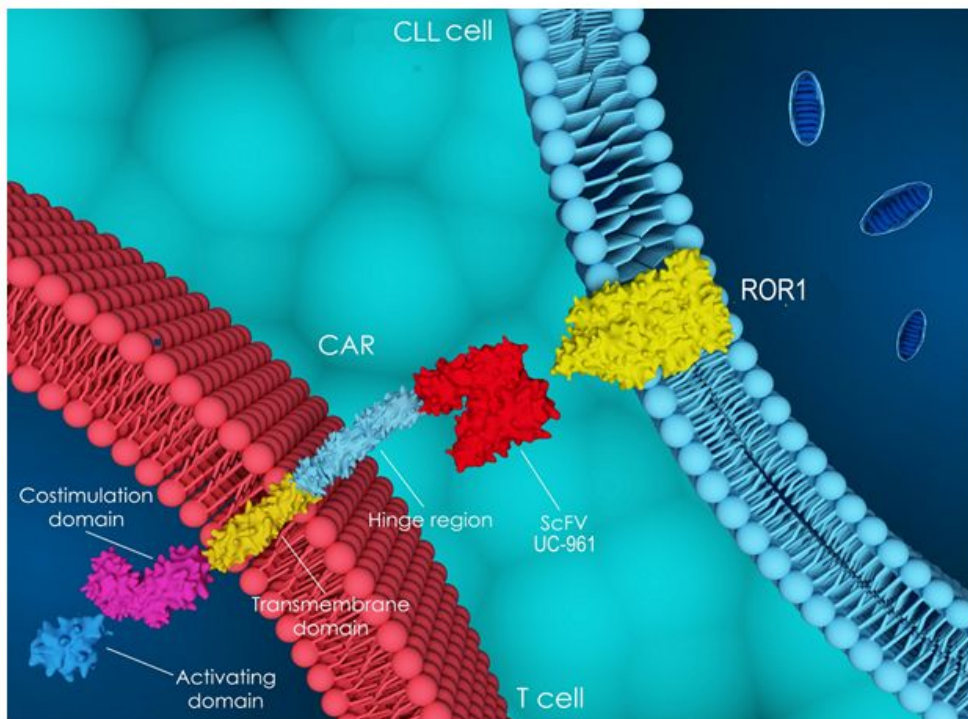
Zöllner 2017 Science Signaling 10(499)



# TK216 Clinical Development Status

- Phase 1 dose escalation study in relapsed Ewing sarcoma
- Next: Expansion cohort using TK216 at RDR plus vincristine to estimate response rate
- Planning to launch Phase 1 trial in relapsed and refractory acute myeloid leukemia (AML)

# CAR-T Construct Elements



- ROR1 is expressed on multiple cancers
- Targeting ROR1 with cirmtuzumab binding region
- UCSD collaboration with CIRM funding
- Candidate genetic construct design completed (left)
- Shanghai Pharma may help manufacture and collaborate on clinical trials

CAR = Chimeric Antigen Receptor

# Oncternal Pipeline

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# Oncternal – GTx Merger Update



# Oncternal – GTx Merger Background

- September 2018: GTx announced negative results for its SARM study
- November 2018: Communications between Oncternal and GTx board members regarding a potential transaction
- March 6, 2019: Merger Agreement signed
  - Oncternal to combine with GTx, Inc. (Nasdaq: GTXI)
  - Initial exchange ratio: Oncternal stockholders would own approximately 75% of the outstanding shares of the combined company, subject to certain cash adjustments; based on an assumed valuation of \$87.7 million for Oncternal
  - Contingent Value Rights Agreement (CVR): GTx stockholders would receive 50% of all proceeds (less certain costs) from the sale or license of GTx's SARD or SARM development programs, or a royalty if the company commercializes a drug itself
- April 30, 2019: Amendment to Merger Agreement signed
  - Final exchange ratio revised so Oncternal stockholders would own 77.5% of the outstanding shares of the combined company
  - CVR Agreement revised such that GTx stockholders would receive 75% of all proceeds (less certain costs) from the sale or license of GTx's SARD or SARM development programs, or a royalty if the company commercializes a drug itself; no obligation for Oncternal to develop SARM technologies



## **SARM (Selective Androgen Receptor Modulator)**

- Enobosarm (GTx-024) failed to achieve statistical significance on the primary endpoint in a study of post-menopausal women with stress urinary incontinence in September 2018
- GTx has discontinued any further development of its SARM program
- Oncternal has no current intent to develop the SARM technology

## **SARD (Selective Androgen Receptor Degradar)**

- GTx has been conducting preclinical studies to determine if it can identify an appropriate SARD compound to move forward
- GTx recently received and evaluated new preclinical data from an academic laboratory showing that the SARD compounds demonstrated partial androgen receptor agonist activity
- Additional preclinical studies are required to better understand SARDs and their mechanism of action, and to reconcile conflicting *in vitro* and *in vivo* findings

# Oncternal Reasons for the Merger

## **Factors considered by the Oncternal Board in deciding to approve the merger include:**

- The potential increased access to sources of capital and a broader range of investors to support the clinical development of Oncternal's product candidates
- The potential to provide Oncternal's current stockholders with greater liquidity by owning stock in a public company
- The board's belief that no alternatives to the merger were reasonably likely to create greater value for Oncternal's stockholders, after reviewing the various financing and other strategic options to enhance stockholder value that were considered by the Oncternal Board
- The cash resources of the combined organization at merger closing
- The expectation that the merger with GTx would be a more time- and cost-effective means to access capital than other options considered by the Oncternal Board, including additional private financings or an initial public offering

# Share Ownership Conversion – Illustrative Only

- Variables for converting Oncternal equity instruments at closing:
  - GTx / Oncternal Exchange Ratio = 22.5% / 77.5%<sup>1</sup>
  - GTx and Oncternal boards have approved a reverse split ranging between 1:6 and 1:8.

Shares in Millions	Total Combined Company	GTx	Oncternal	Individual Oncternal Investor
Shares outstanding at 4-30-19	-	24.2	162.3	100K
Conversion Factor <sup>1</sup>	-	-	.5137	.5137
Estimated outstanding shares at Exchange Ratio 22.5%/77.5% <sup>1</sup>	107.6	24.2	83.4	51,370
Reverse Split at mid-point of range	1:7	1:7	1:7	1:7
Shares outstanding post-closing	15.4	3.5	11.9	7,338

- Oncternal options and warrants will be subject to the same adjustments, and will become options or warrants of the combined company's common stock

# Target Timetable

5/7/19	Amended S/4 declared effective by SEC
5/9/19	Oncternal distributed final information statement and shareholder consents for the merger
6/3/19	Cirmtuzumab poster at ASCO meeting
6/5/19	GTx special stockholder meeting to approve transaction
6/10/19	Estimated closing date of merger
6/10/19	Estimated initiation date of trading Nasdaq: ONCT

# ONCT Post-Merger Board Composition

## Oncternal designees

- David F. Hale, Chairman
- James B. Breitmeyer, M.D., Ph.D.
- William R. LaRue
- Yanjun Liu, M.D., Ph.D.
- Xin Nakanishi, Ph.D.
- Charles P. Theuer, M.D., Ph.D.

## New independent director

- Daniel L. Kisner, M.D.

## GTx designees

- Robert J. Wills, Ph.D.
- Michael G. Carter, M.D., Ch.B., F.R.C.P.

# Oncternal Shareholder Logistics

- Please advise Oncternal immediately if your shareholder information has changed (e.g. entity name, mailing address, tax ID number)
  - Rich Vincent – Rvincent@Oncternal.com
- Oncternal will submit all shareholder information to Computershare prior to the close
- Computershare will establish an account for each shareholder
  - Computershare will provide a letter of transmittal to each shareholder shortly after closing
  - Computershare may use existing accounts
  - Each shareholder needs to return the letter of transmittal to finalize their share position with Computershare
- More details to follow

Thank You!

