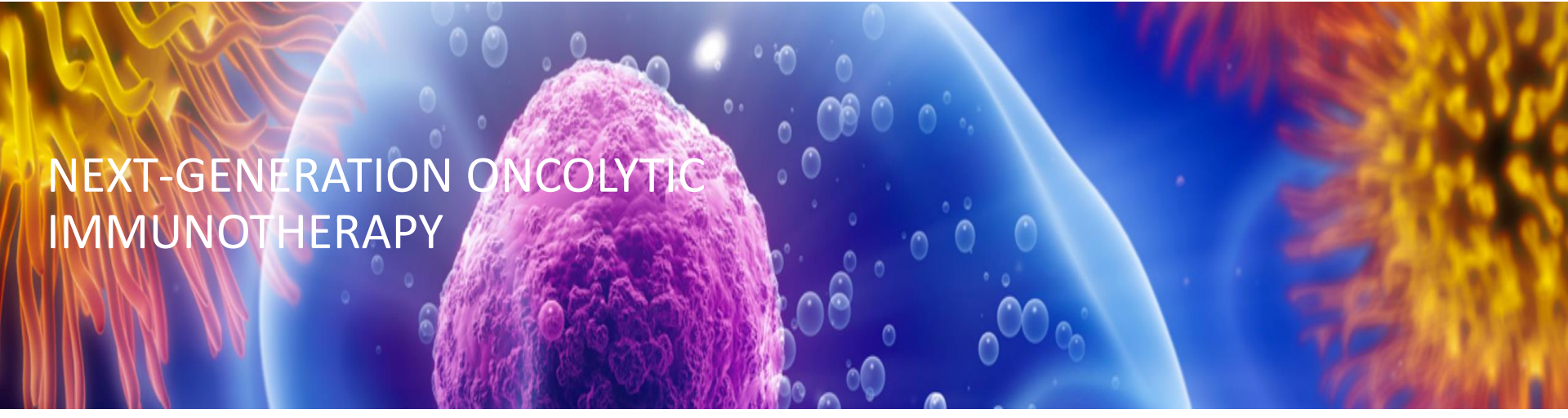
Replimune



December 2019
Piper Jaffray 31st Annual Healthcare Conference

Safe harbor

Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding our expectations about our use of cash, our advancement of our clinical trials, the timing of the release of our clinical data, our goals to develop and commercialize our product candidates, our plans to operate our own in-house manufacturing facility, our proposed scientific presentations, and other statements identified by words such as “could,” “expects,” “intends,” “may,” “plans,” “potential,” “should,” “will,” “would,” or similar expressions and the negatives of those terms. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include risks related to our limited operating history, our ability to generate positive clinical trial results for our product candidates, the costs and timing of establishing, equipping, and operating our planned in-house manufacturing facility, the timing and scope of regulatory approvals, changes in laws and regulations to which we are subject, competitive pressures, our ability to identify additional product candidates, and other risks set forth under the heading “Risk Factors” of our Annual Report on Form 10-K for the year ended March 31, 2019, our subsequently filed Quarterly Reports on Form 10-Q and other reports we file with the Securities and Exchange Commission. Our actual results could differ materially from the results described in or implied by such forward-looking statements. Forward-looking statements speak only as of the date hereof, and, except as required by law, we undertake no obligation to update or revise these forward-looking statements.

- Proprietary 'Immulytic' oncolytic immuno-gene therapy platform
  - Intended to maximally activate the immune system against a patient's cancer
  - Establish Replimune's products as the second cornerstone of immuno-oncology
- RP1 – in multiple clinical trials, with current focus on skin cancers
  - Skin cancer clinical trials underway & planned include
    - Ongoing registration directed Phase 2 clinical trial in CSCC in combination with cemiplimab
    - Potentially registrational clinical trial of single agent RP1 in CSCC in organ transplant recipients (expected start Q1 2020)
    - Potentially registrational clinical trial in anti-PD1 refractory melanoma (expected start H1 2020)
- RP2 & RP3 - intended to treat less immuno-responsive tumors, outside skin cancers
  - Ongoing Phase 1 clinical trial of RP2 alone & combined with nivolumab
  - RP3 intended to enter the clinic in 2020
- Commercial scale manufacturing facility expected to be operational H1 2020
- c.$190m in pro forma cash - 31 September 2019

The most experienced oncolytic immunotherapy team

ROB COFFIN
Chief Executive Officer
Founder & CTO at BioVex, VP at Amgen

PHILIP ASTLEY-SPARKE
Executive Chairman
CEO BioVex, Chairman at uniQure

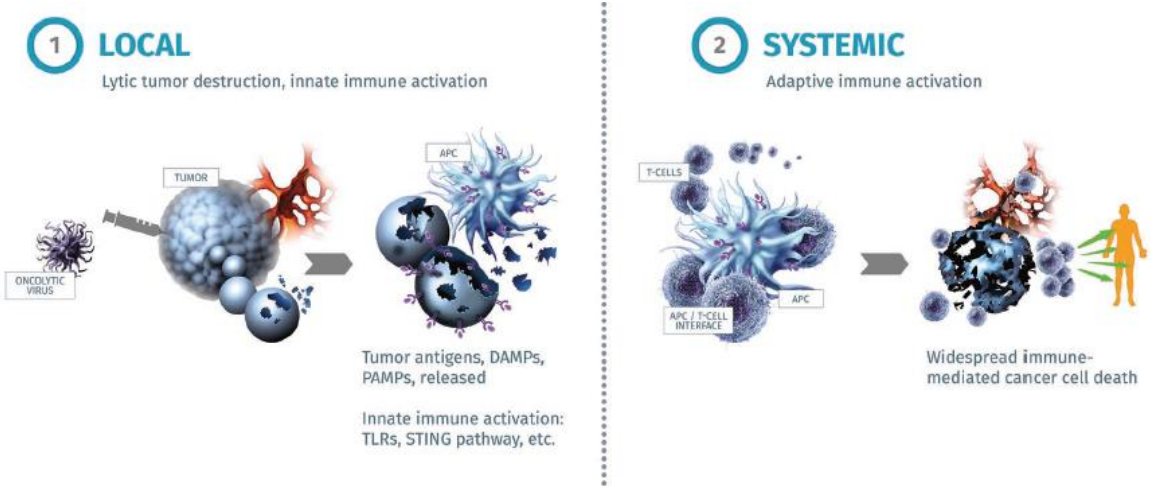
COLIN LOVE
Chief Operating Officer
SVP BioVex; VP at Amgen through T-Vec BLA filing

HOWARD KAUFMAN
Chief Medical Officer
World leading clinical immuno-oncologist; ex-SITC President

PAMELA ESPOSITO
Chief Business Officer
VP BD at BioVex; CBO at Ra Pharmaceuticals

Oncolytic immunotherapy

- The use of viruses that selectively replicate in & kill tumors to treat cancer
  - ✓ Highly inflammatory
  - ✓ Activates both innate and adaptive immunity
  - ✓ Releases the full array of tumor antigens into an inflamed environment
  - ✓ Systemically activates the immune system against the tumor & neo-antigens released
  - ✓ Can be ‘armed’ with additional genes to increase efficacy
- Single agent T-VEC is FDA approved for the treatment of advanced melanoma



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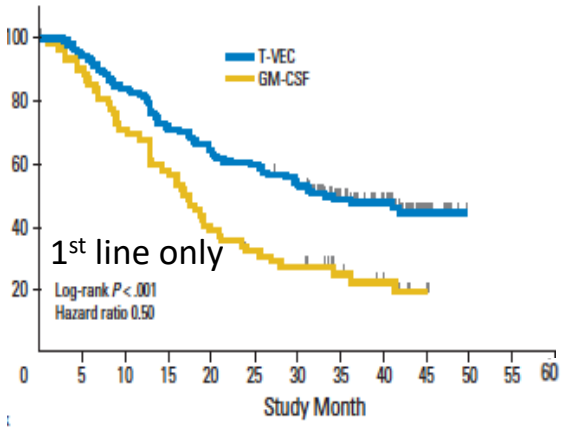
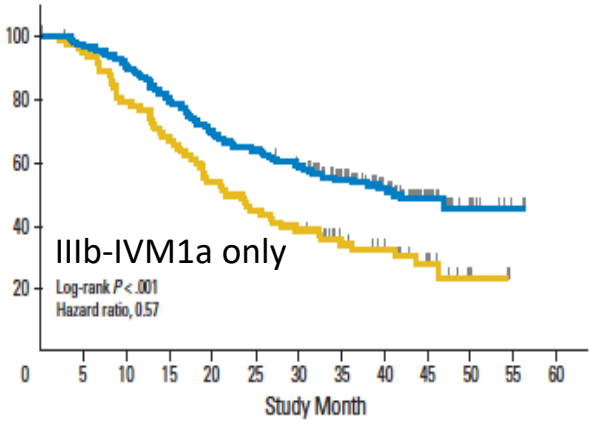
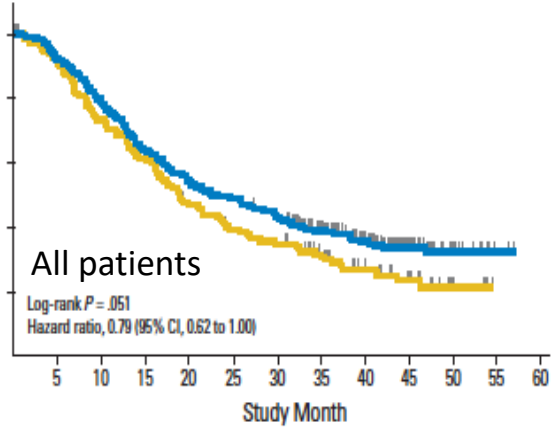
Single agent oncolytic immunotherapy works

T-VEC phase 3 data in melanoma

- 436 pts randomized 2:1 to T-VEC or GM-CSF
- Stage IIIb, IIIc, IVM1a-c; 1st line & previously treated
- DRR **16.3%**; ORR 26.4%; CR rate **17%**
- Median OS (ITT) 23.3 mo vs 18.9 mo (HR 0.79)
- Increased benefit in stage IIIb-IVM1a (**ORR 40.5%**) & first line patients (**ORR 37.7%**)
- OS was also improved in stage IIIb-IVM1a & first line patients (**HR 0.57 & 0.50 respectively**)







Andtbacka et al JCO 2015; Amgen ODAC presentation 2015

Oncolytic immunotherapy + checkpoint blockade

Immune response to neo-antigens, inflamed tumor

- Oncolytic and immune-based efficacy in its own right
- Patient-specific neo-antigen vaccine generated in situ

'Brakes removed' from the immune response generated

- Without a pre-existing neo-antigen response, nothing to remove the brakes from
- Only some patients respond

Oncolytic immunotherapy is expected to be an ideal combination partner for checkpoint blockade therapies

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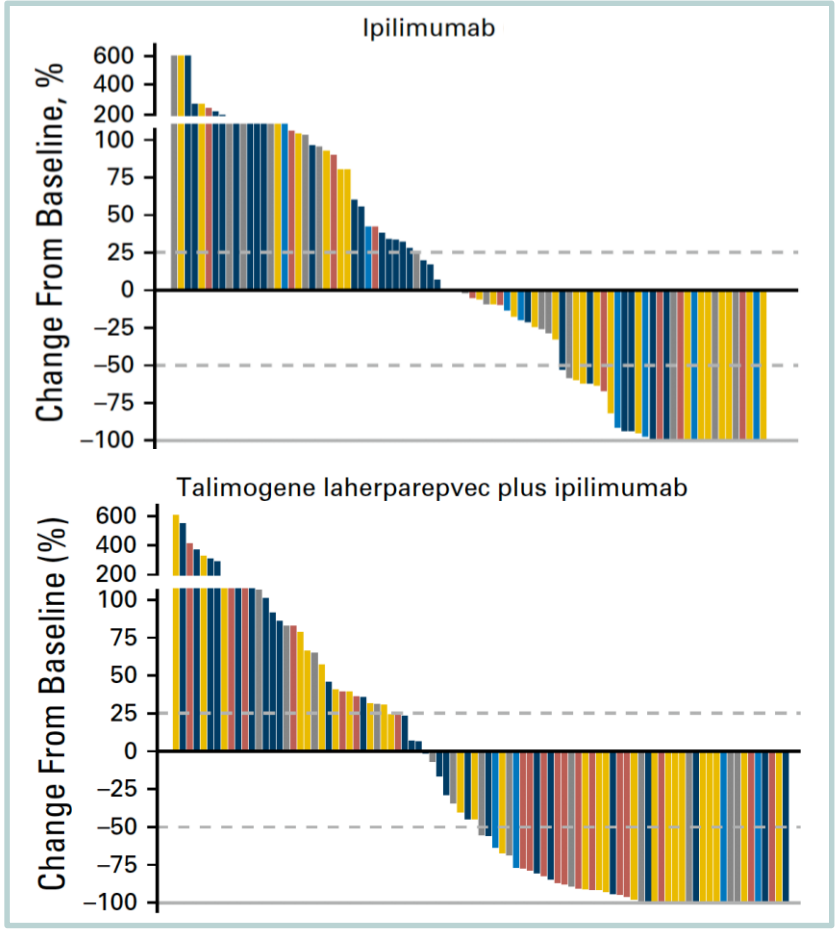
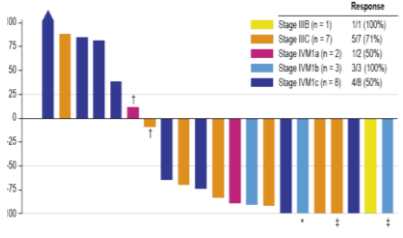
Oncolytic immunotherapy is synergistic with immune checkpoint blockade

- Randomized controlled 198 patient phase 2 study of T-VEC + ipilimumab vs. ipilimumab alone in advanced melanoma
- Response rates more than doubled in combination (38% vs. 18%)
- No additional toxicity as compared to ipilumumab alone Chesney et al JCO, 2017



T-VEC+pembrolizumab ph1b study

Ribas *et al* Cell 2017 170: 1109-1119



67%* response rate; 43% CR rate*

Pembrolizumab+T-VEC currently in a >700 patient phase 3 study *longer term follow up presented at SMR 2018

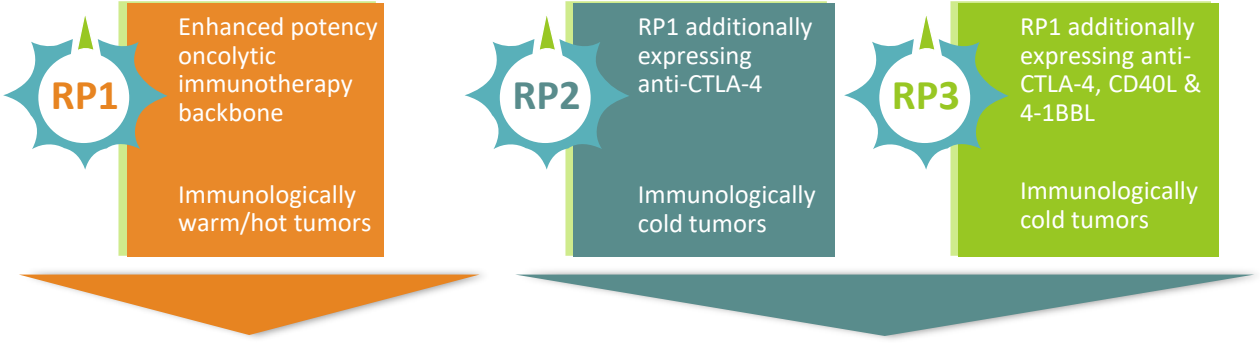
Replimune's Immulytic platform

1. A potent underlying HSV-1 strain

There is great diversity among clinical HSV strains

29 new clinical strains were tested & the most effective selected & engineered for oncolytic use

Our product candidates were then armed with two to four genes to augment tumor killing & the potency of immune activation



2. Increased tumor killing & spread

Armed with GM-CSF & a potent fusogenic protein (GALV)

Provides a substantial increase in direct & immunogenic tumor killing potency

Intended for immune responsive tumor types

3. Delivery of potent immune stimulatory proteins

Focus on pathways where systemic engagement is sub-optimal

Further armed with anti-CTLA-4 & immune-costimulatory pathway activators

Intended for less & non-immune responsive tumor types

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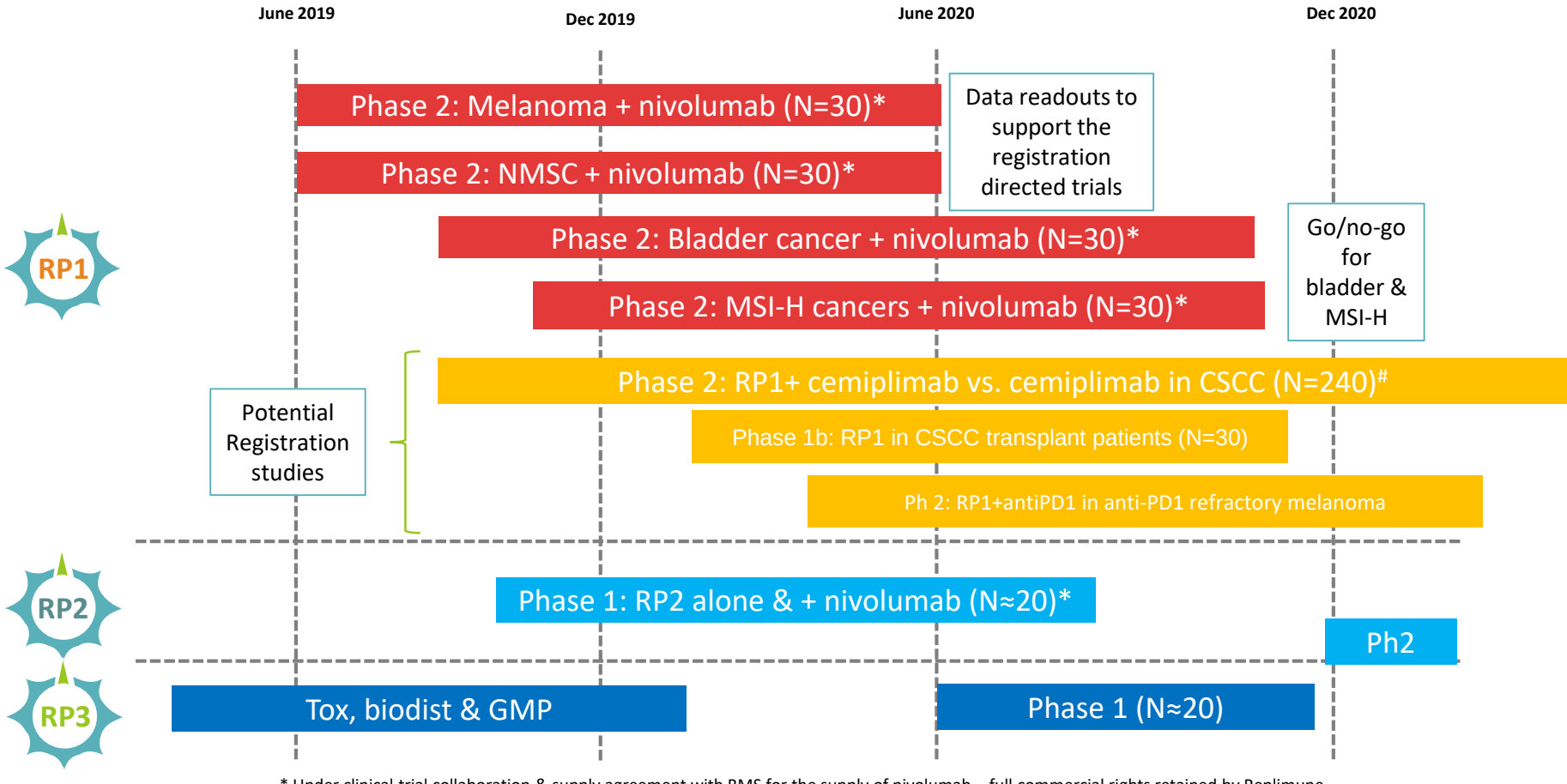
Replimune's overall development plan



* Under clinical trial collaboration & supply agreement with BMS for the supply of nivolumab – full commercial rights retained by Replimune

Under clinical trial collaboration agreement with Regeneron; 50:50 sharing of clinical trial costs – full commercial rights retained by Replimune

Lead indication: CSCC

- 700,000 cases/year in the US; 10% have 'high risk' disease (recur following initial surgery)
- Approximately 7,000 US deaths annually (most conservative addressable population)
- Anti-PD-1 therapy active
  - cemiplimab (Regeneron) demonstrated 46% response rate, but low CR rate
  - Recently FDA approved (only approved therapy)
- 80% of patients die from locoregional progression, not metastatic disease
- Registration-directed randomized controlled phase 2 trial in collaboration with Regeneron
  - 240 patients randomized 2:1 (RP1+ cemiplimab vs cemiplimab alone)
  - Primary endpoint ORR, secondary endpoints including CR rate, PFS, OS
- 30 patient clinical trial of single agent RP1 in solid organ transplant recipients with CSCC*
  - Organ transplant recipients are at increased risk of malignancy, with CSCC most prevalent
  - 70% of patients develop CSCC within 20 years
  - Anti-PD1 therapy contra-indicated due to the risk of organ rejection
  - Clinical data indicates that RP1 has single agent activity in CSCC

* see additional information in the Appendix

Second indication: Checkpoint Failed Melanoma

- Approximately 8,000 US deaths annually (most conservative addressable population)
- Anti-PD-1 therapy activity
  - 40-45% of patients experience no response to therapy – primary resistance
  - 30-40% experience a response but progress
  - i.e. 70-85% of melanoma patients will require additional therapies
- 6-7% of patients respond to a second line of anti-PD1
  - For patients who have clearly progressed (not pseudo) and never responded responses are very rare

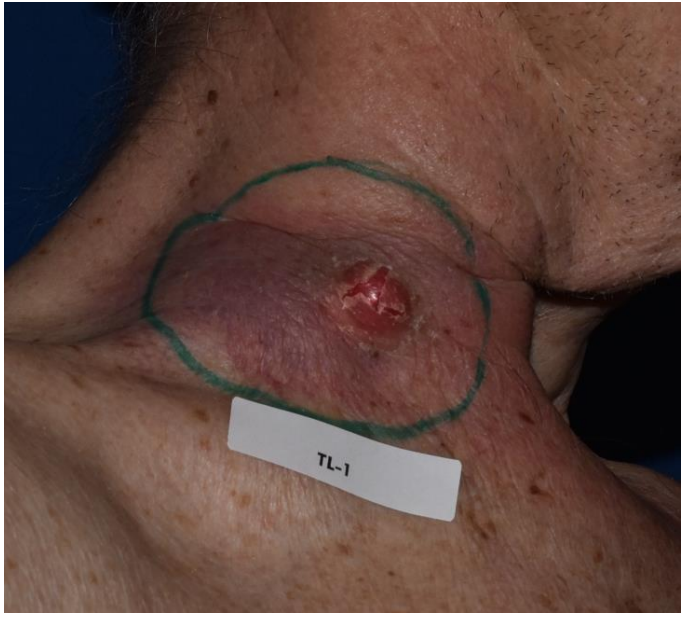
Current clinical focus based on compelling clinical data

- Data from an ongoing Phase 1/2 trial of RP1 alone & in combination with nivolumab
  - Four of five CSCC patients enrolled showing clear clinical response to treatment
  - Responses observed in three of the four anti-PD-1 refractory cutaneous melanoma patients treated with RPI in combination with nivolumab & with follow up scans
  - Seven of eight cutaneous melanoma patients in total (i.e. including treatment naïve) treated with RP1+ nivolumab & with follow up scans in response or tracking to response
    - Full 30 patient cohort expected to be enrolled by year end
  - Abscopal (uninjected) responses seen in multiple patients
  - Biomarker data also indicated robust virus replication & immune activation
  - Includes marked increase in CD8 T cells & PD-L1 staining following treatment across tumor types
- Phase 2 data with RP1 combined with nivolumab in bladder cancer & MSI-H tumors is pending, and depending on results may lead to further registration-directed development

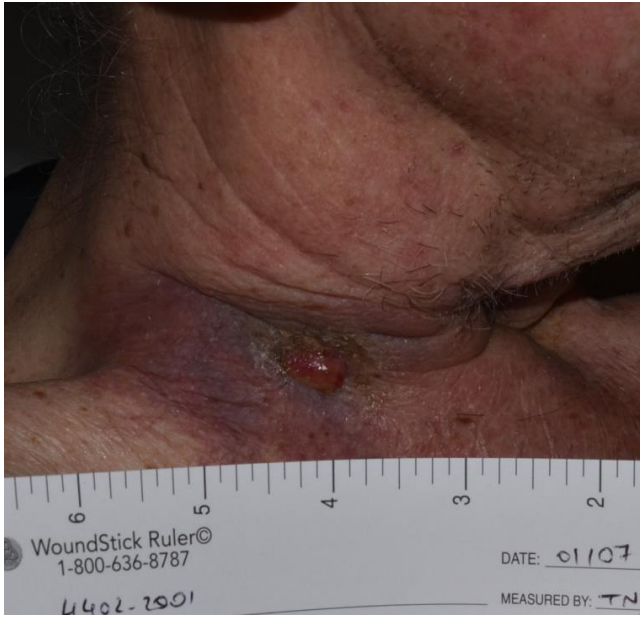
Patient 2 (4402-2001): PR

Patient close to CR – the only remaining lesions are a number of non-measurable bone metastases which are increasingly sclerotic

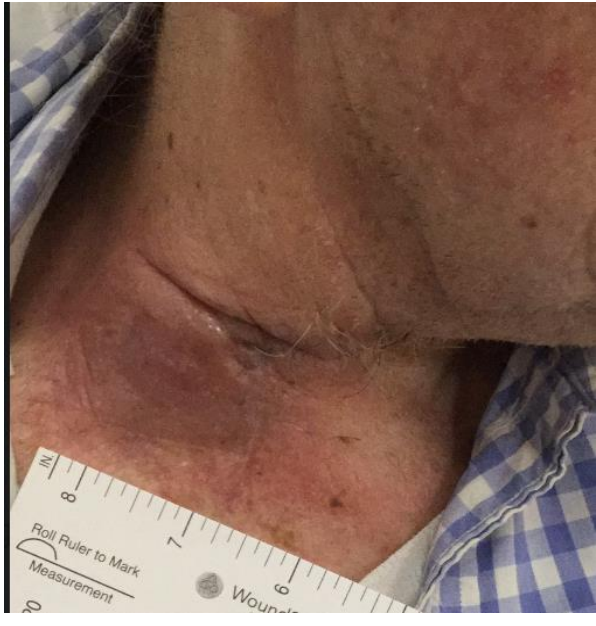
16th June 2019
(baseline)



1st July 2019
(post one dose of RP1, no nivolumab)



16th July 2019
(post 2 doses of RP1 & 1 dose of nivolumab)

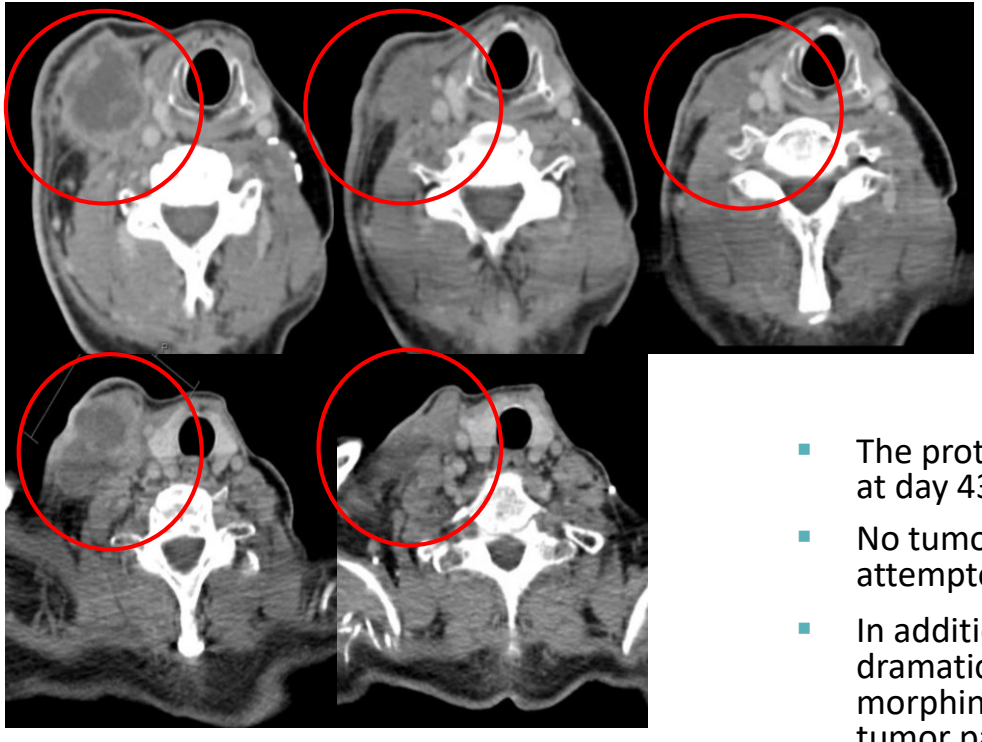


- Patient with recurrent CSCC of the neck (bilateral), previously treated with cisplatin-based chemoradiation & six cycles of carboplatin/5-FU, prior to entering the clinical trial
- Both the large injected tumor & the smaller contralateral uninjected tumor in the neck reduced considerably before the first nivolumab dose, i.e. after the first dose of RP1

Patient 2 (4402-2001): PR

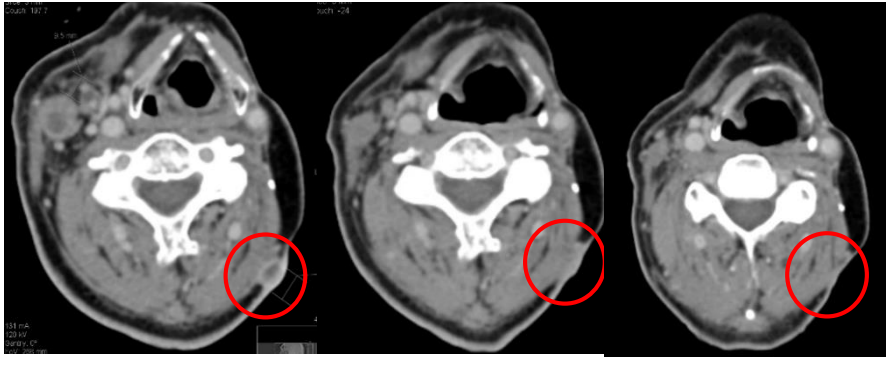
Right neck (injected)

Baseline 8 weeks 16 weeks



Left neck (not injected)

Baseline 8 weeks 16 weeks



- The protocol mandated biopsy of the injected tumor taken at day 43 was tumor free
- No tumor was found to remain when a biopsy was attempted from the left neck
- In addition to the tumor response, this patient has had a dramatic improvement in quality of life & is now off morphine which was previously necessary for substantial tumor pain

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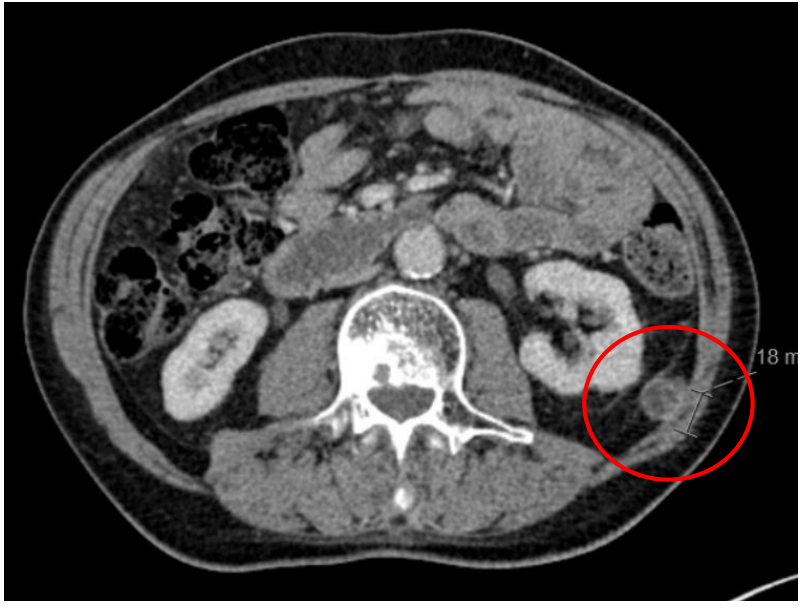
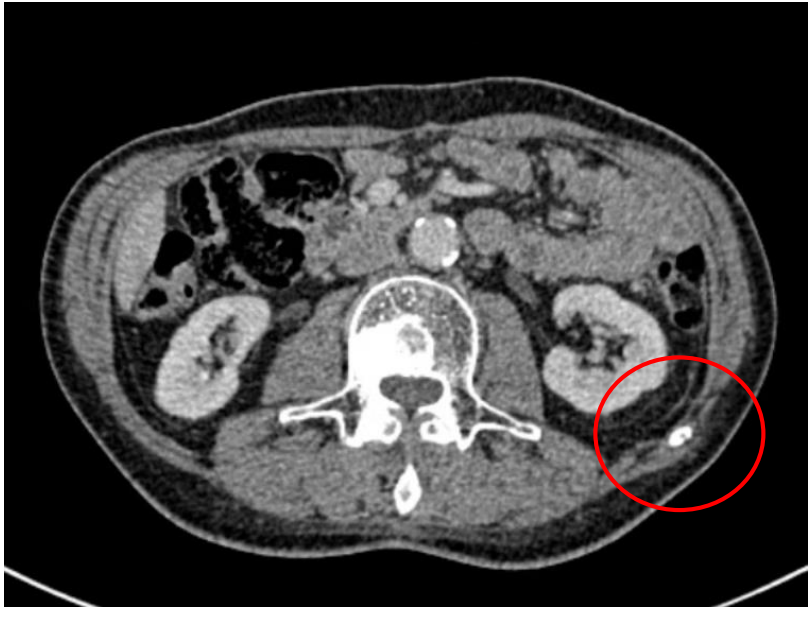
Patient 2 (4402-2001): PR

Baseline

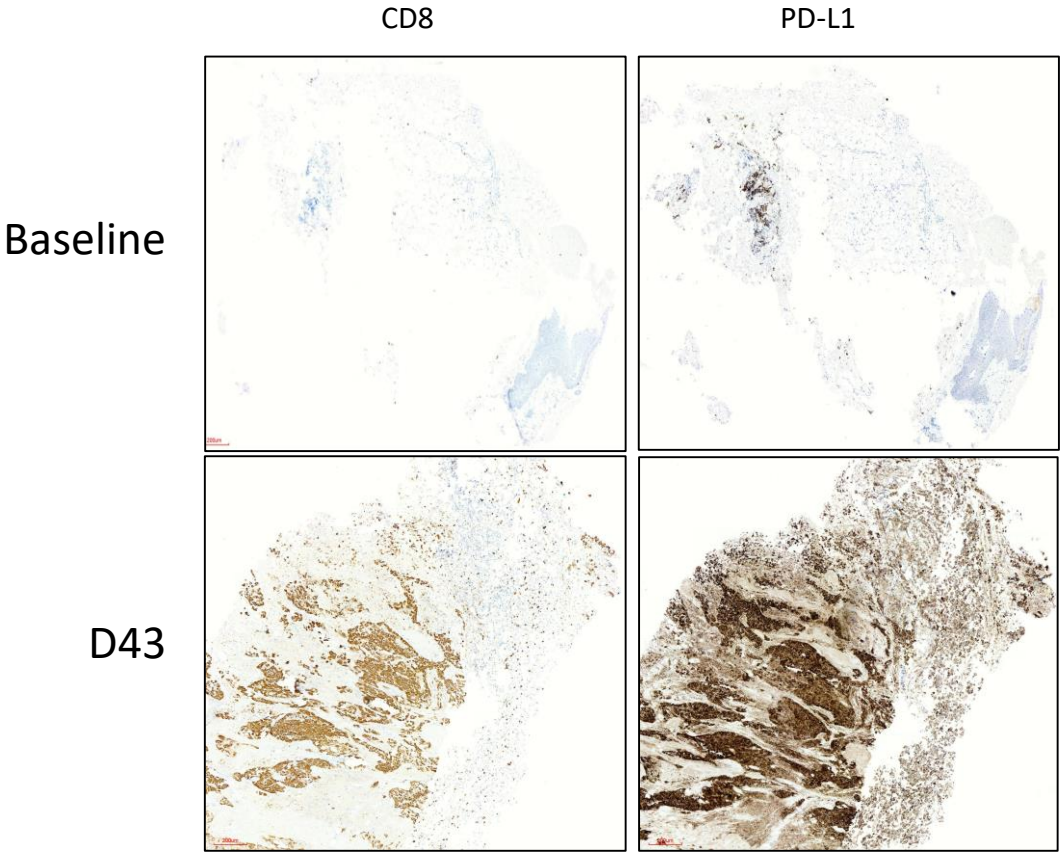


16 weeks



- The patient also had baseline retroperitoneal tumors (uninjected) which have completely resolved
- The only remaining disease are a number of non-measurable bone metastases, which were the main source of the cancer pain which has now resolved
- The bone lesions are increasingly sclerotic by CT scan, also indicative of a treatment response, with Zometa (stimulates bone formation) also now having been withdrawn

Patient 2 (4402-2001): CD8 T cell & PD-L1 staining



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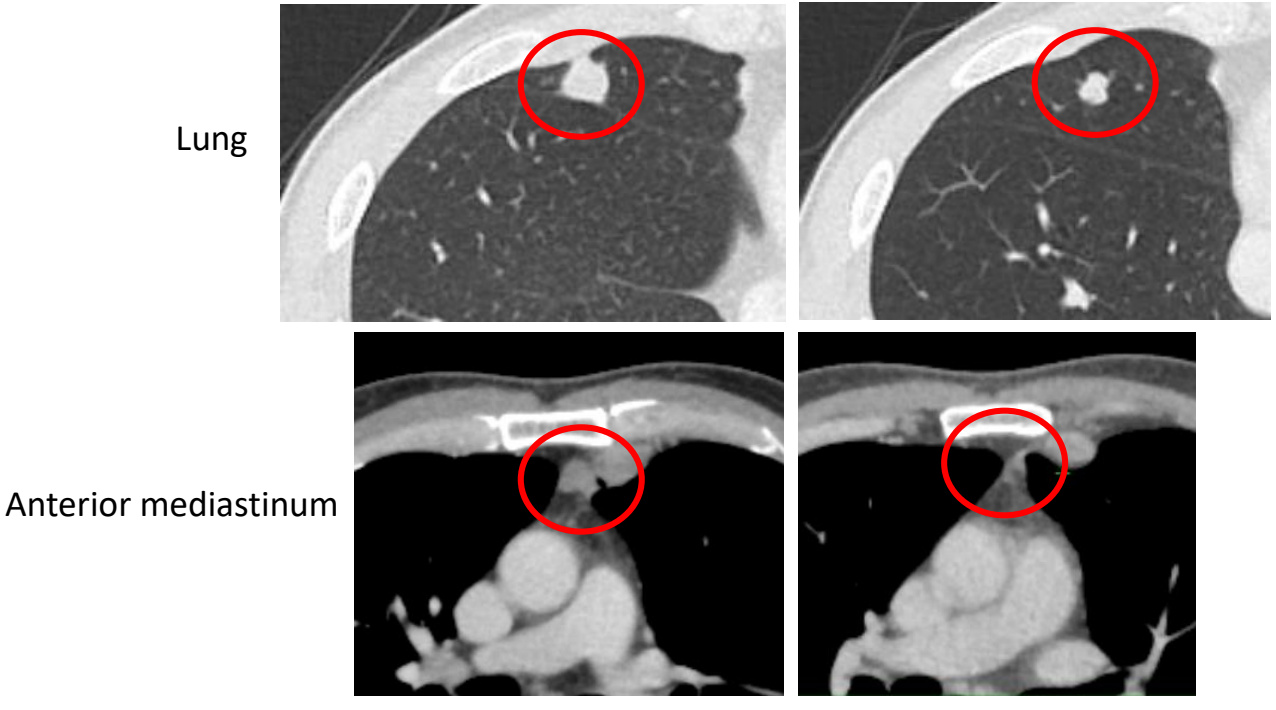
Patient #: 4401-1022 (ipilimumab & pembrolizumab refractory melanoma)

- Disease sites: Breast, lung, mediastinal and peritoneal anterior to the spleen
- RP1 injection site: Lesion behind the left ear

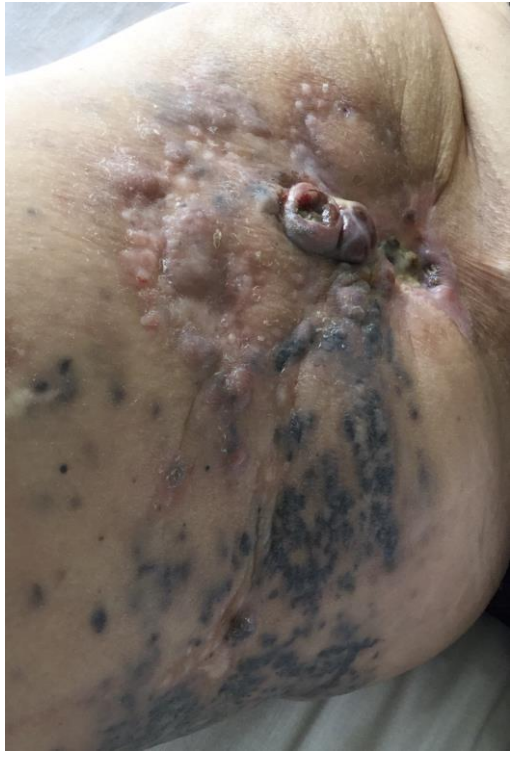


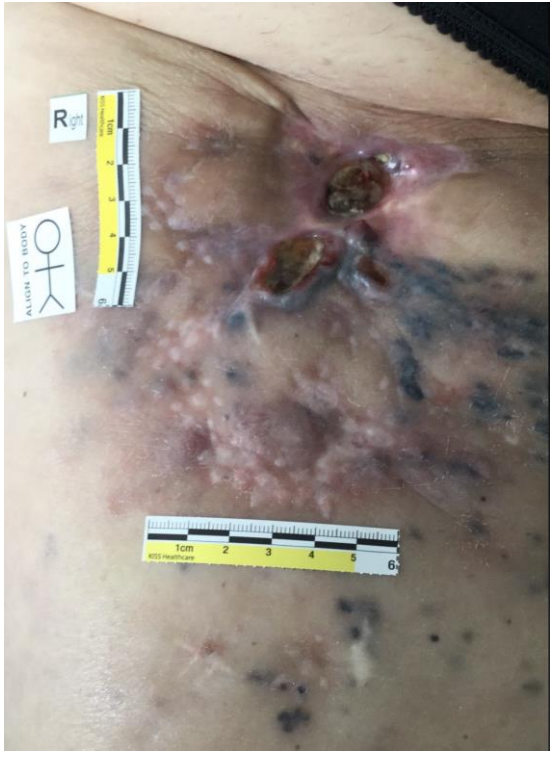
- Confirmed progression on prior immune checkpoint blockade, where two sequential PET scans demonstrated new lesions while also concurrently being treated with local therapy for the lesion behind the ear, then entry into the RP1 clinical trial
- Ongoing PR
- Patient remains on treatment at 11 months

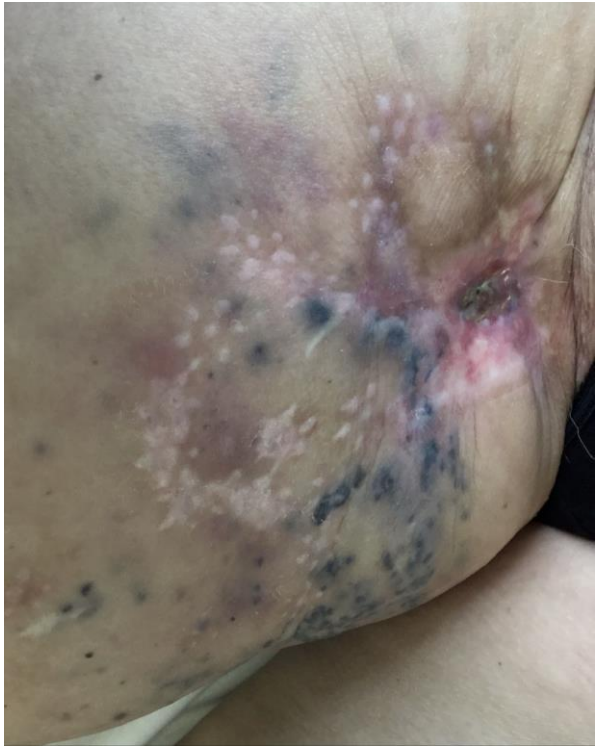
Replimune

Patient #: 4403-1003 (ipilimumab/nivolumab refractory melanoma)

10th June 2019 | 24th June 2019 (pre nivolumab) | 2nd September 2019







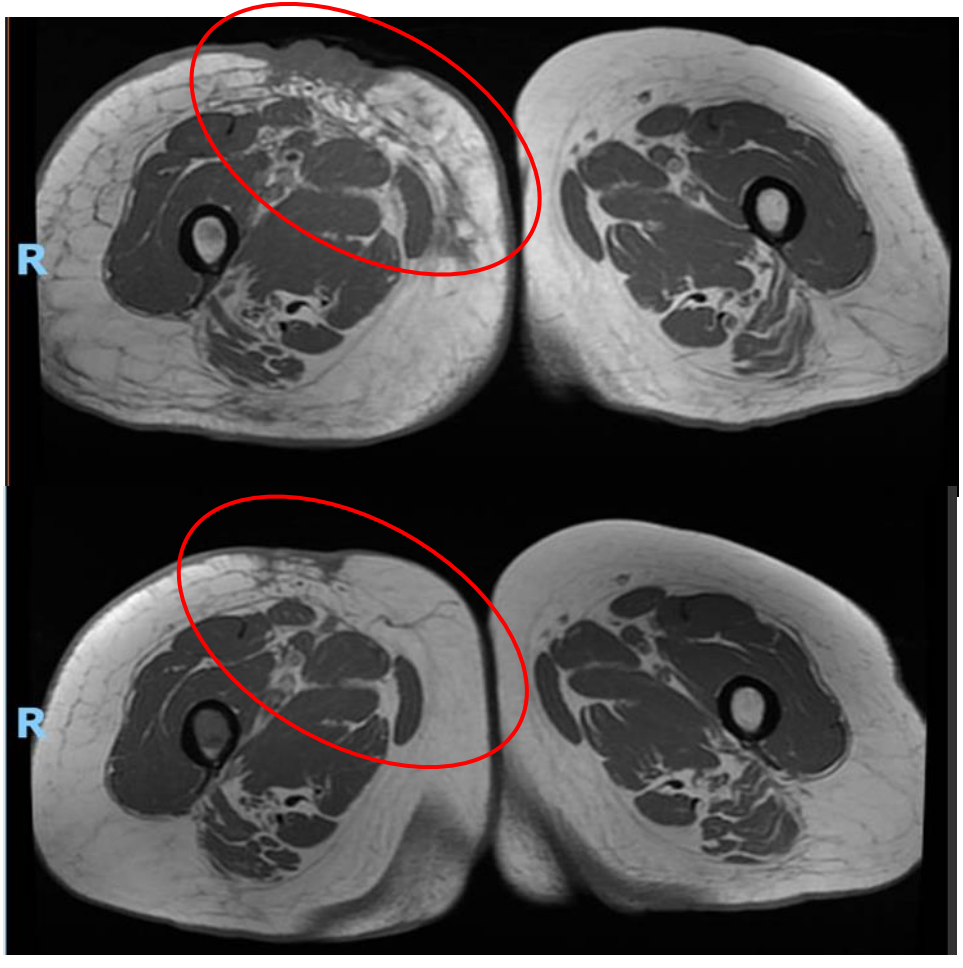
Patient history: Metastatic disease initially treated with ipili/nivo with best response of SD, then clear progression in the groin & thigh when radiotherapy followed by electrochemotherapy was added to continued nivolumab; following further clear progression, enrolled into the current trial

All tumors flattened after the first dose of RP1, i.e. prior to nivolumab & extensive oedema rapidly reduced

Patient #: 4403-1003 (ipilimumab/nivolumab refractory melanoma)

May 2019
(Baseline)

August
2019



- Patient also had nodes in the groin which increased and are now reducing and lung metastases which following no change for prior 18 months are now reducing
- Patient quality of life has also greatly improved, from being essentially immobile at baseline to now able to go on long country walks
- Patient remains on treatment at 5 months

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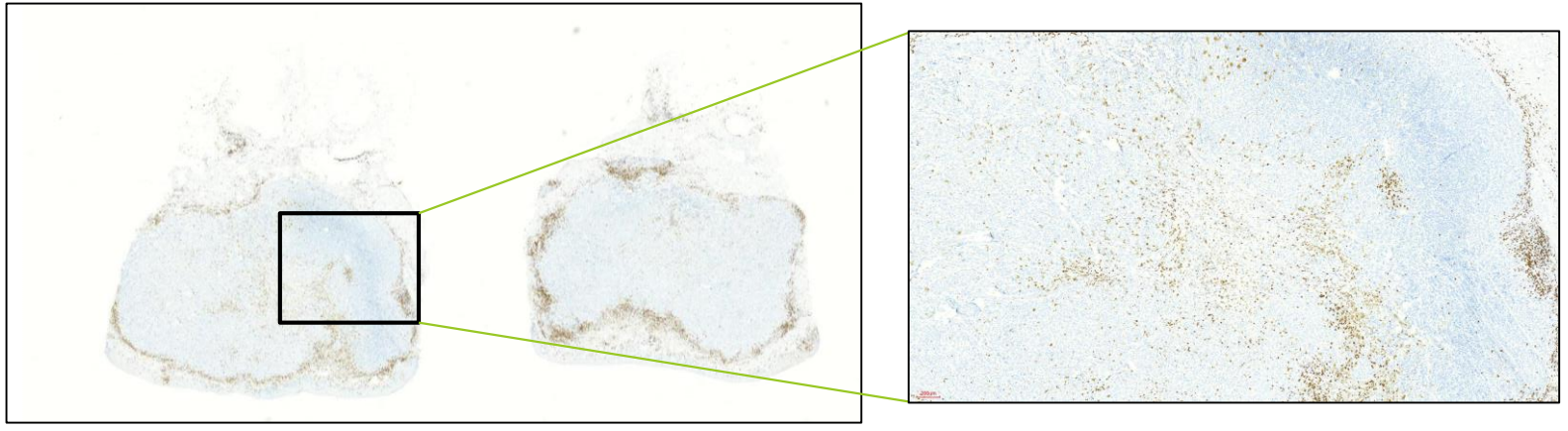
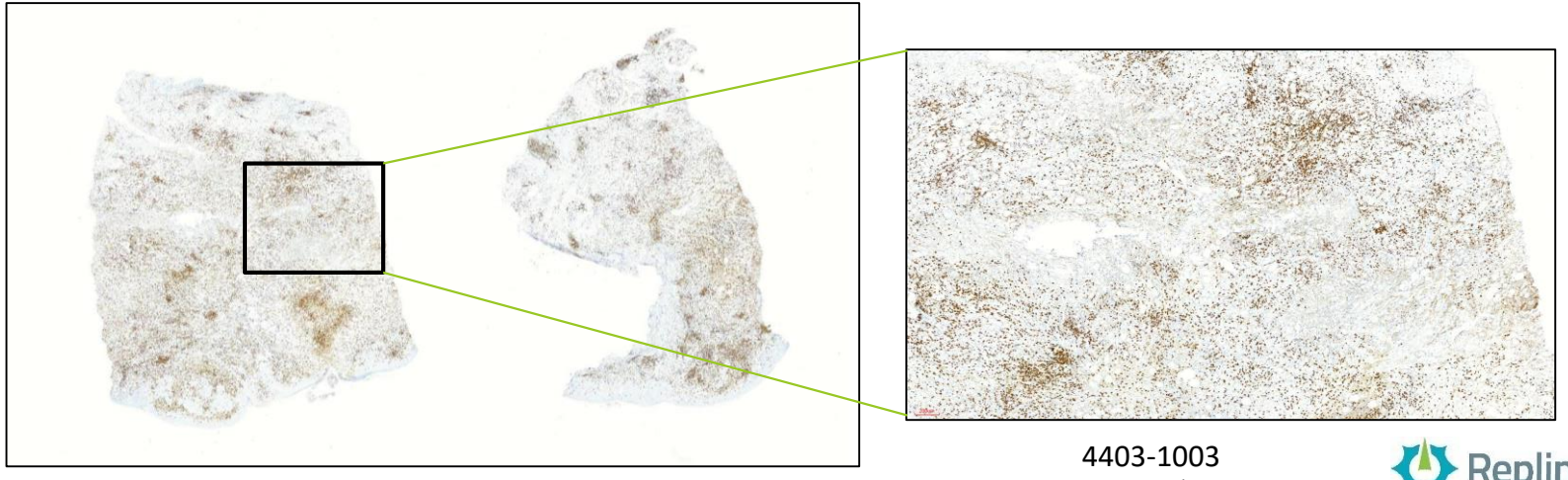
Reversal of T cell exclusion with RP1 combined with nivolumab

CD8
Baseline
biopsy



CD8
Day 43
biopsy



4403-1003
Cutaneous melanoma
(ipilimumab/nivolumab refractory)

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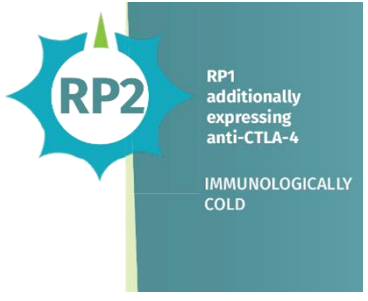

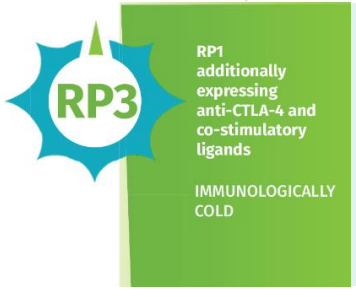

RP2/3: Target anti-PD1/L1 non-responsive or less responsive tumor types

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Intratumoral anti-CTLA-4 & co-stimulatory pathway agonists

- Focus on delivery of proteins which act <u>as the immune response is being generated</u>
  - Systemic antibody approaches probably don't act at the right place or the right time
  - Potential for toxicity
- RP2
  - Delivery of anti-CTLA-4 directly into the tumor
  - Blocks Treg activation/inhibition of T cell activation at the site of immune response initiation
  - Retain the efficacy of ipilimumab alone & in combination with anti-PD1 but reduce toxicity
    - Potential for improved activity as compared to combination anti-CTLA-4/anti-PD1
- RP3
  - Delivery immune co-stimulatory pathway activating ligands
  - Antibody approaches have given indications of activity, but toxic
    - Considerable pharma interest in these pathways
  - RP3 encodes GALV-GP-R-, anti-CTLA-4, CD40L & 4-1BBL
    - CD40L: Broadly activates both innate & adaptive immunity
    - 4-1BBL: Promotes the expansion of cellular & memory immune responses

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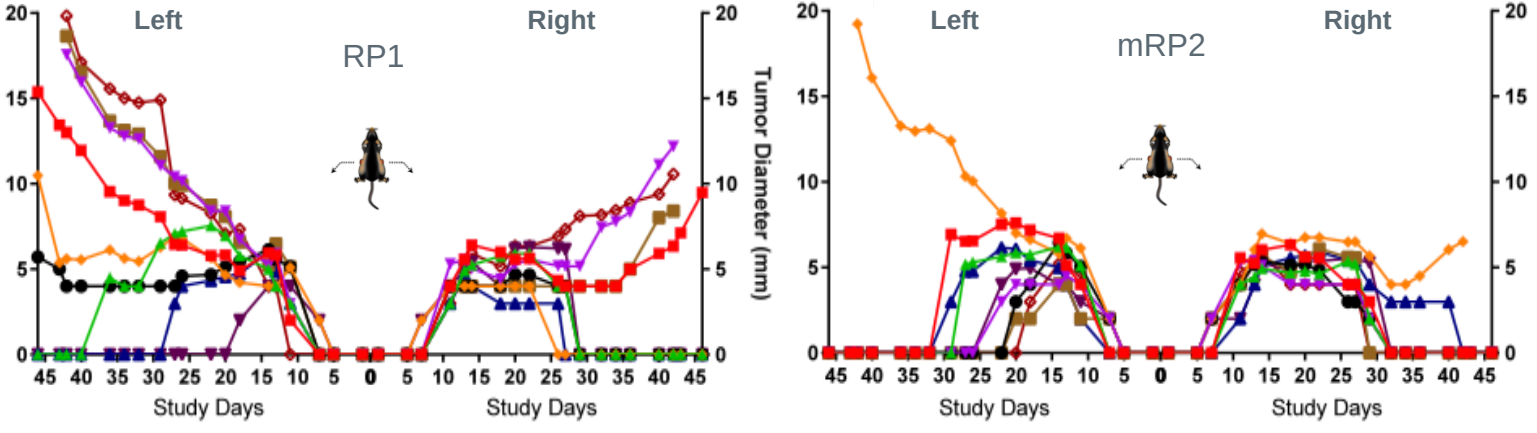
Expression of anti-mCTLA4 enhances efficacy



Immune competent A20 mouse tumor model
Subtherapeutic dose for RP1 ($5x10^4$ pfu) injected 3x into the right tumor only

Critical focus on manufacturing

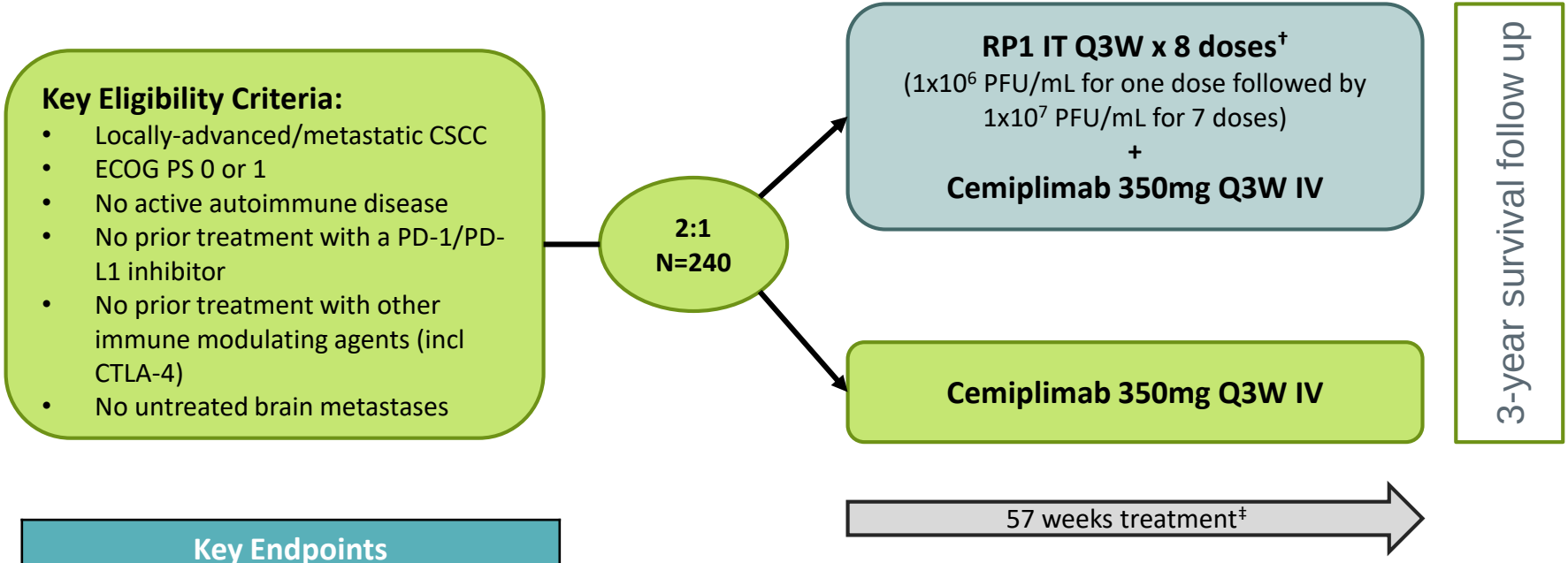
- Product candidates currently manufactured by a CMO for ongoing clinical development
- For later stage development & commercialization, in-house manufacturing is preferable
- The team has extensive manufacturing experience
- 63,000 ft^2 manufacturing facility leased in July 2018 in Framingham, MA, appropriate for multi-product production – intended to include translational biomarker lab
- Of sufficient scale to cover full global commercialization of Replimune's products
- Expected to be on-line to produce clinical product in H1 2020

Milestones in 2020

- Initiate & complete the single agent RP1 potentially registrational clinical trial in organ transplant recipients with CSCC
  - Initial data read out H2 2020
  - Additional CSCC data from Phase 2 in combination with nivolumab expected mid-2020
- Initiate registration-directed trial in anti-PD1 refractory melanoma
  - Additional melanoma data from Phase 2 in combination with nivolumab expected; mid-2020
- Complete Phase 2 MSI-H and bladder cancer cohorts + nivo and determine go/no-go
- RP2 Phase 1 data
- RP3 to enter the clinic

Appendix

Randomized controlled Phase 2 study in CSCC (CERPASS)



Key Endpoints

Primary: ORR (RECIST v1.1)
Secondary: DOR, PFS, OS, Disease-Specific Survival, safety/tolerability

†First dose of RP1 to be given as monotherapy with cemiplimab to be given with second dose of RP1
‡57 weeks treatment for the combination arm; treatment duration for cemiplimab-only arm is 54 weeks

Phase 1b clinical trial in solid organ transplant recipients with CSCC

Key Eligibility Criteria:

- Locally-advanced/metastatic CSCC
- ECOG PS 0 or 1
- Renal or hepatic organ allograft recipients on stable immunosuppressive regimen for ≥12 mos
- No prior systemic anti-cancer treatment for CSCC
- No transplant-related viral infections (such as BK, EBV, CMV) within 3 months
- No untreated brain metastases

RP1 IT Q2W x 26 doses
($1x10^6$ PFU/mL for one dose followed by $1x10^7$ PFU/mL)

50 weeks treatment

3-year survival follow up

Key Endpoints

Primary: Safety and tolerability
Secondary: ORR (RECIST v1.1), DOR, Disease-Free Survival, incidence/severity of graft rejection

Replimune