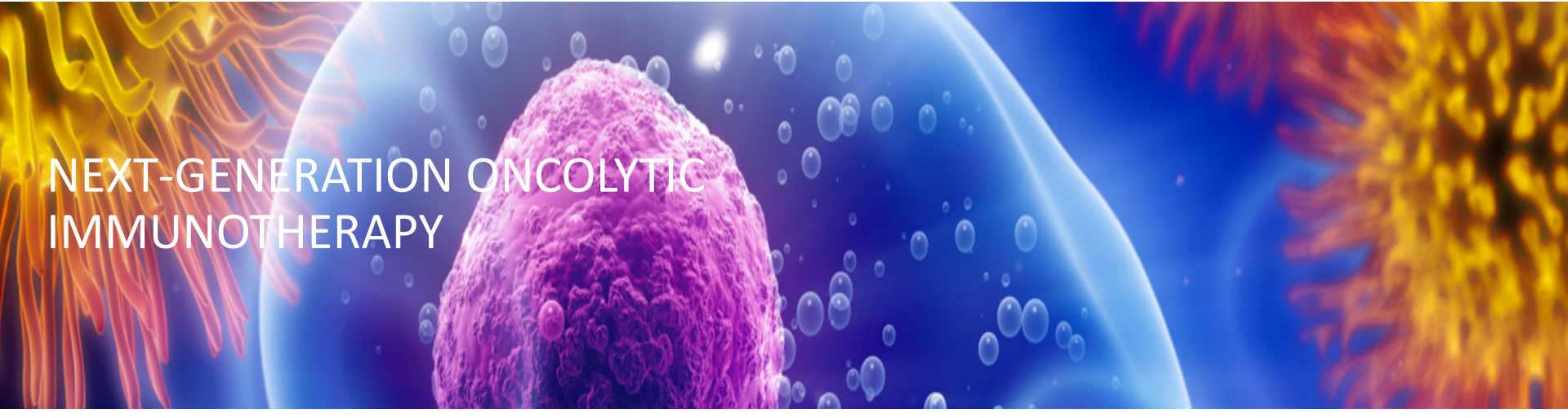
Replimune



Corporate Presentation August 2019

Safe harbor

This presentation contains forward-looking statements, including statements regarding our expectations about the advancement of our clinical trials, our goals to develop and commercialize our product candidates, our plans to establish our own in-house manufacturing capabilities, our proposed scientific presentations, our use of cash, and other statements identified by words such as “could,” “expects,” “intends,” “may,” “plans,” “potential,” “should,” “will,” “would,” or similar expressions. 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 Quarterly Report on Form 10-Q for the quarter ended December 31, 2018. 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.

- Founded in 2015 by the ex-BioVex management team
- Proprietary 'Immulytic' oncolytic immunotherapy platform intended to maximally activate the immune system against a patient's cancer
- RP1 being studied in multiple tumor types in Part 2 of an ongoing 150 patient clinical trial combining with nivolumab - *collaboration with BMS*
- RP1 also soon to enter a 240 patient randomized controlled registration directed phase 2 clinical trial in cutaneous squamous cell carcinoma (CSCC) combining with cemiplimab - *collaboration with Regeneron*
- RP2 (additionally expresses anti-CTLA-4) intended to enter the clinic in 2019
- RP3 (additionally expresses immune co-stimulatory pathway activating ligands) intended to enter the clinic in 2020
- Commercial scale manufacturing capability being established
- IPO in July 2018 (Nasdaq: REPL); 30 June 2019 cash balance ≈$121m (e)
- Headquartered near Boston, MA, labs in the UK, ≈ 70 employees

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

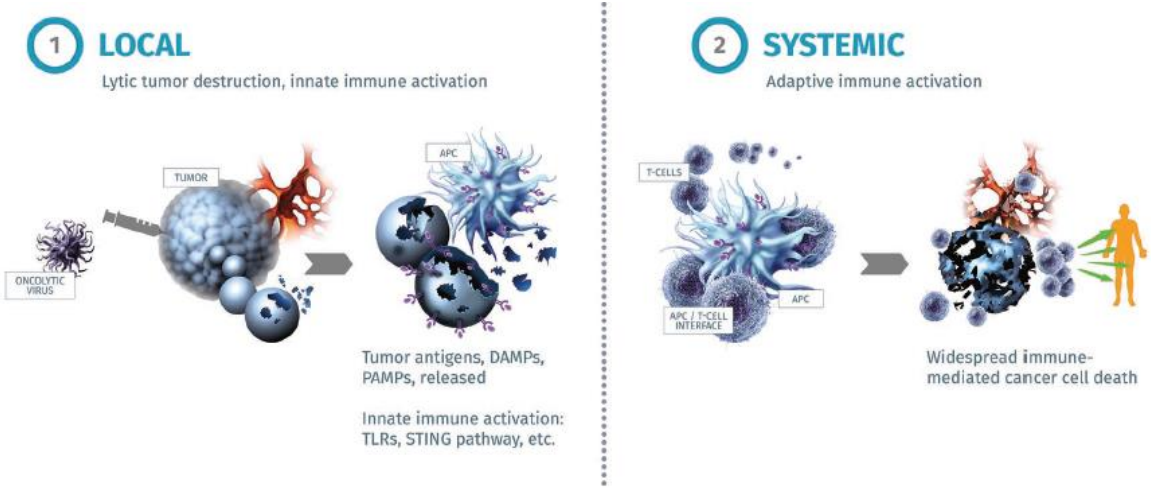
COLIN LOVE
Chief Operating Officer
SVP BioVex; VP at Amgen through T-Vec BLA filing

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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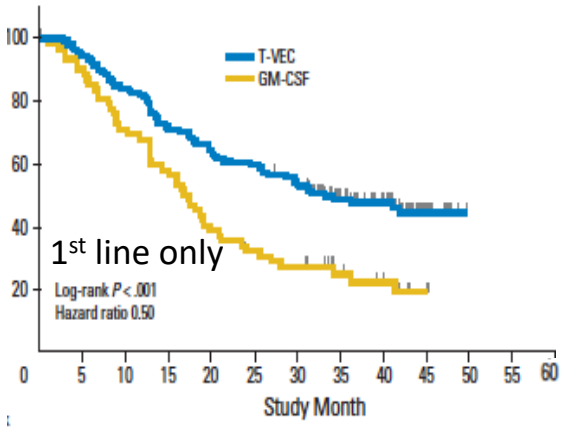
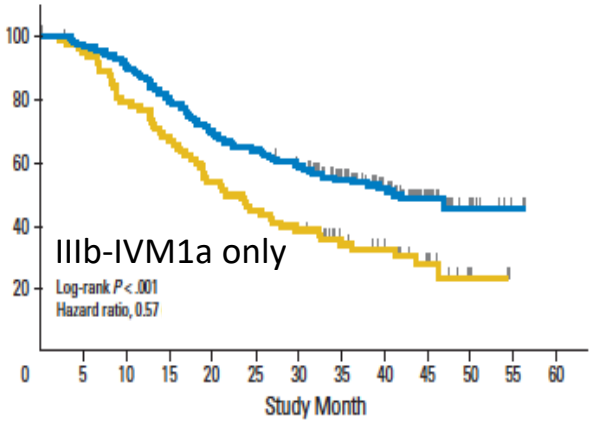
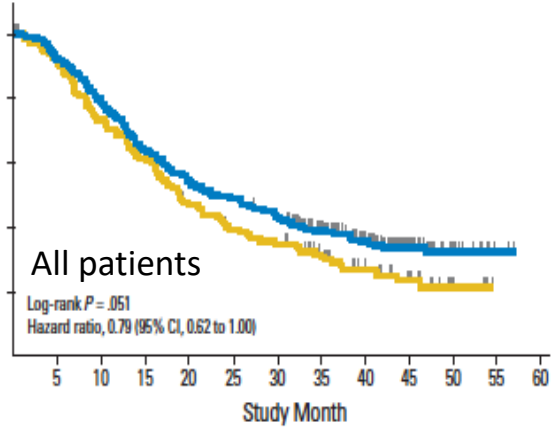
Single agent oncolytic immunotherapy works

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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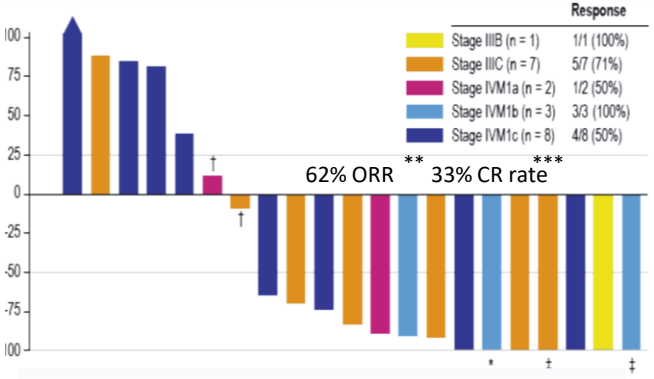
Oncolytic immunotherapy is synergistic with checkpoint blockade

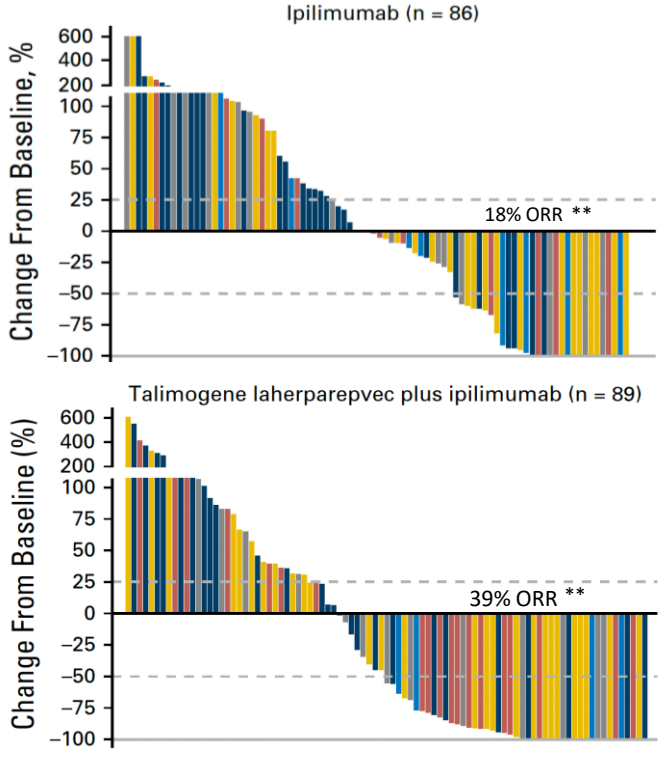
T-vec+pembrolizumab

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



T-vec+ipilimumab

Chesney et al JCO, 2017*



*Studies conducted in patients with melanoma
** ORR = Overall response rate
*** CR = Complete response

No added toxicity reported

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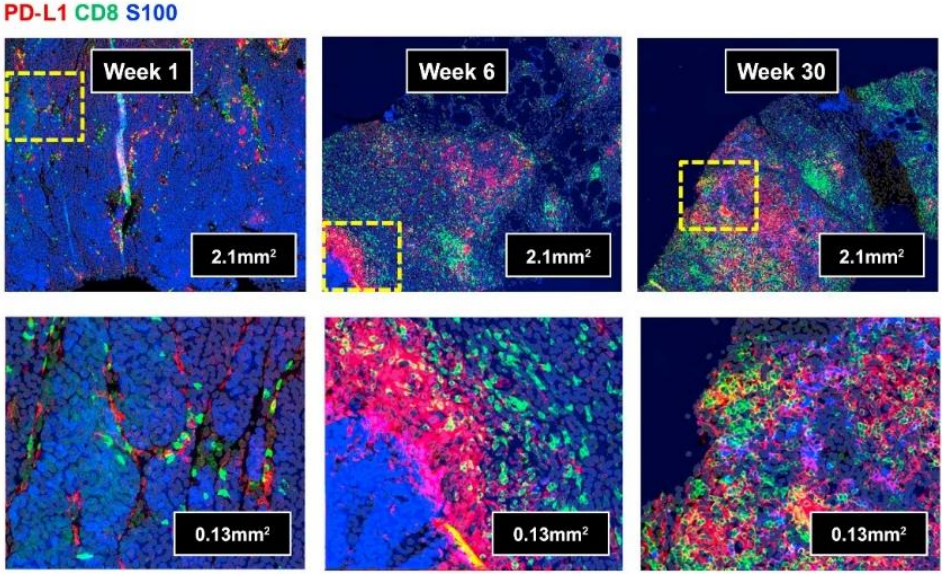
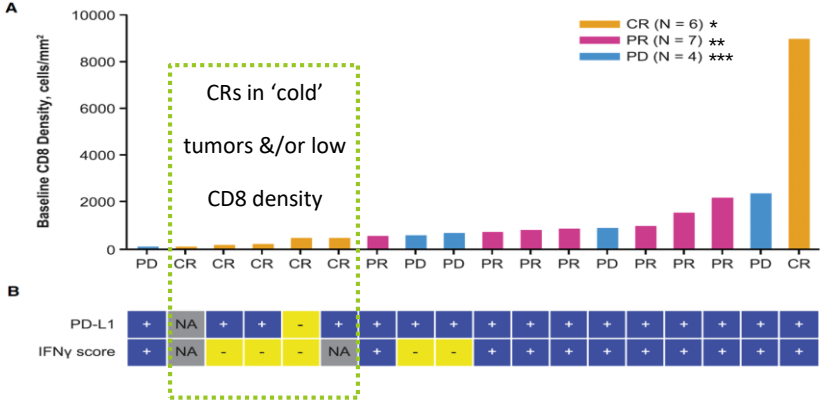
Oncolytic immunotherapy turns “cold” tumors “hot”

T-Vec+pembrolizumab

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



Baseline | After T-VEC alone | After T-VEC+ pembrolizumab



* CR = Complete response
** PR = Partial response
*** PD = Progressive disease

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Our Immulytic platform uses HSV

- HSV as an oncolytic agent has ideal properties for cancer immunotherapy:
  - Biology & disabling mutations well understood
  - Genetically stable, non-integrating
  - Improves safety & efficacy, including in combination with checkpoint blockade
  - Infects human tumor cells broadly, highly lytic & inflammatory, kills mainly by necrosis
  - Potent activator of innate immunity, including through STING/cGAS & TLRs
  - Large viral genome with the capacity to package multiple genes
    - These are then delivered and expressed in the tumor and draining lymph nodes – the optimal sites for anti-tumor immune response induction

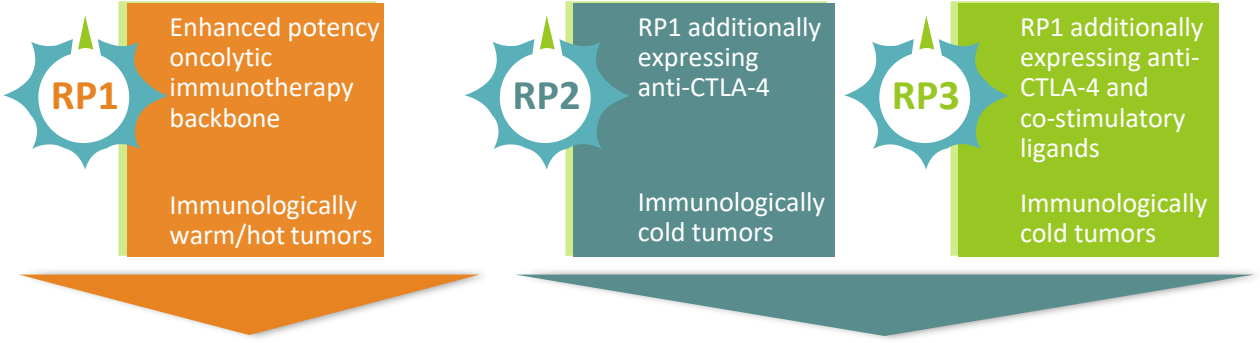
Our Immulytic platform

1. A potent underlying HSV-1 strain

There is great diversity among clinical HSV strains

We tested 29 new strains & selected the most effective

We have armed all of our product candidates with two to four genes encoding therapeutic proteins



2. Increased tumor killing & spread

In addition to the potent cytokine GM-CSF, a modified fusogenic protein (GALV) is expressed

Large bystander effect, highly immunogenic cell death

Provides a substantial increase in direct tumor killing potency

3. Delivery of potent immune stimulatory proteins

Focus on pathways where systemic engagement is sub-optimal

CTLA-4 blockade, immune-costimulatory pathway activation

Delivery directly to the tumor

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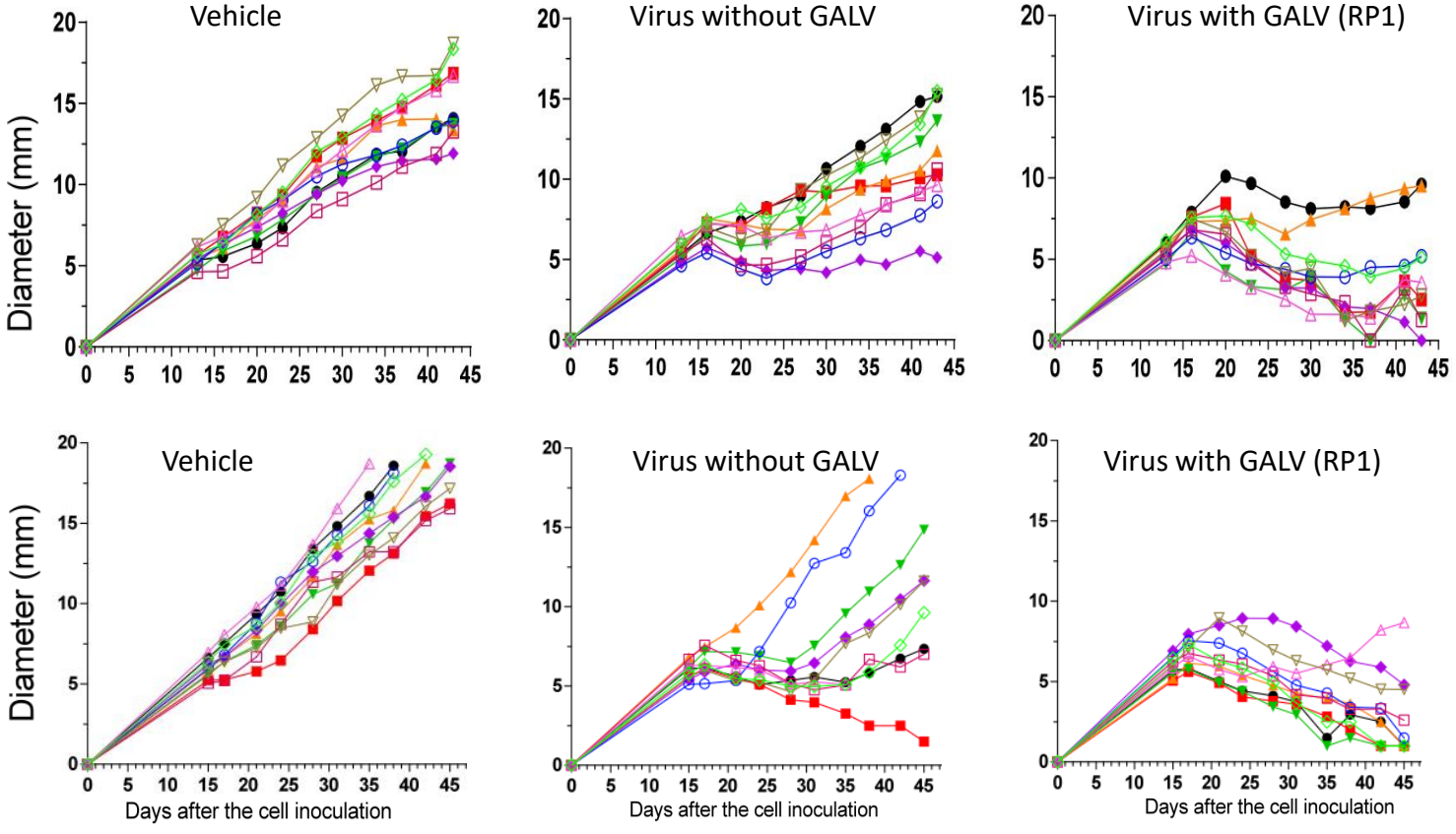
GALV enhances efficacy in vivo

A549
lung cancer

MDA-MB-231
breast cancer



3 injections over 1week; virus dose 5x10^3 pfu

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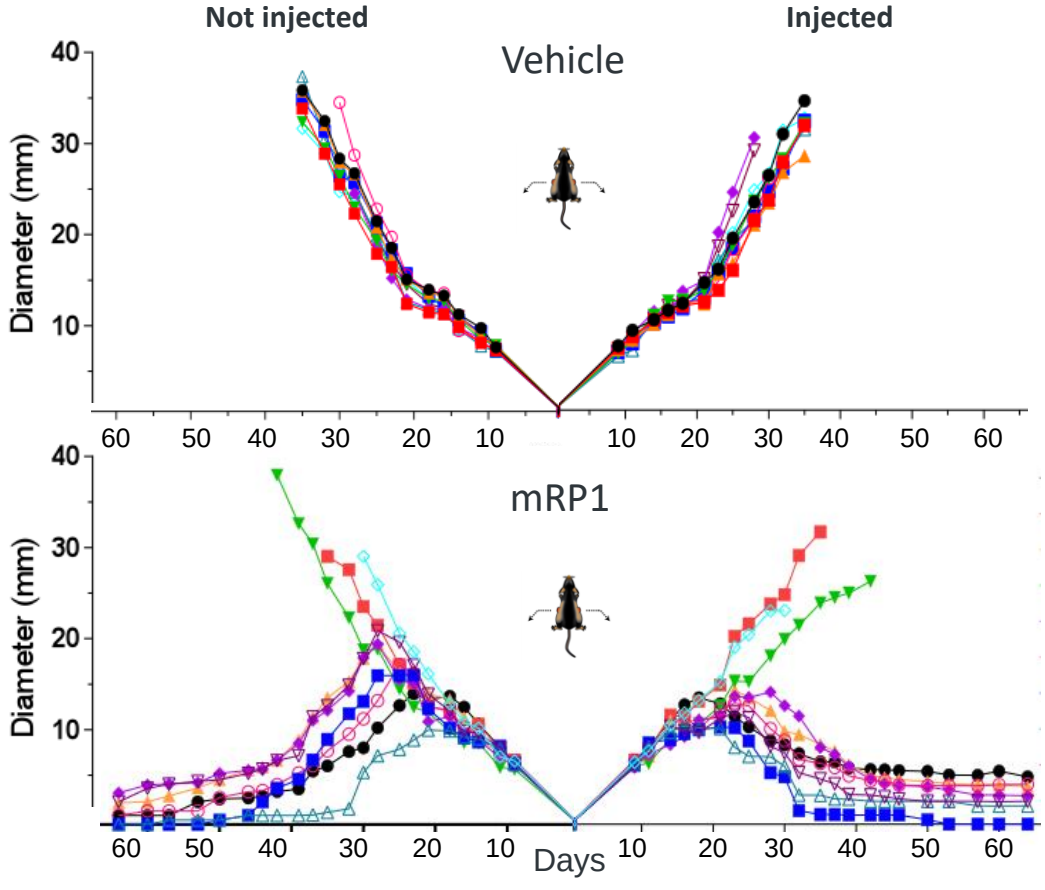
RP1 treats large injected & uninjected tumors



Immune competent rat model (dual flank)

Right flank tumors injected 5x with 5x10^6 pfu

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RP1: Developing for tumor types with underlying sensitivity to anti-PD1

Potential rapid path to initial approval

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RP1 clinical strategy

Phase 1 (complete except MSI high**)**
Safety confirmation & determination of dose for phase 2, all comers
(N≈30)

Phase 2 (underway except MSI high**)**
Defined indications
(N≈30 patients per group)

Phase 1/2 clinical trial in ≈150 patients

Single agent RP1

RP1 + nivolumab*[1]

Melanoma + nivolumab*[2]

NMSC[3] + nivolumab*[2]

Bladder cancer + nivolumab*[2]

MSI-H cancers + nivolumab*[2]

EXPAND PROMISING COHORTS (dependent on data & FDA input)

initiates Q3 2019

Randomized, controlled Phase 2 clinical trial in ≈240 patients with CSCC

RP1+ cemiplimab vs. cemiplimab alone#

[1] Includes biomarker component to confirm MOA [2] Efficacy to be assessed by ORR, CR rate and biomarker analysis [3] Non-melanoma skin cancers

* Under clinical trial collaboration & supply agreement with BMS for the supply of nivolumab

Under clinical trial collaboration agreement with Regeneron; 50:50 sharing of clinical trial costs
(part of a broader collaboration under which clinical trials in additional tumor types may also be conducted)

CSCC – potential path to initial approval

- 4,000-9,000 US deaths annually
- Anti-PD-1 therapy active
  - Cemiplimab (Regeneron) demonstrated 46% response rate, but low CR rate
  - BLA filed
- Tumors are frequently accessible for direct intra-tumor injection
- We believe CSCC provides a rapid route to market for RP1
- Preparing for a potentially 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

RP2/3: Target anti-PD1/L1 non-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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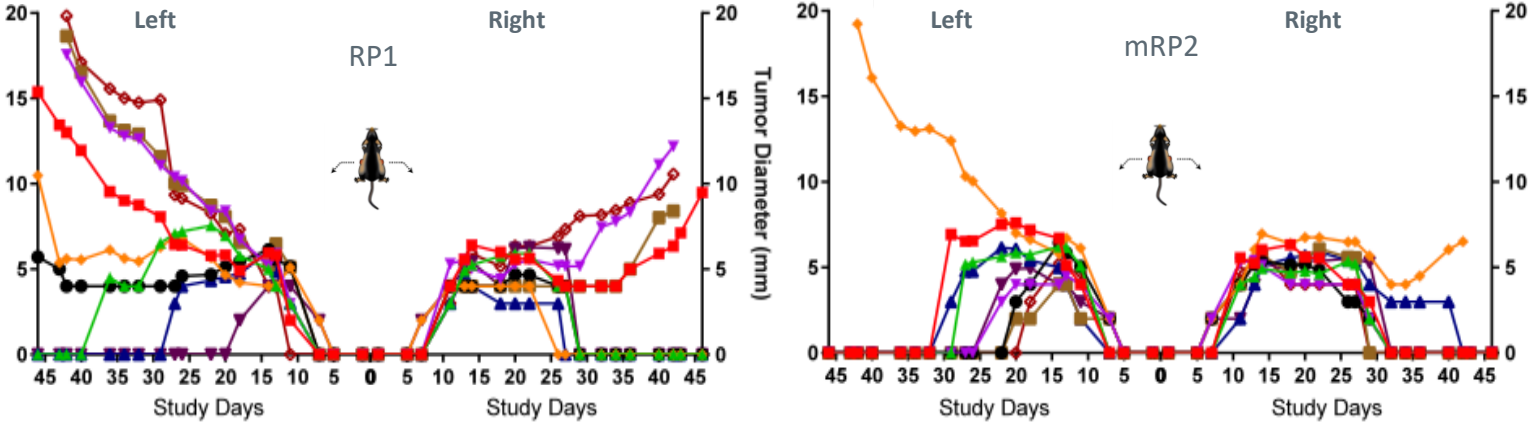
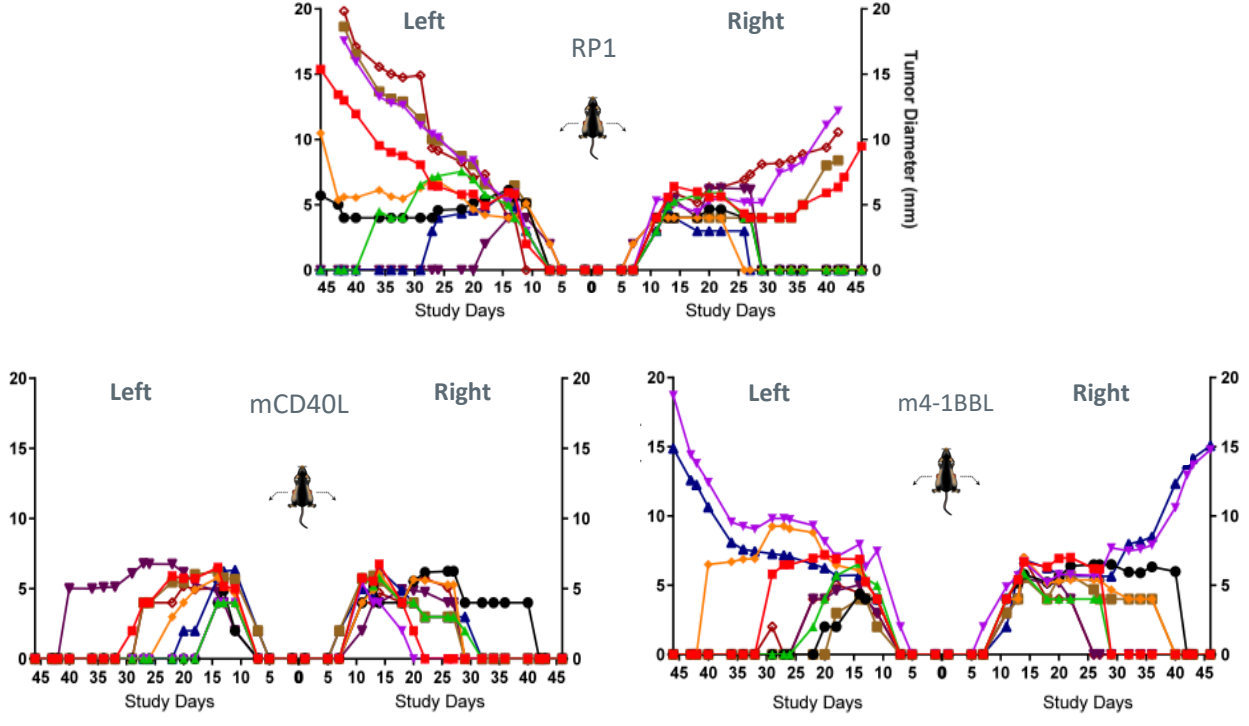
Expression of anti-mCTLA4 enhances efficacy



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

Similarly increased effects with co-stimulatory pathway ligands

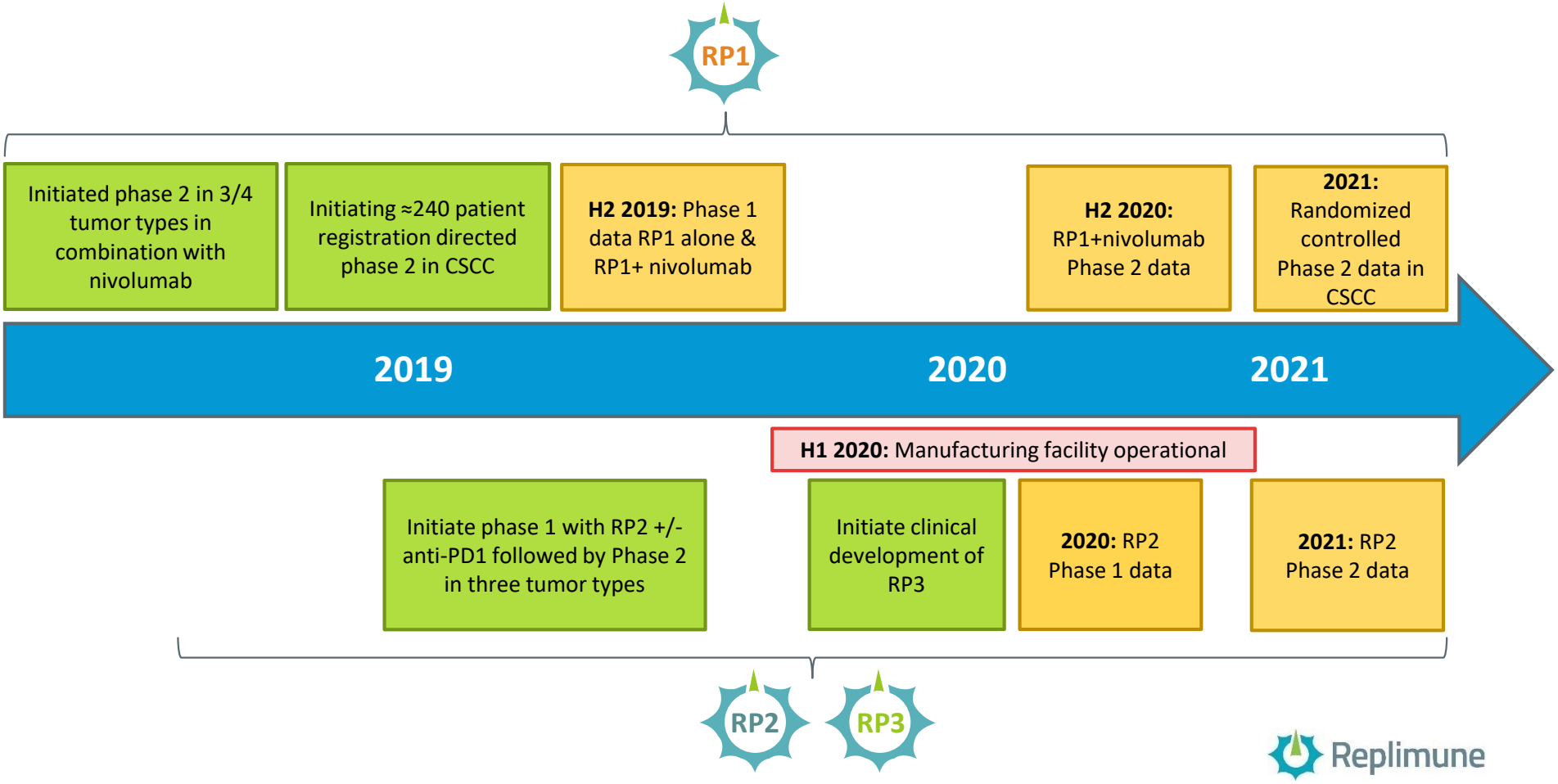


Critical focus on manufacturing

- 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
- Expected to be on-line to produce clinical product in H1 2020

* Rendered depiction of the intended final facility

Key target milestones



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Maximally activating the immune system against cancer

- Multi-product candidate oncolytic immunotherapy platform company
- Broad clinical development program underway
- RP1 intended to enter a registration-directed 240 patient phase 2 clinical trial in cutaneous squamous cell carcinoma (CSCC) imminently (collaboration with Regeneron)
- RP1 being studied in an additional four tumor types in part 2 of an ongoing 150 patient clinical trial combining with nivolumab (collaboration with BMS)
- RP2 & RP3 for PD-1/L1 less responsive tumors expected to enter the clinic in 2019/20
- Further product candidates intended
- Commercial scale manufacturing capability being established
- Aim to become a universal combination partner for PD-1/L1 therapies potentially applicable to all solid tumors