PharmaIN

Proprietary Peptide Drugs for In-Home Therapy

Non-Confidential Presentation 2024

INnovation is in our DNA

- Founded in 2000 as a drug delivery provider, located near Seattle in Bothell, WA
- Recently evolved to become a proprietary superior peptide-based drug developer for in-home therapy
- Asahi-Kasei, PeptiDream, and Shionogi are our publicly announced partners/investors
- Two lead programs in development:
  - ▶ **PHIN-214**
    - Treatment of Liver Refractory Ascites
    - Phase 1b Clinical Trial in US in compensated and decompensated cirrhotic patients
  - ▶ **PHIN-1314**
    - Immuno-Oncology Therapy for Solid Tumor
    - Pre-IND stage

Two Products with 6+ Indications

PHIN-214	Refractory Ascites P1b is ongoing	Undisclosed	Undisclosed
PHIN-1314	Oncology Solid Tumors IND in 2024	Oncology Combination with Checkpoint Inhibitors	Inflammation and Fibrosis

PHIN-214 Opportunity

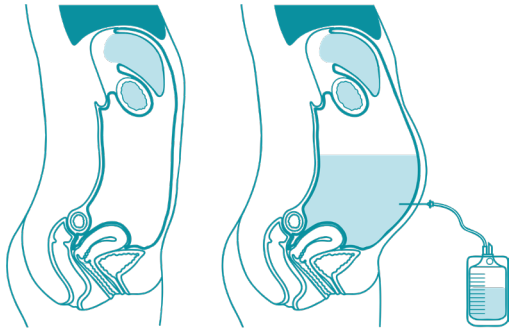
Refractory Ascites Opportunity

▶ **PHIN-214** is a synthetic derivative of Vasopressin effective at controlling hemodynamics

- New Chemical Entity / new composition of matter
- Significant safety / durability improvements over Terlipressin*
  - Single subcutaneous injection provides greater sustained PK, and enables long term therapy at home
  - Milder vasopressor activity reduces risk of ischemia
  - Broader therapeutic index

▶ Clinical development

- Phase 1b in compensated and decompensated cirrhotic patients is ongoing
- Phase 2 initiation in cirrhotic patients in 2025

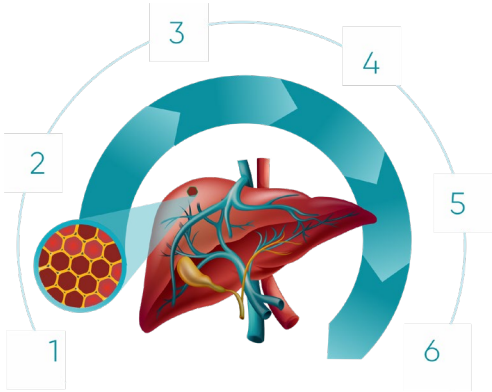


** Approved in US, EU countries, and Australia*

Large and Unmet Medical Need

- 1st Indication – *Refractory Ascites in late-stage liver cirrhosis*
  - Large unmet medical need worldwide, primarily in the US (>13,000 patients) and Japan
  - Addressable market in the US alone: $1.0B+*
- 2nd Indication – *Progressive Liver Disease / Ascites*
  - 10x larger market (130,000+ patients in the US)
  - Opportunity for Orphan Drug Designation (FDA)
- Additional indications
  - *Immune-Mediated Vascular Leakage / Cytokine Storm*
  - *Hepatorenal Syndrome (HRS)*
  - *Esophageal Variceal Bleeding (EVB)*
  - *Left Ventricular Assist Device Orthostatic Hypotension*

ASCITES DEVELOPMENT



1. Liver is clogged by cirrhosis causing portal vein pressure (portal hypertension)

2. Blood pooling / vasodilation beneath liver

3. Decreased effective blood volume

4. Activation of neurohormonal systems (RAAS)

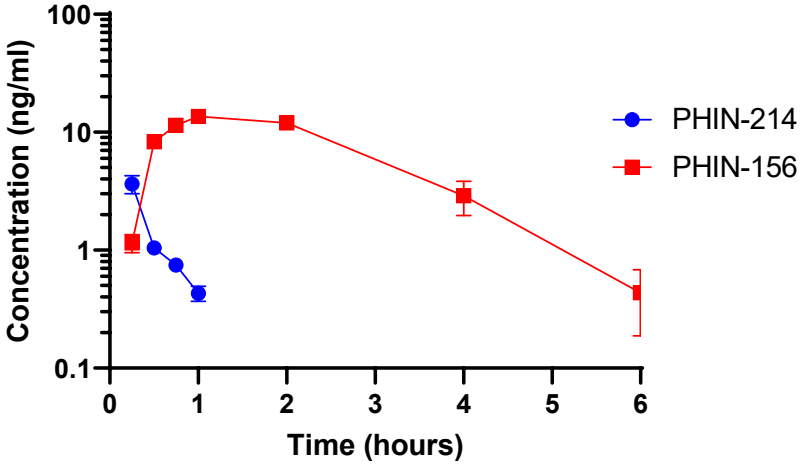
5. Sodium and water retention

6. ASCITES

* *J.Vasc Interv Radiol 2018*

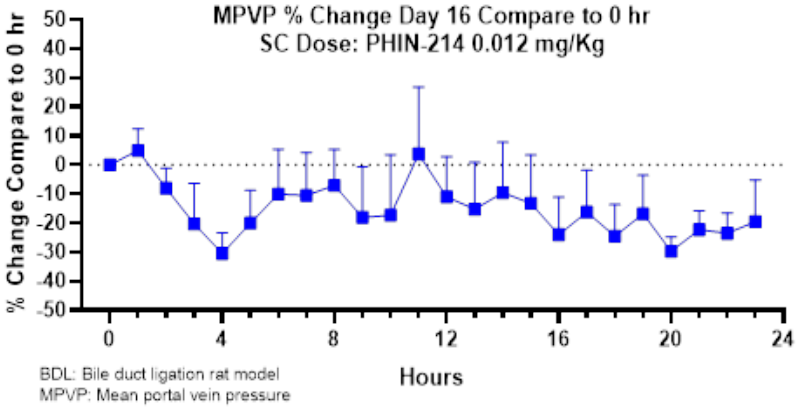
PHIN-214's Metabolite, PHIN-156, Has Long Lasting PK and PD

PHIN-214 0.1 mg/kg SC (n=6)
GLP study



AUC (hr*ng/mL) per 0.1 mg/kg dose
PHIN-214: 1.34 (T1/2 = 0.365 hr)
PHIN-156: 34.8 (T1/2 = 0.7 hr)

Mean Portal Venous Pressure % Change compared to baseline
PHIN-214 0.012 mg/Kg



BDL: Bile duct ligation rat model
MPVP: Mean portal vein pressure
SC: Subcutaneously
Data presented as Mean ± SEM
0 hour data is the average of 45 min to 15 min prior to dose
In BDL MPVP group, animal 003 was excluded due to more than 50% difference than the animals in the same group

Summary

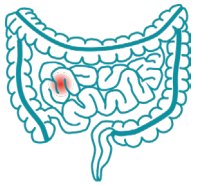
- First-in-class, subcutaneous, long-term home therapy for Cirrhotic Ascites
- Expandable to other indications, HRS, EVB, catecholamine-resistant hypotension, cytokine storm-induced hypotension
- Blockbuster opportunity for multiple unmet medical needs

PHIN-1314 Opportunity

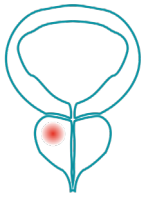
Safe, Effective, Proprietary Peptide for Treatment of Cancer

- Unparalleled Anti-Tumor Response
  - Vascular-targeting Mechanism of Action (MoA) distinct from Avastin
  - Demonstrated single-agent activity in mouse syngeneic solid tumor models including:
    - Osteosarcoma, Breast, Colon, Melanoma, and Prostate
  - Modifies tumor microenvironment
  - Synergy with approved Immuno-Oncology (I-O) drugs
  - Broad application across solid tumors
  - Subcutaneous administration

BREAST



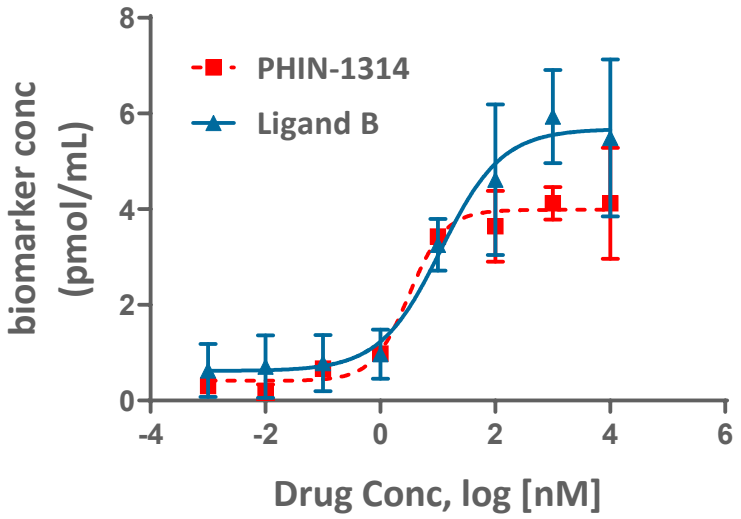
INTESTINE



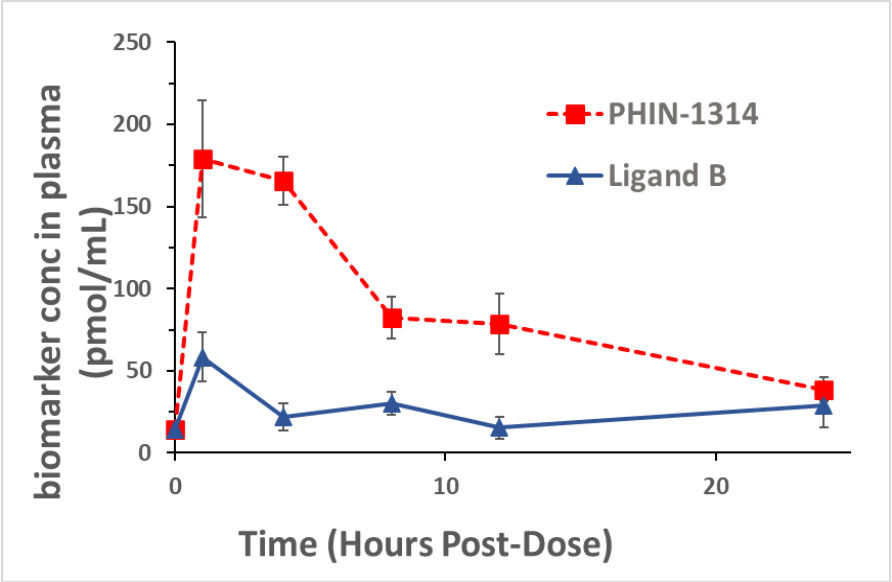
PROSTATE

PHIN-1314 Has Higher Potency than Ligand B

In vitro activity (Receptor B specific)



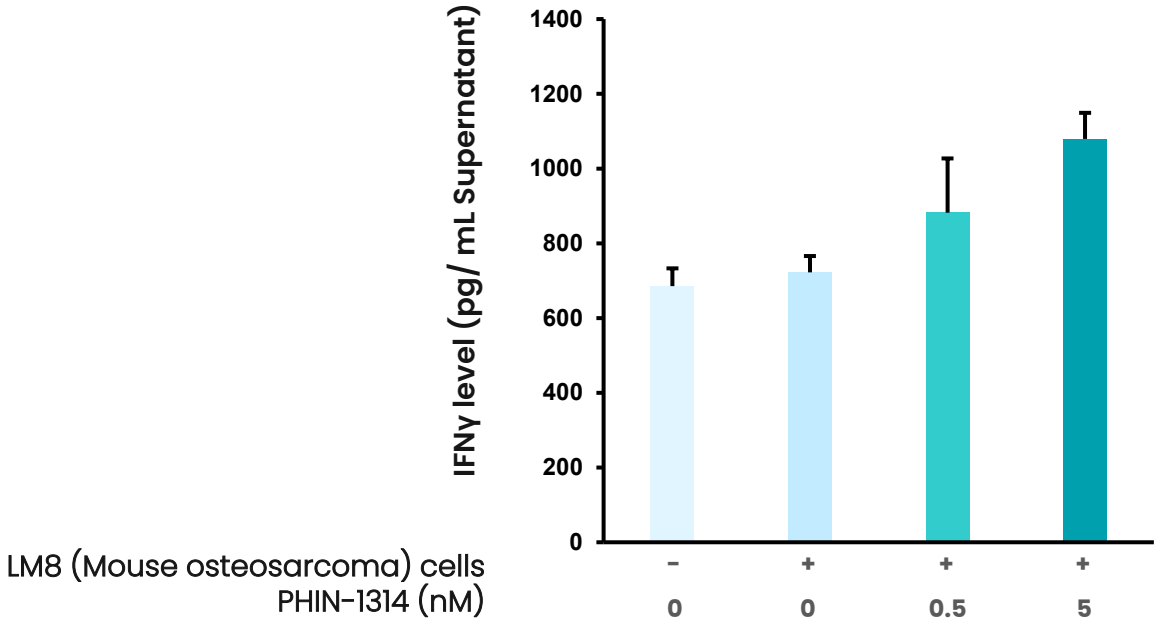
In vivo PD study in mice (n=5)



2 mg/kg via SC

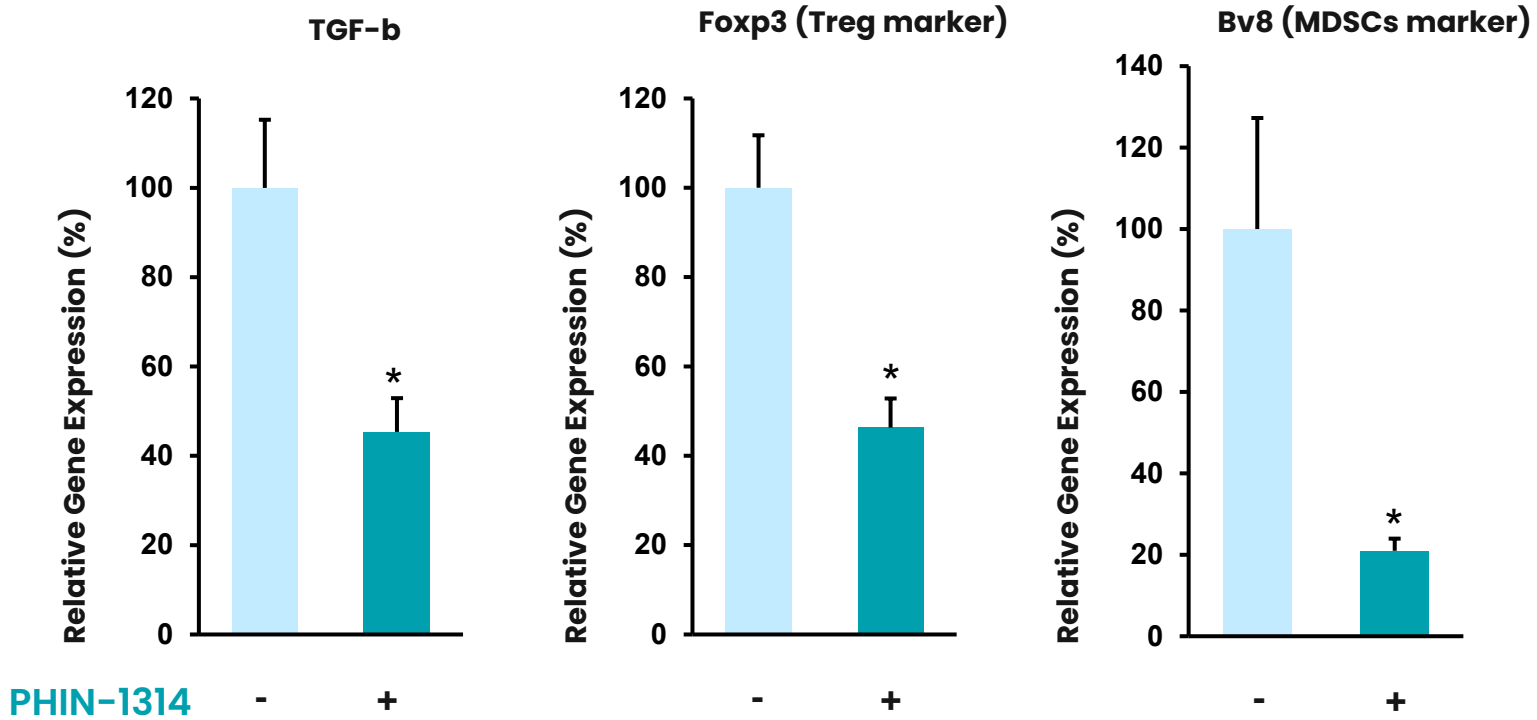
PHIN-1314 is a derivative of Ligand B with potent and extended activity in vivo.
No biomarker signal was detected in cells displaying other receptor family members treated with PHIN-1314.

PHIN-1314 Drives IFNg Production by Splenocytes from Tumor-Bearing Mice



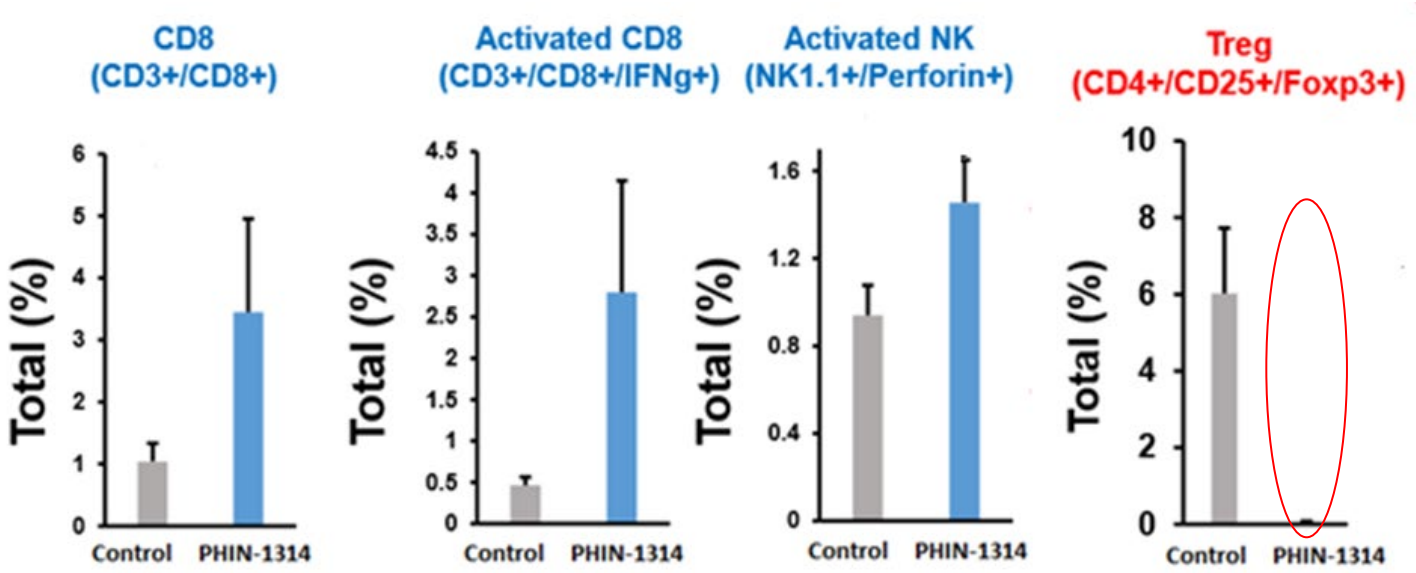
Mouse Osteosarcoma cancer LM8 cell line were maintained in complete media and seeded into 96-well plates (10,000 cells/well with 1,000,000 cells splenocytes derived from LM8 tumor-bearing orthotopic mice). Cells were treated with PHIN-1314 for 96 hrs. IFNg levels were measured by ELISA assay (R&D) (*n* = 4).

PHIN-1314 Down-regulates Key Immuno-Suppressive Factors



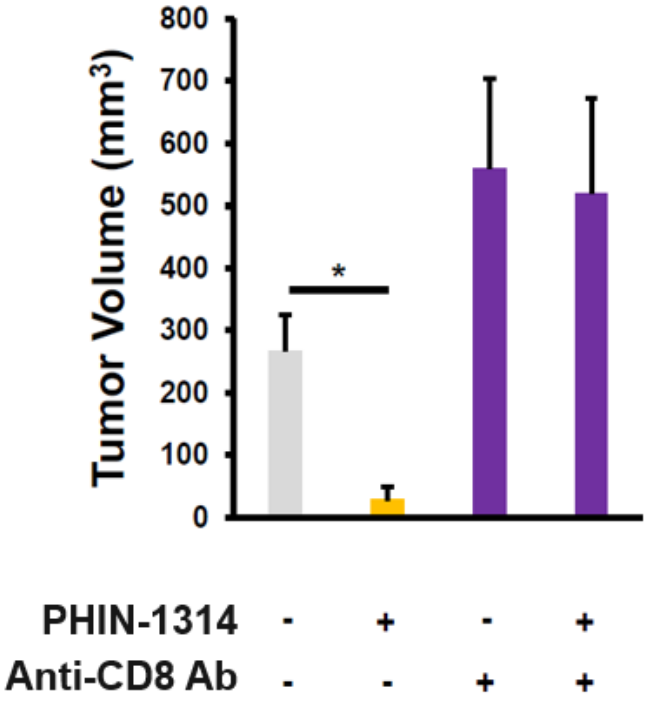
Mice bearing subcutaneous LM8 osteosarcoma tumors were treated with 1 mg/kg PHIN-1314. Small intestine were excised and analyzed for lymphocyte and cytokine markers by qPCR. (*Actb* gene as a marker)

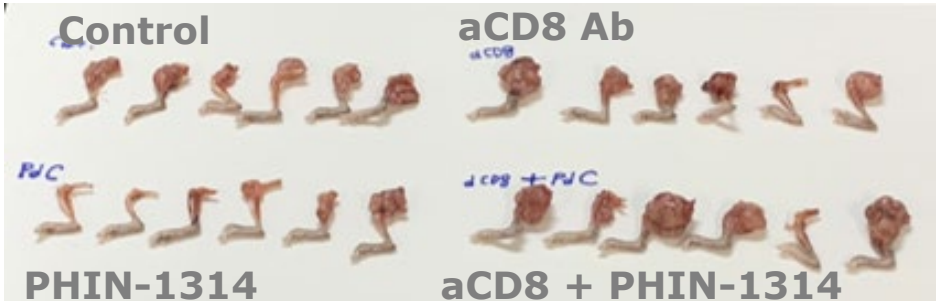
PHIN-1314 Alters the Tumor Microenvironment



Mice bearing subcutaneous E0771 mammary tumors were treated daily with PHIN-1314 for 2 weeks. Tumors were removed and immune cells within the tumor were measured by flow cytometry. PHIN-1314 treatment (0.3 mg/Kg via SC) resulted in increased levels of $CD8^+$ T cells and NK cells within the tumor, coincident with reduced levels of Tregs. The receptor for PHIN-1314 is known to be expressed on these immune cell types.

Anti-tumor Activity is T cell-Mediated



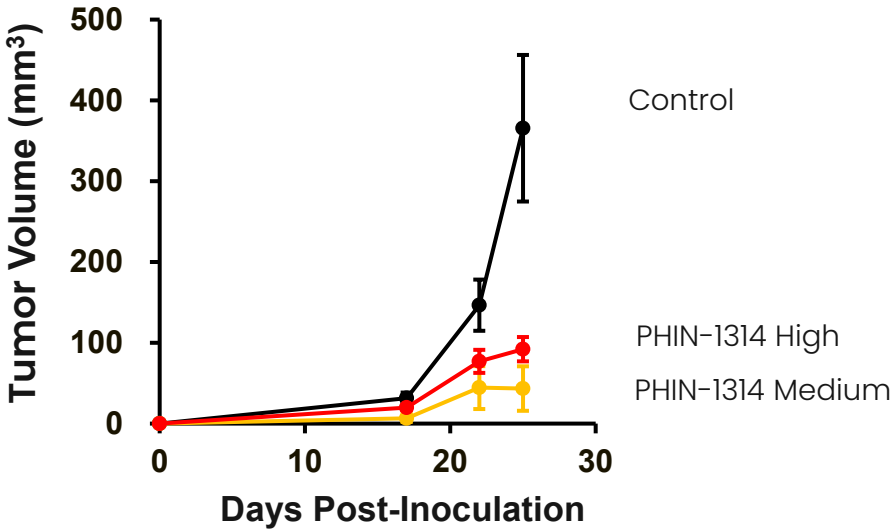


LM8 Osteosarcoma cell line were implanted in femurs of C3H/He mice ($1x10^6$ cells) n=6/group.
Mice with established tumors were treated subcutaneously with PHIN-1314 QDx5 for 2 cycles

CD8 serves as a co-receptor for the T-cell receptor, and defines an effector T cell population
* P<0.01

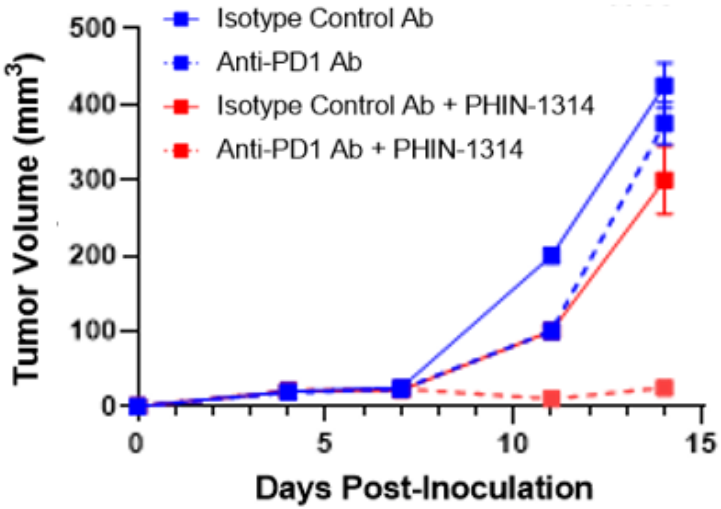
Synergy in Combination with PD-1

Single agent: Osteosarcoma



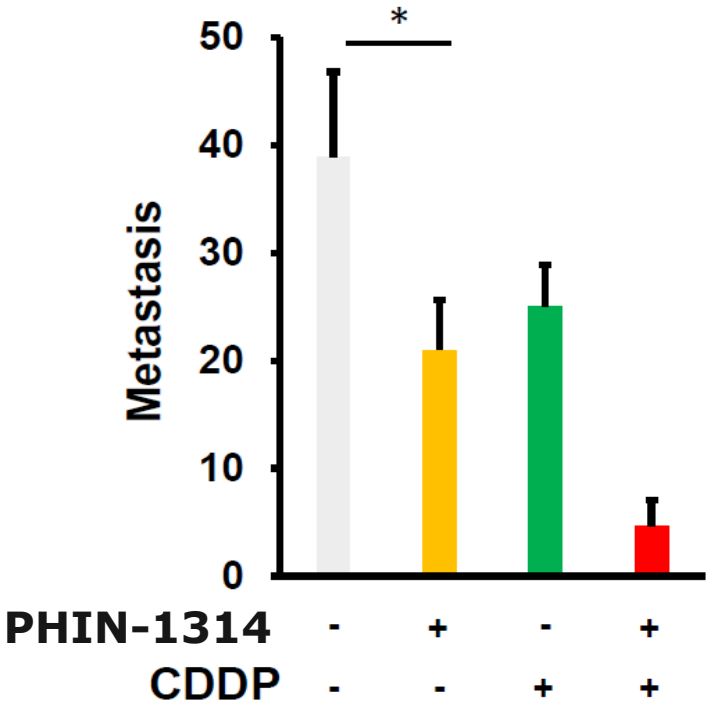
Balb/c mice were implanted with mouse osteosarcoma cell line K7M2 (SC implantation) and treated API 5 times a week starting on Day 4.

PHIN-1314 + anti-PD1 in resistant tumor



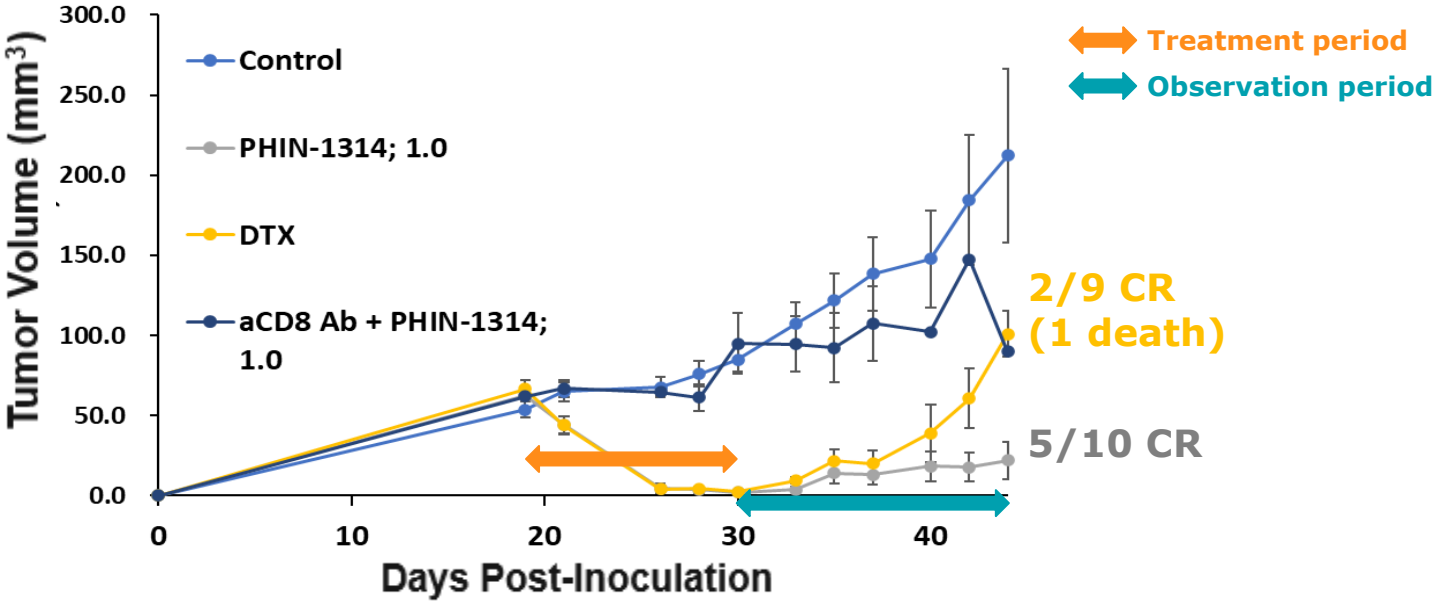
The mouse breast tumor E0771 model is refractory to either aPD-1 or PHIN-1314. Mice implanted with E0771 and treated with anti-PD1 and PHIN-1314 produced true combination synergy. Similar combined effects are observed in other syngeneic models including B16 melanoma and MC38 colon cancer, and with PHIN-1314 combined with anti-CTLA-4.

Antimetastatic When Combined with Cisplatin



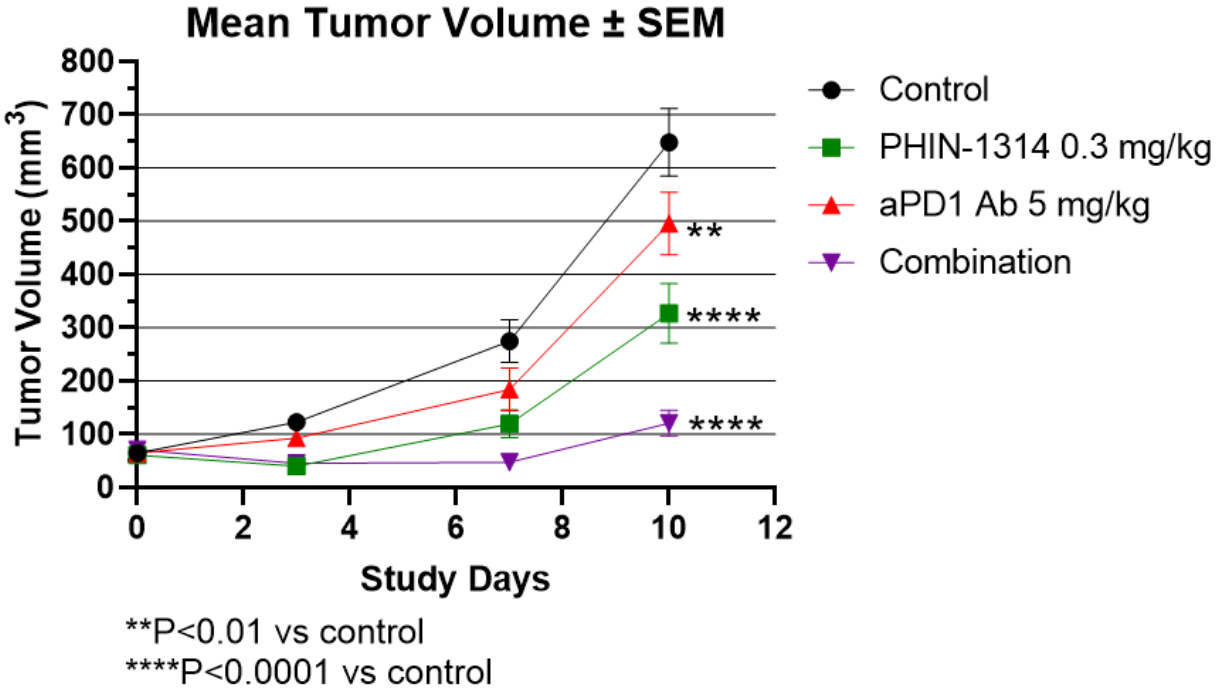
Syngeneic LM8 Osteosarcoma cells ($1x10^6$ cells) were implanted in the femurs of C3H/He mice. Established tumor-bearing animals were treated with Cisplatin (CDDP) 6 mg/kg (IP, QDx6) and/or PHIN-1314 0.3 mg/kg (SC, QDx5 for 2 cycles), followed by assessment of lung metastasis
*P<0.05

Confirmed Single Agent Activity in Established Prostate Tumors



Mice bearing SC TRAMP-C1 prostate tumors were treated (SC, QDx5, 2 cycles) with PHIN-1314 starting on Study Day 19 (~70 mm3 tumors), followed by a 2-week observation period. PHIN-1314 treatment (1.0 mg/Kg SC) resulted in significant tumor reduction with 5/10 Complete Responses (CR). Antitumor activity was dependent on presence of CD8 T cells. Docetaxel (DTX) treatment at MTD resulted in 2/9 CR (one death in DTX group). No unanticipated activity noted in PHIN-1314 groups.

Combination Therapy in Established Prostate Tumors



**P<0.01 vs control
****P<0.0001 vs control

Methods

6-week male C57BL/6J mice were inoculated with RM1 prostate cancer cells (500,000 cells/mouse sc) in the right flank and treated with from the day tumor volumes are reached to 80 mm3 (Day 0), mice were treated with PHIN-1314/ Anti-PD1 Ab.

Summary

- First-in-class, subcutaneous, long-term home therapy for Solid Tumors
- Effective in multiple tumor models alone or in combination with approved I-O treatments
- Unparalleled MoA
- Pre-IND
- Seeking co-development partners

We look forward to working with you!

Thank you!

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