TaiMed Biologics

用於重大疾病的生物製劑發展
Development of Biologic Therapeutics for Critical Diseases

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TaiMed Biologics Mission and Business Model

- TaiMed is committed to finding safe and effective treatments for those patients suffering from HIV/AIDS
- Development led by science
- Develop licensed assets from bench through the clinic
- Smart business development
  - In-license quality molecules
  - Outlicense / codevelop with the right partners
- Return value to our investors

Corporate Structure

TaiMed Biologics Inc. Taiwan

- Headquarters
- Finance & Accounting
- Collaborative Discovery Research
- Preclinical Development
- GMP Manufacturing/Testing Facility
- Quality Assurance

TMB USA Irvine, CA

- Subsidiary of TaiMed Biologics, Inc.
- Clinical
- Regulatory
- Virology
- Business Development

Financial Status

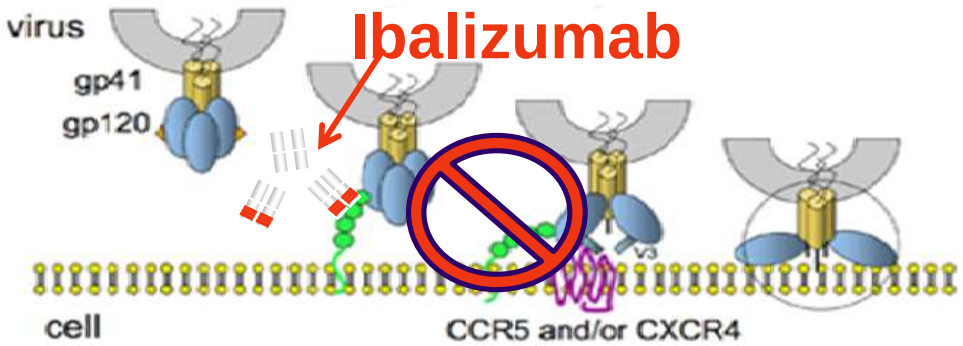
- TaiMed has been a publicly traded company on the Taipei stock exchange (stock code: 4147) since 2010
- IPO on Nov 23, 2015 and traded on the Taipei Exchange Market (OTC)
- Current market cap is approximately USD$1.45B, with an average daily trading volume of approximately 1.05 million shares (Oct 2017)
- Ruentex holds ~18% of TaiMed
- National Development Fund hold ~16.5% of TaiMed
- Shareholders exceed 20,000

Fundraising History

- Raised a total of USD$208M through four fundraising rounds:
  - First round (2007-2008) USD$30M
  - Second round (2010) USD$22M
  - Third round (2014) USD$46M
  - Fourth round for IPO (2015) USD$110M
- Cash in hand as of 11/30/2017: USD$123M
- Total shares outstanding: 250M

Ibalizumab – Our Lead Product

- Humanized monoclonal antibody being developed for the treatment of multidrug resistant (MDR) HIV-1 infection
- Binds primarily to the second extracellular domain of CD4+ T cell receptor, away from MHC II molecule binding sites
- Prevents HIV from infecting CD4+ T cells while preserving normal immunological function



Exploring “Clever” Pathways with US FDA

- In 2011, Ibalizumab Phase II was completed and we had very little business case to move the IV program forward given the large number of patients needed for Phase III
  - We presented our intention to focus on SC or IM alternate routes of administration
  - HIV guidelines on clinical trial design were changing
    - Short-term monotherapy lead-in
- FDA presented
  - Orphan Drug Designation
  - Breakthrough Therapy

Orphan Drug Designation

- Agency Objective
  - To encourage the development of drugs for the treatment of rare diseases
- Criteria
  - Disease prevalence must be under 200,000
- Advantages include
  - 50% tax credit on the cost of clinical trials in the US
  - 7 year marketing exclusivity
  - Fast-track reviews for registrational filings
  - More flexibility with trial design
  - Possibly fewer trials needed, smaller trials
  - User fee waivers
  - Grant funding for clinical trials up to $500,000 per year
- Ibalizumab granted orphan drug designation in October 2014
  - For the treatment of HIV-1 infection in treatment experienced adult patients with documented multi-antiretroviral class resistance and evidence of HIV-1 replication despite ongoing antiretroviral therapy
  - First HIV treatment to be given orphan drug designation

Expedited Approval Pathways with US FDA

	Fast track	Accelerated Approval	Priority Review	Breakthrough Therapy
Eligibility	A drug that treats a serious condition and for which nonclinical or clinical data demonstrate the potential to address an unmet need	A drug that treats a serious condition, provides meaningful therapeutic benefit over available therapies and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit	A drug that offers major advances in treatment over existing therapies or provides a treatment where no adequate therapy exists	A drug that treats a serious condition and for which **preliminary clinical evidence** indicates that the drug may demonstrate substantial improvement over available therapies
Designation	Can be requested at any time; 60 day response time	No formal process.	Requested at time of new drug or biologic application submission; 45 day response time	Can be requested at any time after IND application; 60 day response time
Clinical Development	Earlier and more frequent communication	Conditional approval granted using surrogate endpoint(s) from P2 or interim P3 data; confirmatory trials with hard clinical endpoints required	Standard.	Abbreviated or condensed development, with earlier and more frequent communication and delegation of senior reviewers and a cross-disciplinary review team.
Review Process	Option for rolling data submission; standard review after last data submitted	Data submitted in one-package; standard 10-month review	Data submitted in one-package; review time shortened to 6-months	Data submitted as they are accumulated; review time shortened
Established	1988	1992	1992	2012

Source: Friends of Cancer Research's Conference on Clinical Cancer Research Issue Brief, Developing Standards for Breakthrough Therapy Designation, Nov 2012

Breakthrough Therapy

- “All hands on deck” approach to drug development
- Signal from the Agency that you have unprecedented activity and they want to work with you to find the best course forward
- Ibalizumab received breakthrough designation in 2015 (previously had fast-track, accelerated approval and priority review)

Our Experience thus far

- Statuses and designations have been extremely helpful through the BLA process
  - 2 meetings thus far; mid-cycle and late-cycle reviews
  - FDA working with us to ensure an appropriate application is submitted
  - Label discussions

Ibalizumab - Clinical Program

- Evaluated in 247 patients prior to Phase III
- Phase III trial
  - 40 patients
  - 24-week study (first dose at day 7)
- Primary endpoint at Day 14
  - % of patients achieving > 0.5 $\log_{10}$ decrease in viral load
- Secondary endpoints at Week 25
  - Safety and efficacy data

Ibalizumab - Phase III Results

- Primary endpoint results
  - 82.5% success rate (33/40, $p < 0.0001$)
  - Average viral load reduction was 1.1 $\log_{10}$ after 7 days
  - Well tolerated in the first week of treatment (No treatment related SAEs)
- Secondary endpoint results
  - Mean reduction in viral load – 1.6 $\log_{10}$
  - 43% of patients achieved undetectable viral load (<50 copies/mL) with a mean reduction of 3.1 $\log_{10}$

Moving forward with Ibalizumab

- Many firsts for TaiMed and ibalizumab
  - First BLA filed with FDA on May 3, 2017 (Priority review)
  - First new anti-retroviral class in 10 years
  - First monoclonal antibody for HIV
  - First non-daily treatment regimen for HIV
  - First HIV product to receive orphan drug designation
  - First FDA approved protein drug product for Taiwan
- On the horizon
  - PDUFA date – April 3, 2018
  - the global HIV Market is ~$25 billion and dominated by a handful of companies
  - Niche segments are overlooked
  - Partnered with Theratechnologies to market ibalizumab

Market Research

- Firm up our understanding of MDR HIV setting
- Two market studies with physicians
  - Qualitative : Exposure to ibalizumab and reaction (n=10)
  - Quantitative : Assessment of patient population (n=100)
- Results confirmed by internal review of published data

- Payer research
  - Interviews with payers
  - N=20
  - Lives covered – 190 M

Market Research – Qualitative Study Findings

- Multidrug resistance arises through non-compliance
- Unmet medical need for these patients:
  - New therapeutic class
  - Less frequent dosing
- Ibalizumab seen as very useful (8.3/10 in the US - 7.6/10 in Canada)
  - No cross resistance
  - Dosing schedule
  - New therapeutic class
  - Efficacy
  - No drug-drug interactions
- Need for new therapeutic option outweighs IV requirements
- Majority of physicians expect ibalizumab to be included in treatment guidelines
- Ibalizumab was highly likely to be prescribed (rating > 7/10)

Market Research – Quantitative Study

- Patient population
  - Median number of managed HIV patients = 80 per month
    - Number of patients on antiretroviral treatment (ART) = 55
    - Number of patients resistant to at least two classes = 6
    - Number of patients with triple class MDR HIV-1 = 2
- Approximately 4% of ART treated patients are triple class resistant
- Internal research validates these findings

Market Research

- Estimated number of treated HIV-1 patients in the US = 450,000 to 650,000
- Percentage with triple class MDR HIV-1 = Approx. 4%
- Approximate number of triple class MDR HIV-1 patients = 20,000 to 25,000
- Percentage with viral failure during any 48 week period = 50% to 56%
- Ibalizumab, yearly addressable market = Approx. 10,000 to 12,000

Data reference:

NCHHSTP HIV Atlas

CDC. Vital Signs: HIV Diagnosis, Care, and Treatment Among Persons Living with HIV — United States, 2011. MMWR 2014;63(Early Release):1-6.

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Market Research

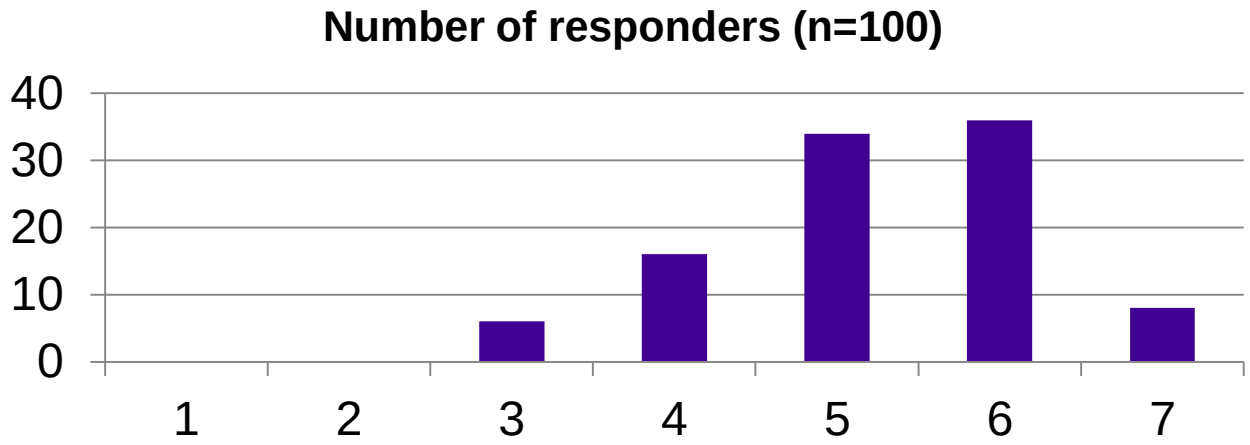
- Quantitative study
  - Treatment goal for triple class MDR HIV-1 patients
    - Virological suppression/reduction: 58%
    - Bring to undetectable load: 18%
    - Control symptoms: 16%

Market Research

- Most important attributes in treatment selection
    1. Clinical evidence of efficacy in MDR HIV-1 patients
    2. Determining virus resistance profile
    3. Improvement in patients quality of life
    4. Safety/side-effect profile of the drug
    5. New option for MDR HIV-1 patients

Market Research

- Level of unmet need in treating triple class MDR HIV-1 patients (7 point scale)



- 78% of physicians reported high unmet need for MDR HIV-1 patients

Market Research

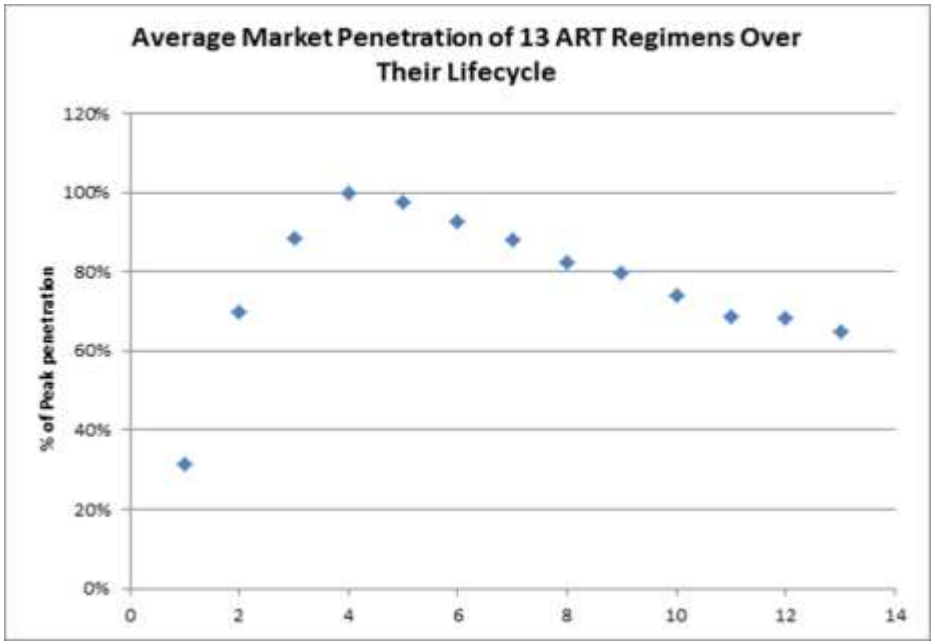
- After being exposed to the ibalizumab profile
  - Ibalizumab was very highly rated to treat MDR HIV-1 patients (5.3/7)
    - Fared even better in most of the key attributes:
      1. Clinical evidence of efficacy in MDR HIV-1 patients (6.0/7)
      2. Determining virus resistance profile (5.7/7)
      3. Improvement in patients' quality of life (4.9/7)
      4. Safety/Side-effect profile of the drug (5.4/7)
      5. New option for MDR HIV-1 patients (5.4/7)

Market Research

- Physicians expressed an intention to prescribe ibalizumab to approximately 50% of their MDR HIV-1 patients experiencing virological failure
- Ramp-up of use would be quite rapid
- Willing to bear the burden of any potential payer-imposed restrictions

Market Research

- Physicians have told us they expect to adopt ibalizumab quickly
- Broader use will come after initial clinical experience with the product
- We believe ibalizumab could mimic other successful HIV product launches



Payer Research

- Sample evenly split between Medicaid, Medicare and private payers
  - In-depth telephone interviews
    - General discussion on HIV treatments
    - Multidrug resistance discussion
    - Product profile presentation
    - Discussion on pricing
    - Coverage intentions

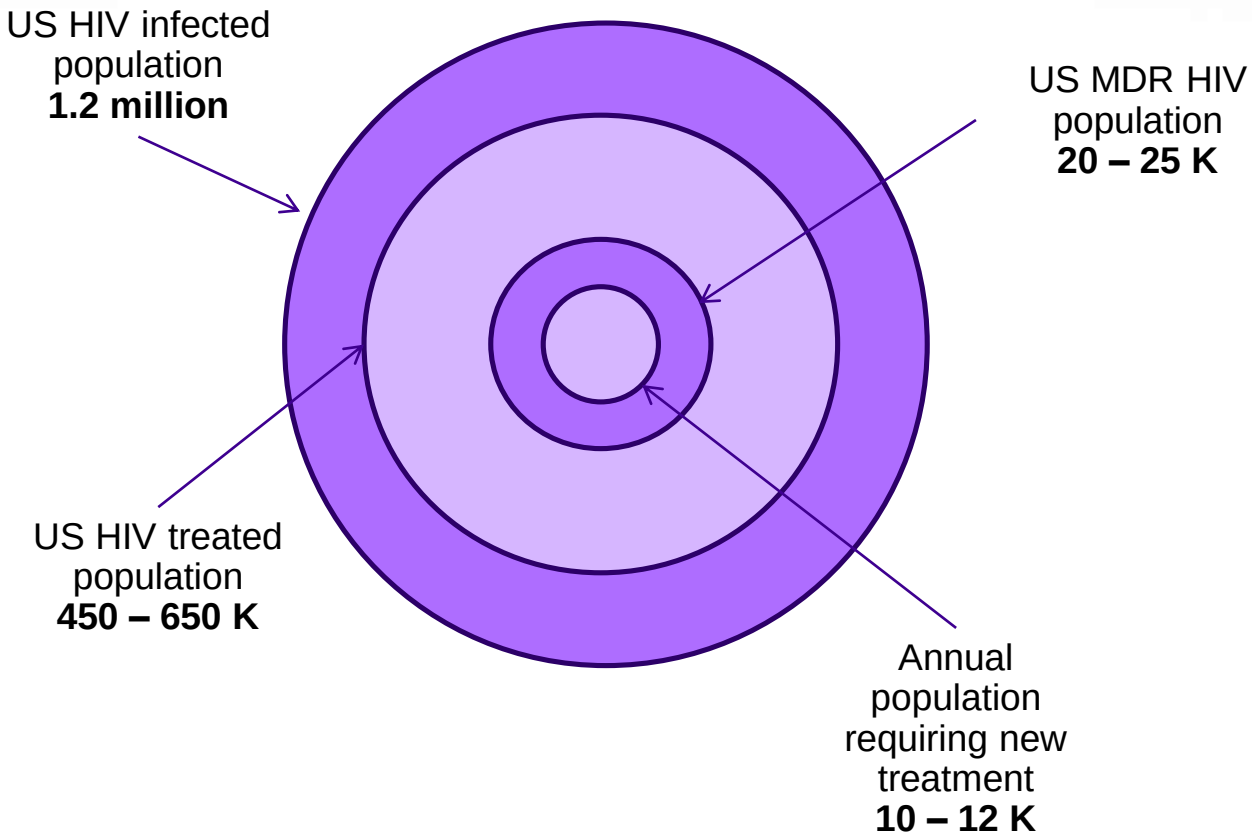
Payer Research

- Virtually all payers felt ibalizumab addressed unmet needs for MDR HIV-1 patients
- Ibalizumab had an 8.1/10 average usefulness rating from payers
- Most attributes score high ratings (> 6.0/10)
  - Safety and tolerability (7.5)
  - Overall efficacy (7.4)
  - Overall clinical trial setup (7.2)
  - Mechanism of action (monoclonal antibody) (6.4)
  - FDA Breakthrough therapy status (6.0)

Payer Research

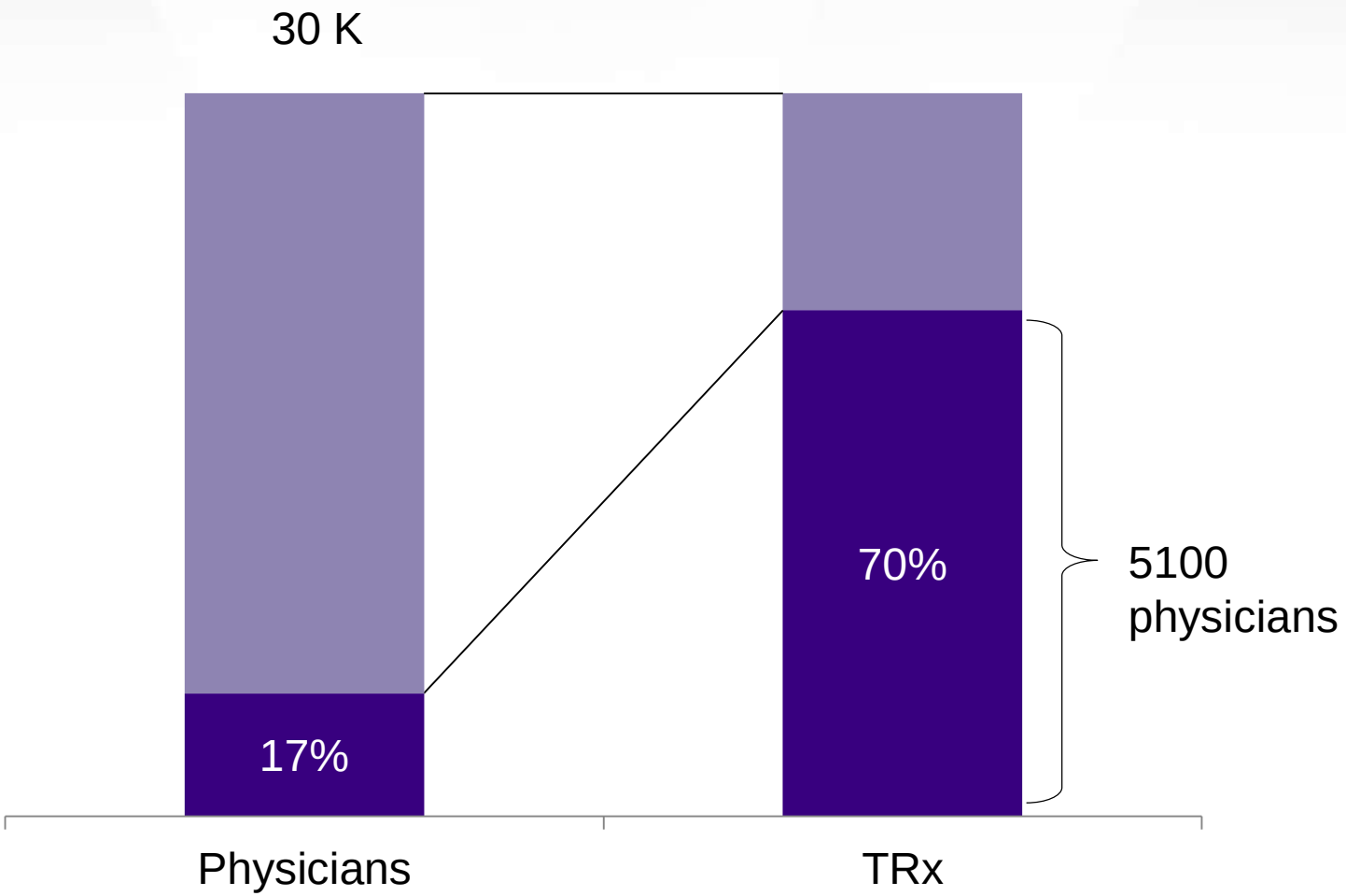
- Overall efficacy and safety/tolerability will be the determining factors when considering ibalizumab for reimbursement
- Cost was not raised as a primary concern
- Majority of plans expected ibalizumab to be priced at a premium to other HIV therapies
- 17 out of 20 payers said ibalizumab would fall under medical benefits, as opposed to pharmacy benefits
  - Considered an act performed by the physician
  - More difficult for insurers to refuse coverage
  - Fall under Medicare, part B
- Restrictions would be minimal, if the product is used according to the label
- All plans intend to cover the cost of ibalizumab

Ibalizumab – US Addressable Market*



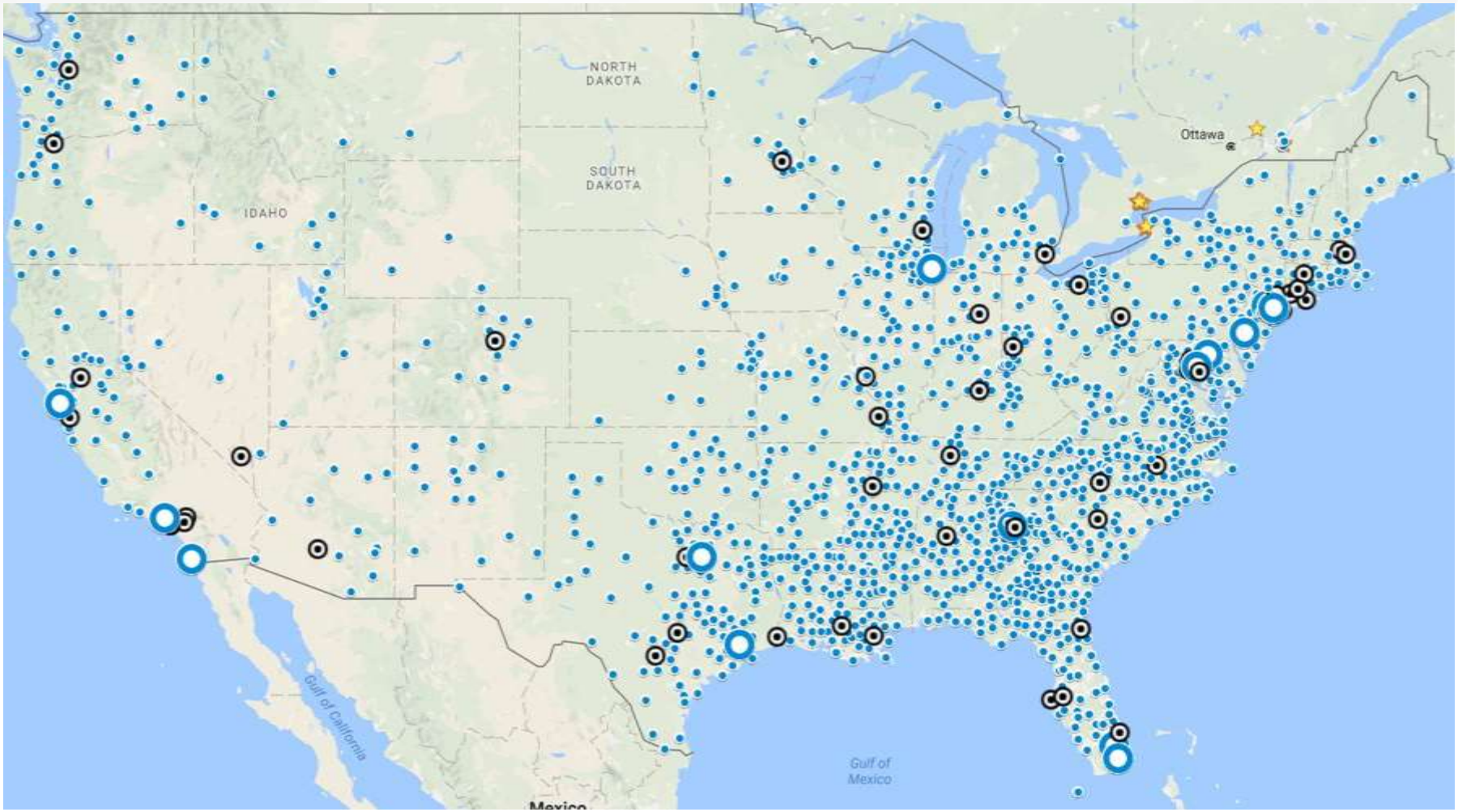
*EU patient population is of similar size

MDR Prescriber Statistics



source: IMS prescription level data

Triple Class Resistant Patient Map



>200 TCR 50-200 TCR ~50 TCR

source: 2013 CDC county data

Theratechnologies Sales Team Expansion for Launch

FUNCTIONS	2016	2017
Sales team	12	41
Reimbursement team	2	5
Medical Science Liaison	2	6

- Expansion to support launch of ibalizumab
- Currently focused on *EGRIFTA*® and building network until approval of ibalizumab
- Reach 95% of 5,000 most important physicians treating HIV and Key Opinion Leaders (KOL)
- Sales force to start detailing immediately after approval
- Goal is to maximize patient access
  - Reach patients where they are
  - Ensure financial accessibility
  - Offer wide distribution (home infusion, physician office, infusion centers)

Theratechnologies Partnership

	North American Agreement	European Agreement
Date of agreement	March 18, 2016	March 6, 2017
Term	12 years from FDA approval	12 years from approval (country-by-country basis)
Transfer Price	52% of Net Sales	52% (57% of annual sales exceeding US$50M in European Territory
Payment at signature	US$1M (cash)	US$3M (common shares)
Upfront and launch milestone	US$4M (common shares) US$5.5M (cash – payable through an increase in transfer price)	US$5M (cash – payable one year after launch) US$5M (cash – payable once EU sales reach US$50M)
Development milestones	US$3M (Intramuscular administration approval)	50% of European clinical trial costs (if any)
Commercial milestones	Up to US$207M upon reaching various sales levels (up to US$1B) and label expansion objectives	Up to US$80M upon reaching various sales levels (up to US$1B)

TaiMed Is Committed to HIV Drug Development with a Solid Pipeline

TMB-607

- Protease inhibitor
- Phase I clinical trial underway (IND sponsored by Temple University)

TMB-365

- Ibalizumab-based, IgG1-scaffold, also blocks domain 2
- FcRn, LM52 glycan modifications
- Broader, wider viral coverage range and higher, greater anti-infectivity against HIV
- PK/GLP Tox study underway
- Phase I start Q2 2018 (Australia)

TMB – Bispecific

- Bispecific neutralizing antibody targets two different antigens
- One targets CD4 like ibalizumab while the other targets gp120
- Currently in preclinical development

TMB – ADC

- Antibody-drug conjugate
- Tripartite drugs comprising a target-specific mAb conjugated to a potent HDAC inhibitor via a stable linker
- Currently in discovery

Building out Our Manufacturing Capabilities

- Current CMO WuXi Biologics
  - Experience has been positive but we can use our last round of funding towards reducing future costs
- Construction of a new cGMP manufacturing plant is currently underway in Taiwan (4 x 2000L, 50L, 200L, and 500L bioreactors)
  - A $35M investment; ~$20M already spent
  - Support our portfolio of biologics
- Build complete in-house protein drug manufacturing capability by hiring additional CMC personnel to help with this plant AND oversee production at WuXi in the near future

New 60,000 sq. ft. Manufacturing Facility in Taiwan

– Ensure Full cGMP Compliance from Design Stage

- Facility design with Nova Pharma Solutions (formerly known as NNE Pharmaplan, Denmark) and BPTC (Boston, MA)
  - cGMP standard of USFDA, EMA, and PIC/S
- Conceptual Design (Nova Pharma Solutions), 12/2016 – 3/2017
  - layout and process design, clean utility and HVAC concept, and cleanroom concept
- Basic Design (Nova Pharma Solutions), 4/2017 – 10/2017
  - detail layout design, relook into process design, user requirement specifications, equipment piping & instrumental diagrams, and process equipment list and utility consumption list
- Detail Design (local construction company), 6/2017 - present
  - mechanical and electrical detail design, and finalization of equipment list and utility consumption list

Timeline for cGMP Manufacturing Facility

9/10/2017

10/19/2017

Construction complete (except clean rooms)
3/2018

Clean room complete
8/2018

IQ/OQ/PQ
6/2018 – 3/2019

PD/Tech Transfer from WuXi
8/2018 – 6/2019

3 PPQ batches & 12 months stability data
7/2019 – 12/2020
- **FDA Inspection**

Thank You