Issuer Free Writing Prospectus
Filed Pursuant to Rule 433
Dated September 24, 2018
Registration Statement No. 333-226368
Relating To Preliminary Prospectus dated September 24, 2018

Free Writing Prospectus
Tiziana Life Sciences plc – Investor Presentation

This free writing prospectus relates to the proposed public offering of ordinary shares ("Ordinary Shares") in the capital of Tiziana Life Sciences plc (the "Company") in the form of American Depositary Receipts ("ADRs"). The Ordinary Shares are being registered on a Registration Statement on Form F-1 (No. 333-226368) (the "Form F-1") and the ADRs are being registered on a Registration Statement on Form F-6.

This free writing prospectus should be read together with the preliminary prospectus dated September 24, 2018 included in that Registration Statement, which can be accessed through the following link:

https://www.sec.gov/Archives/edgar/data/1723069/000121390018012939/ff12018a2_tizianalife.htm

The Company has filed a Form F-1 (including a preliminary prospectus) and Form F-6 with the SEC for the offering to which this communication relates. Before you invest, you should read the preliminary prospectus in that Form F-1 (including the risk factors described therein) and other documents the Company has filed with the SEC for more complete information about the Company and this offering. You may get these documents for free by visiting EDGAR on the SEC Web site at www.sec.gov. Alternatively, the representative of the underwriters will arrange to send you the prospectus if you request it by contacting Laidlaw & Company (UK) Ltd., Attention: Syndicate Department, 521 Fifth Avenue, New York, NY 10175, by telephone at +01 (0)212 953 4917 or by email at syndicate@laidlawltd.com.

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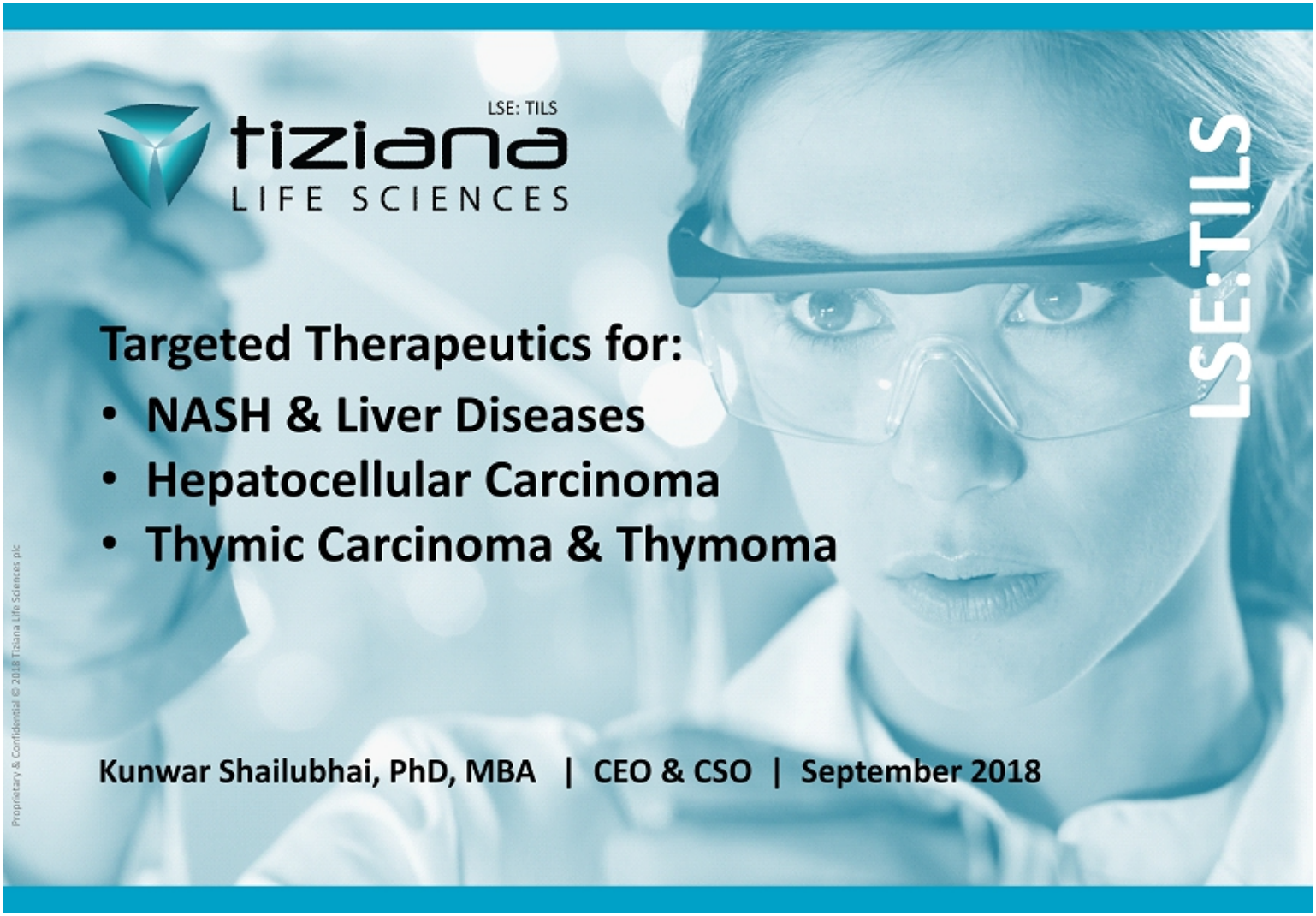

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# BACKGROUND STORY OF THE COMPANY

- Founded in 2013 as a London Stock Exchange AIM-listed biotechnology company (LSE: TILS)
- Focus on therapeutics and diagnostics for cancer and immune diseases
- December 2014: Licensed Foralumab, a fully human anti-CD3 mAb, from Novimmune
- January 2015: Licensed Milciclib, a pan-CDKs inhibitor, from Nerviano Medical Center
- December 2016: Licensed a fully human anti-IL6R mAb from Novimmune
- May 2017: Hired Kunwar Shailubhai as CEO and CSO

# DO IT AGAIN WITH PROVEN BUSINESS STRATEGY

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### Management Strategy
1. Focused primarily on liver diseases
2. Strong pipeline with range of candidates
3. Supported by world renowned academics through advisory board

### Proprietary technologies (Strong IP)
1. Targeting large markets with unmet medical need (HCC, NASH and CD)
2. Innovative and bold therapeutic approaches
3. Continually enhancing intellectual property

### Exemplary BOD with SAB

### Experienced management team
1. Successful record in 'Bench to Market' (Trulance marketed)
2. Including co-founders of Synergy Pharmaceuticals (NASDAQ: SGYP)

## Our Mission

Develop innovative therapies for inflammation and oncology indications

# LEADERSHIP TEAM & BOARD OF DIRECTORS

## MANAGEMENT

**Kunwar Shailubhai PhD, MBA**
CEO & CSO

- Co-founder , EVP & CSO of Synergy Pharmaceuticals, NASDAQ: SGYP
- The pioneer of GC-C agonist technology inventor of TRULANCE® approved for Chronic constipation and IBS-C
- VP, Callisto Pharmaceuticals
- Group Leader, Monsanto Co.

**Tiziano Lazzaretti**
Chief Financial Officer

- Previously Group Finance Director at Pharmentis –Teva Ratiopharm spin off
- Executive Director at Alliance Boots, Snia, Accenture and FIAT Group
- MBA, Bocconi University, Milan
- Corporate Finance, London Business School. BSc Accounting and Finance

### Key Strengths of the Management Team

- Successful credentials in entrepreneurship
- Strong history in biotechnology deals
- Proven 'Bench to market' record
- Strong credentials in Science and Business

## BOARD

**Gabriele Cerrone**
Executive Chairman

- Proven track record & experience in financing biotechnology companies
- Served as chairman of 2 biotech companies with market cap over $2Bn
- Inhibitex sale $2.5Bn
- Synergy / Trovagene / Gensignia / Rasna / Contravir / Siga Technologies
- MBA, Stern School of Business, NY, USA

**Leopoldo Zambeletti**
Non-Executive Director

- Former head of Life Sciences M&A for Credit Suisse, EU
- Investment Banking experience at JP Morgan and Credit Suisse
- Non-exec. director several biotech companies

**Riccardo Dalla-Favera MD**
Non-Executive Director

- Member of National Academy of Sciences
- Leader in molecular oncology
- Prof & Director, Institute for Cancer Genetics, Uris Prof of Pathology; Columbia Medical Center, US
- 2014 presented with Oncomed Giants of Cancer Care Award

**Willy Simon**
Non-Executive Director

- Career as a executive in the banking and corporate finance sector and director of publicly listed companies
- Kredietbank N.V., Citibank, Generale Bank NL, CEO of Fortis Investment Management
- Chairman of Bank Oyens & van Eeghen, Partner at Redi & Partners

# SCIENTIFIC ADVISORY BOARD

SCIENCE ADVISORY

**Howard Weiner, MD**

- Professor of Neurology at Harvard Med
- Director and Founder of the Partners MS Center and Co-Director of the Ann Romney Center for Neurologic Diseases
- Pioneered investigation of the mucosal immune system for the treatment of autoimmune and other diseases

**Kevin Herold, MD**

- Professor of Immunobiology and Medicine and Deputy Director, Yale Center for Clinical Investigation
- Director of the Yale Diabetes Center and Director of the TrialNet Center at Yale
- Expert in autoimmune diseases and anti-CD3 monoclonal antibody therapies

**Arun Sanyal MD**

- Charles Caravati Distinguished Professor and Chair, Division of Gastroenterology, Hepatology and Nutrition at Virginia Commonwealth University School of Medicine
- World leader in the field of liver diseases

**Napoleone Ferrara MD**

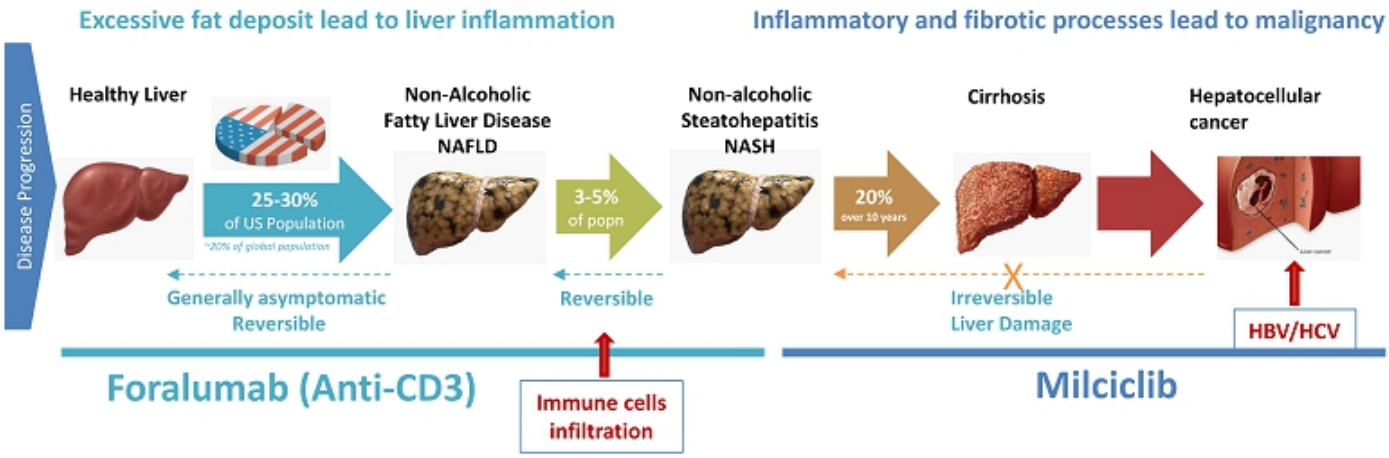
- Inventor of Avastin® ($6.67Bn/yr)*; 2010 Lasker Award
- Senior Deputy Director Basic Sciences, Moores Cancer Center, UC San Diego
- Distinguished Prof of Pathology, School of Medicine, UC San Diego

**Alessandro Padova PhD**

- Senior executive, managerial and scientific roles in the pharmaceutical and biotechnology sector
- Peptide Therapeutics, Medivir UK, Astex Technology, C4T S.C.ar.l., Siena Biotech and IRBM Science Park

* Roche Investor Update – February 2018

# FOCUSED ON LIVER DISEASES




- **Non-alcoholic fatty liver disease (NAFLD) the most common liver disease**, affecting one-third of the Western world, driven by obesity and diabetes epidemic[1]
- **NASH predicted to become leading cause of liver transplantation** in USA by 2020[2]
- **Hepatocellular carcinoma (HCC) is primary cause of obesity-related cancer death** in middle-aged men in the USA[1]
- **No currently approved drugs** – liver transplant only option for end-stage patients



1 Transparency Market Research "Nonalcoholic Steatohepatitis Therapeutics Market - Global Industry Analysis, Size, Share, Growth, Trends, and Forecast 2015 – 2025
2 Y Ilan. Aliment Pharmacol Ther 44 (11-12), 1168-1182. 2016
3 Wree A, Broderick L, Canbay A, Hoffman HM, Feldstein AE. From NAFLD to NASH to cirrhosis-new insights into disease mechanisms. Nat Rev Gastroenterol Hepatol 2013; 10: 627–36.

# MAJOR ACHIEVEMENTS & ANTICIPATED NEAR TERM MILESTONES 2019

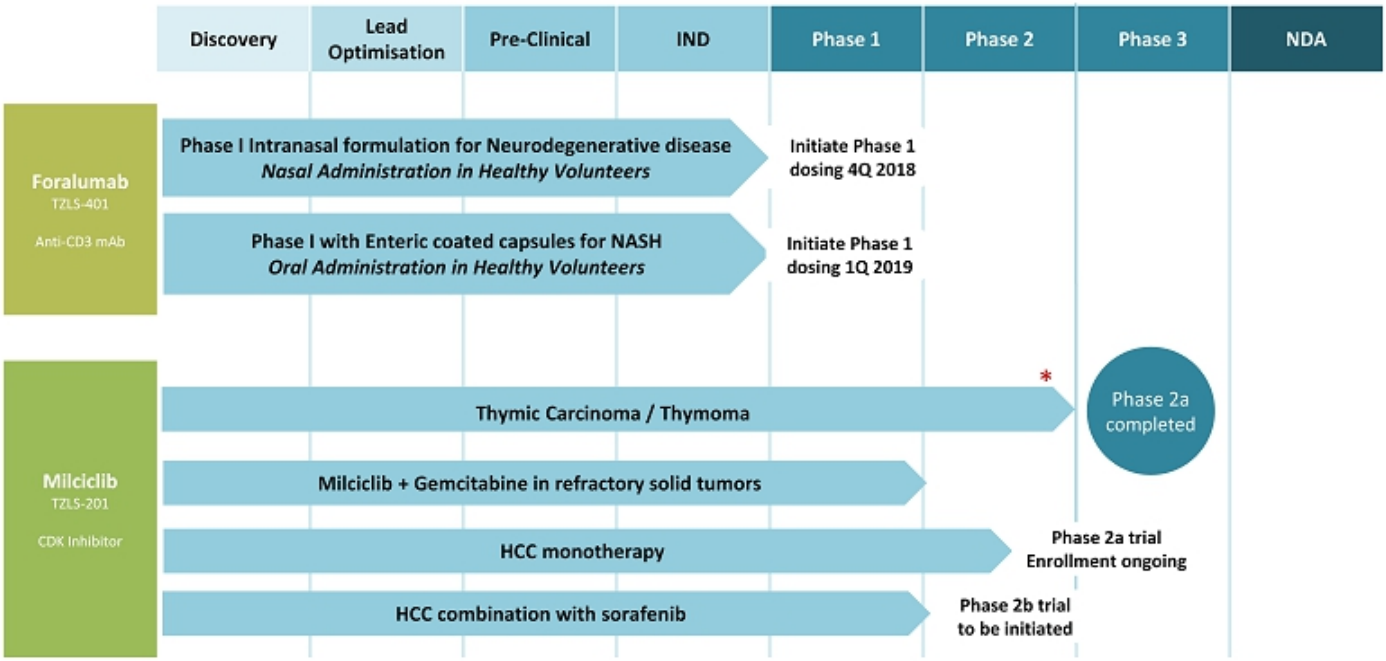
## Foralumab (TZLS-401)

| | |
|---|---|
| • Complete enteric coated capsule formulation and manufacture cGMP clinical supply | 4Q 2018 |
| • Submit IND for oral administration with Foralumab capsules | 4Q 2018 |
| • Initiate Phase 1 dosing in healthy volunteers with enteric coated capsules | 1Q 2019 |
| • Report topline data from phase I dosing in healthy volunteers with intranasal formulation | 4Q 2018 |

## Milciclib (TZLS-201)

| | |
|---|---|
| • Report Phase 2 Data from Thymic cancer and Thymoma | 4Q 2017 |
| • Initiation of Phase 2a monotherapy trial in patients with HCC | 1Q 2017 |
| • Topline data from HCC trial with milciclib monotherapy | 2Q 2019 |
| • Initiation of Phase 2b combination therapy (milciclib + sorafenib) trial in patients with HCC | 2Q 2019 |

# CLINICAL DEVELOPMENT PIPELINE




* We will seek guidance from regulatory authorities for next steps

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## CLINICAL DEVELOPMENT PIPELINE

**Foralumab: A fully human anti-CD3 mAb licensed from Novimmune**

- **Phase 1 trials in NASH and Crohn's Disease with an enteric coated capsule formulation for oral administration**
- **Phase 1 trial in neurodegenerative disease with an intranasal formulation for nasal delivery**

# Several current blockbuster drugs are humanized monoclonal antibodies


- **#1**: **Humira (Adalimumab):** Humira topped the global prescription-drug list and had annual revenue growth of 14.6% to reach global revenue of USD 18.43 billion.
- **#4**: **Rituxan (Rituximab, MabThera)**: Rituxan held 4th position in the global prescription drug market with revenues amounting to USD 8.11 billion.
- **#6**: **Herceptin (Trastuzumab):** Herceptin sales were up by 15.98%, to reach global revenue of USD 7.55 billion.
- **#8**: **Avastin (Bevacizumab):** Avastin global sales grown by 10.75% in the 2017 to reach revenue of USD 7.21 billion.
- **#9**: **Remicade (Infliximab):** Remicade sales reached global revenue of USD 7.16 billion.

**Tiziana Life Sciences in-licensed from Novimmune fully-humanized anti-CD3 mAb Foralumab designed to be administered orally and nasally to induce site-specific immune tolerance for treatment of autoimmune and inflammatory diseases**

# Tiziana in-licensed Fully Human mAbs Foralumab and anti-IL6R from Novimmune

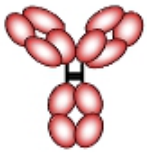
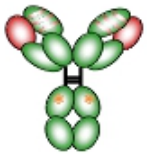
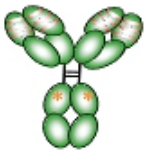
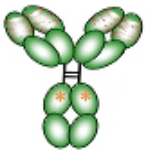
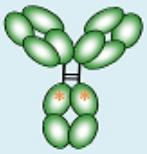
- Championed the monoclonal and bispecific antibody generation platforms designed to streamline the identification, production and characterization of fully-human antibodies

- Novimmune partnered with Genentech to develop:
  - Anti-IL-17 mAb for treatment of autoimmune diseases
  - Anti-TLR4 mAb for treatment of rheumatoid arthritis

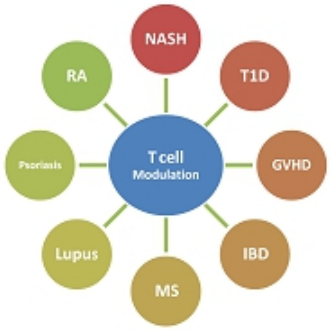
- Novimmune partnered with Shire to develop a bispecific antibody for treatment of hemophilia A.

# FORALUMAB – THE ONLY FULLY HUMAN ANTI-CD3 MAB

## CD3-specific monoclonal antibodies in clinical development[1]

| OKT3 Muromonab | ChAglyCD3 Otelixizumab | Nuvion Visilizumab | hOKT3γ1(Ala-Ala) Teplizumab | NI-0401 Foralumab |
|---|---|---|---|---|
|  |  |  |  |  |
| IgG2a | IgG1 *Agly | IgG2 *AA | IgG1 *AA | IgG1 *AE |
| *Fully Mouse* | *Chimeric & Humanized* | *Humanized* | *Humanized* | *Fully Human* |
| Approved by the FDA for solid organ transplantation immuno-suppression | | | | |

**Oral and Nasal Administration**




Oral and nasal administration with foralumab could potentially be a game changer to enhance efficacy and reduce toxicity

Source: (1) Therapeutic anti-CD3 monoclonal antibodies: from bench to bedside, Kuhn C, Weiner HL, Immunotherapy, 2016 Jul;8(8):889-906.

# HOWARD WEINER - TOP TIER KEY OPINION LEADER IN MS AND AUTOIMMUNE DISEASES

- Director of Multiple Sclerosis Program, Department of Neurology, Brigham and Women's Hospital (BWH).
- Robert L Kroc Professor of Neurology, Harvard Medical School.
- Co-Director , Ann Romney Center for Neurological Disease, BWH.
- Founder, Partners MS Center.
- Has pioneered immunotherapy in MS and has investigated immune mechanisms in nervous system diseases including MS, Alzheimer's Disease, ALS, stroke and brain tumors.
- Has pioneered the investigation of the mucosal immune system for the treatment of autoimmune and other diseases and the use of anti-CD3 to induce regulatory T cells for the treatment of these diseases.
- Author of the book "*CURING MS*" and the award winning film documentary "*WHAT IS LIFE? THE MOVIE*".
- Dr. Weiner is the 2007 recipient of the John Dystel Prize for MS Research and in 2012 he received the NIH Director's Transformative Research Award for investigating the innate immune system in Alzheimer's disease.

# ORAL TREATMENT WITH MURINE ANTI-CD3 (OKT3) EFFECTIVE IN A PHASE II TRIAL WITH NASH[1]

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## Study design

- 36 subjects with NASH and type II diabetes
- Randomized, single-blinded
- 9 per group, not powered for statistical significance
- 0.2, 1.0, 5.0 mg or placebo daily for 30 days
- Primary endpoints: safety and trends in immunomodulation
- Secondary endpoint: indication or trend of efficacy through biomarkers
- Follow up: Days 0, 14, 30, 60
- Hadassah Medical Center, Jerusalem Israel

## Safety

- No treatment-related adverse events
- Well tolerated
- No change in CD3+ lymphocyte count
- Normal blood chemistry and blood cell counts

## Immunological

- Increases in T reg markers consistent with induction of Tregs
- Anti-inflammatory markers ↑
- CD4+CD25+LAP+ Treg cells ,TGFβ ↑

## Efficacy biomarkers

- Positive trends, some of which were statistically significant
- AST ↓ – liver enzyme indicating reduced liver inflammation
- Glucose ↓ – favorable for subjects with type-2 diabetes
- Insulin ↓ – favorable for subjects with type-2 diabetes

OKT3 withdrawn from the market due to severe side effects being a murine mAb
Foralumab is fully human anti-CD3 mAb



Source: (1) Lalazar, G., Mizrahi, M., Turgeman, I., Adar, T., Ya'Acov, A. B., Shabat, Y., . . . Ilan, Y. (2015). Oral Administration of OKT3 MAb to Patients with NASH, Promotes Regulatory T-cell Induction, and Alleviates Insulin Resistance: Results of a Phase IIa Blinded Placebo-Controlled Trial. Journal of Clinical Immunology, 35(4), 399-407.

# KEY PUBLICATION OF PRE-CLINICAL EFFICACY

## Oral Treatment with Foralumab, a fully human anti-CD3 monoclonal antibody, prevents skin xenograft rejection in mice with human immune systems

Mineko Ogura, Songyan Deng, Paula Preston-Hurlburt, Hideki Ogura, Kunwar Shailubhai, Chantal Kuhn, Howard L Weiner, and Kevan C. Herold

*Clinical Immunol, 2017. 183: 240-246*


Clinical Immunology

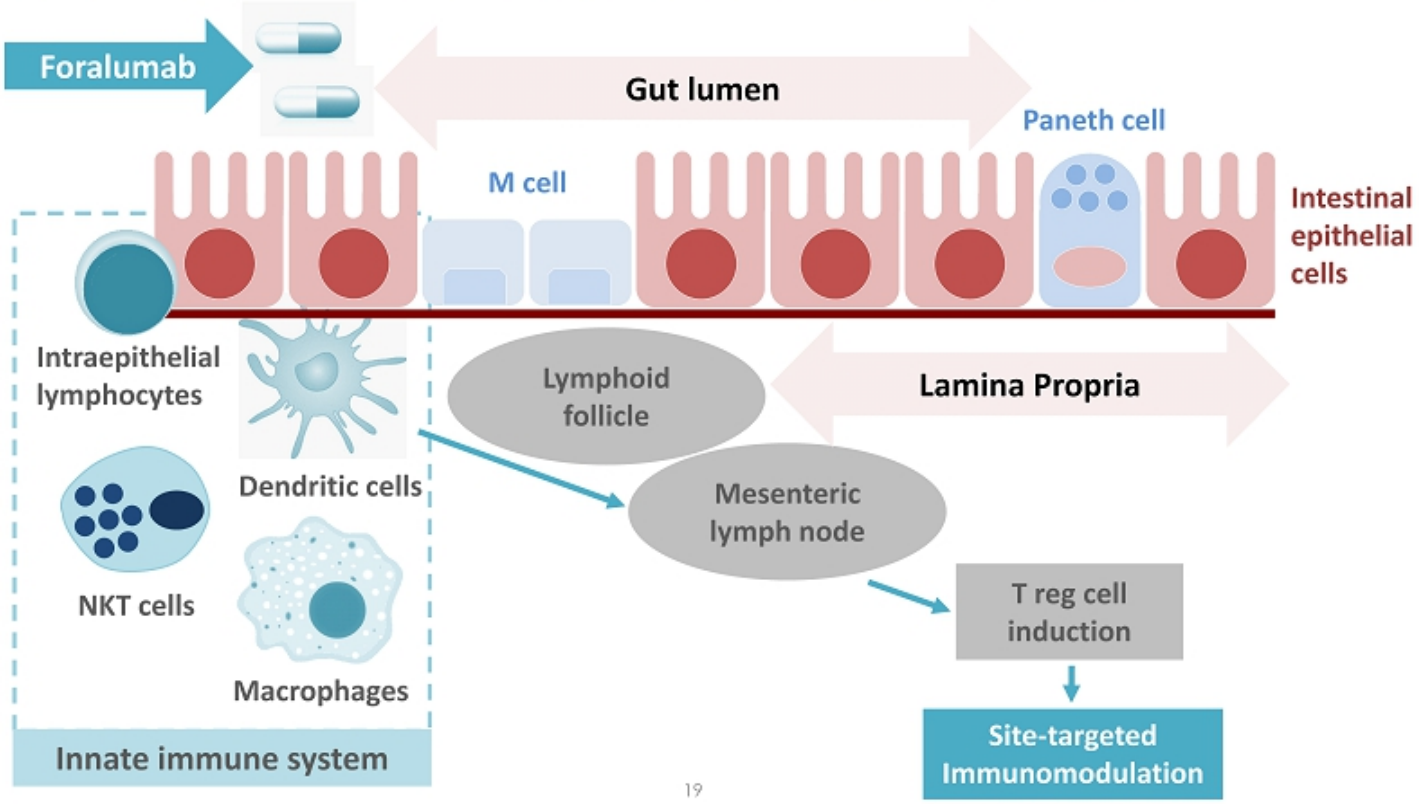
Oral treatment with foralumab, a fully human anti-CD3 monoclonal antibody, prevents skin xenograft rejection in humanized mice

### Key Findings

- **Foralumab is as potent as OKT3**
- **Oral treatment with Foralumab is effective in animal studies**
- **Mechanism of action is *via* activation of T regs that systemically circulate to elicit targeted immunomodulation**

# HOW DOES ORALLY ADMINISTERED FORALUMAB WORK?

## A novel method for immune modulation without immune suppression



# ORAL AND NASAL FORMULATION OF FORALUMAB

## Nasal administration of Foralumab

- Successfully developed nasal formulation of Foralumab
- Proof-of-concept for nasal administration demonstrated in animal studies
- IND for nasal administration for neurodegenerative diseases with BWH, Harvard University. Submitted on May 31,2018.
- In-licensed nasal delivery technology from Brigham and Women's Hospital, Harvard Medical School

## Patent on Oral administration

**ANTI-CD3 ANTIBODY FORMULATIONS**

US Non-Provisional Patent Application No.:62/380,652, filed August 29, 2017

PCT Application PCT/US2017/049211, filed, Aug 29, 2017

***Claims***

- Composition of matter of a first oral formulation of the fully human antibody, foralumab comprising an enteric-coated lyophilized capsule with stabilizers and antioxidants to treat autoimmune and inflammatory diseases such as NASH
- General methods for the production of a lyophilized NI-0401/CD3 antibody dosage form for use in oral formulation

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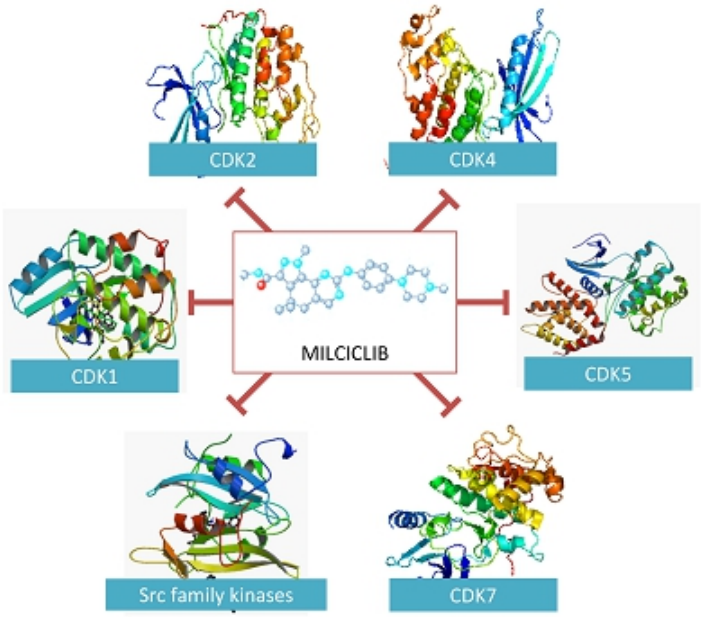
# CLINICAL DEVELOPMENT PIPELINE

## Milciclib: A pan-inhibitor of CDKs, TRKs and Src kinase

- Phase IIa trial in HCC with Milciclib (Italy, Greece & Israel)
- Phase IIb trial with combination of Milciclib and Sorafenib (Italy, Greece, Spain and Israel)

# MILCICLIB, A SMALL MOLECULAR PAN-INHIBITOR OF CDKS

- A novel small molecule with potent anti-tumor activity in a wide range of animal models with remarkably low toxicity
- Inhibitor of a wide range of kinases associated with cancer cell growth including CDK2, CDK1, CDK4 and CDK5 and src-family kinases
- Treatment of cancer cells with milciclib induces reduction in STAT3, MAPK, AKT, YES and S6, effectors of signaling pathways relevant to hepato-carcinogenesis
- Shown to be well tolerated in over 296 patients, supplied for oral administration – a key issue for patients with underlying liver disease
- Anticipated improved toxicity profile over the current standard of care




Potentially the next-gen Sorafenib/Nexavar with fewer side effects

# MILCICLIB INHIBITS MIR221/222 TO SUPPRESS HCC TUMOR GROWTH IN MICE

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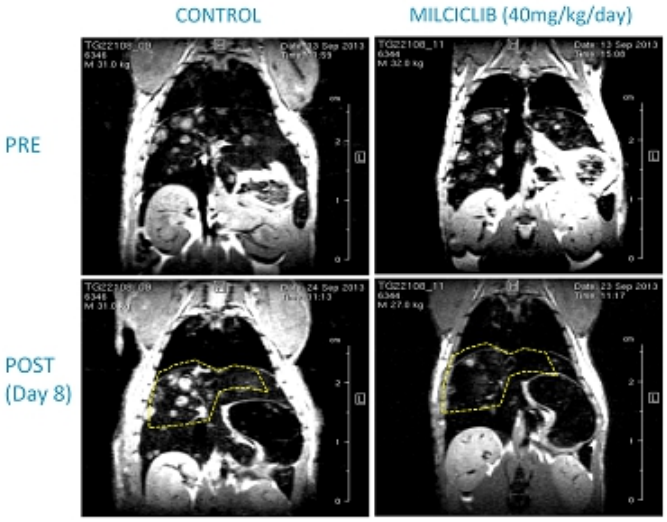
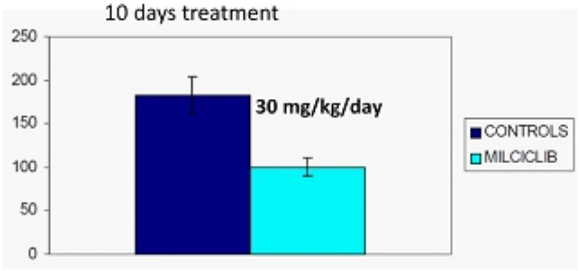
## MR images, control vs. milciclib treated mice, pre-/post-treatment




## % tumor growth, pre-/post- treatment

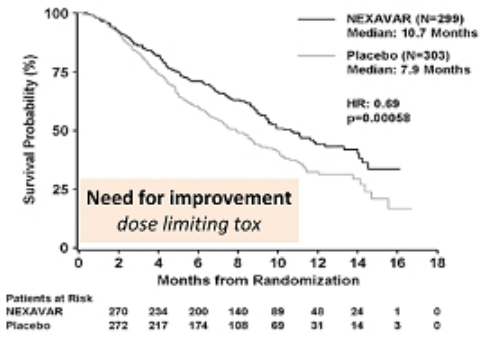


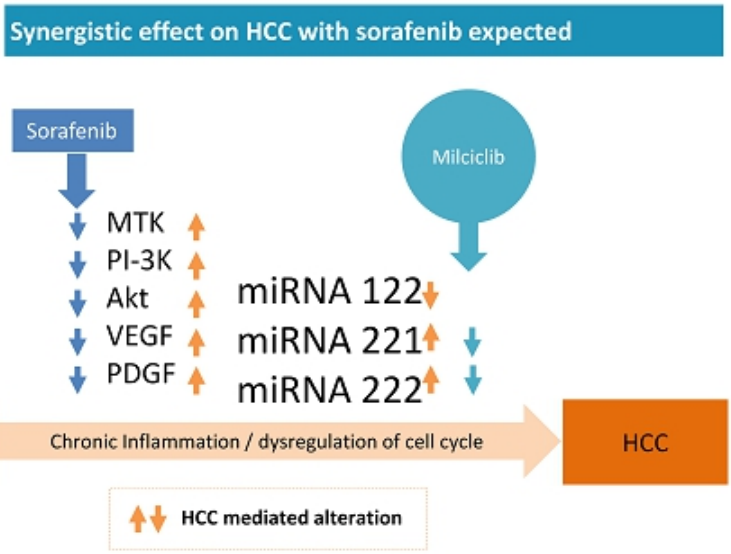

**TG 221/DENA mice**

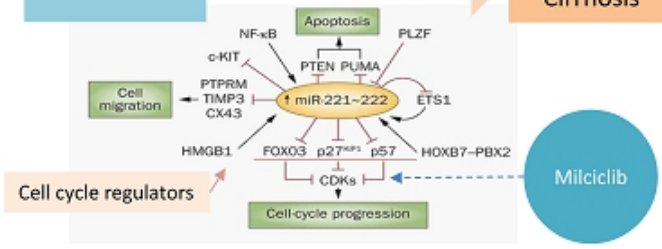
- Short and robust MOA based transgenic mouse model for HCC development, dependent on mir221 expression
- Tumor development is induced by DENA

***Impressive milciclib effect, with clear reduction in the number and volume of lesions observed after treatment***

# MILCICLIB AND SORAFENIB MAY HAVE SYNERGISTIC EFFECT



## Key Findings

- Milciclib was well-tolerated with manageable side effects in patients with refractory solid tumors
- Oral treatment with milciclib in combination with gemcitabine demonstrated clinical activity in patients who were non-responder to existing chemotherapeutic drugs
- Recommended phase II dose was found to be 150 mg/day (7 day off/7day on cycle)
- Overall response rate was 36%
- Results suggest further evaluation of milciclib in other solid cancers either as monotherapy or combo-therapy

Cancer Chemother Pharmacol (2017) 79:1257–1265
DOI 10.1007/s00280-017-3303-z

CLINICAL TRIAL REPORT

**Phase I dose-escalation study of milciclib in combination with gemcitabine in patients with refractory solid tumors**

Sandrine Aspeslagh[3] · Kunwar Shailubhai[2] · Rastilav Bahleda[1] · Anas Gazzah[1] · Andréa Varga[1] · Antoine Hollebecque[1] · Christophe Massard[1] · Anna Spreafico[3] · Michele Reni[3] · Jean-Charles Soria[1]

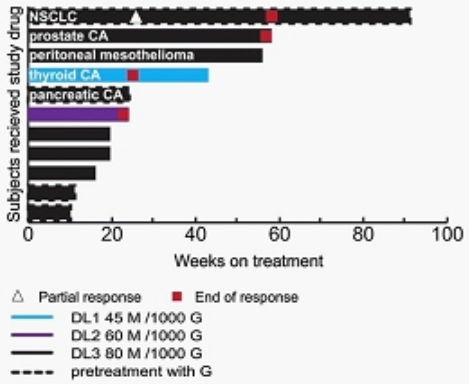



**Fig. 1** Swimmerplot showing treatment duration. Tumor type was indicated for patients having a prolonged stable disease or a partial response. *M* milciclib; *G* gemcitabine

# RECENT PRESS RELEASES

**Tiziana Life Sciences Announces that Milciclib Met its Primary Endpoint in Two Phase II Clinical Trials in Patients with Thymic Carcinoma and Thymoma**

November 23, 2017

*With long-term safety and efficacy profile, Milciclib could potentially be the first-in-class targeted therapy for patients with thymic carcinoma and thymoma without any satisfactory treatment option today*

**Tiziana Life Sciences Announces Safety of Milciclib in a Phase 2a Trial in Unresectable or Metastatic Hepatocellular Carcinoma (HCC) Patients**

December 8, 2017

*Demonstration of safety, a pre-requisite to initiate a Phase 2b trial evaluating combination of Milciclib with sorafenib (Nexavar®; Bayer Germany (BAYN.GR)) in HCC patients, is an important milestone*

**Tiziana Life Sciences Announces a Poster Presentation on Phase II clinical data with Milciclib in Thymic carcinoma and Thymoma patients at the American Society of Clinical Oncology (ASCO) Meeting (June 1-5, Chicago IL)**

April 9, 2018

*Milciclib met the primary endpoint and secondary endpoints in two phase II multi-centered clinical trials in thymic carcinoma (TC) and Thymoma (B3T) patients*

*Percentage of patients with stable disease, complete response and partial response was 69.2% in both trials for TC and 80.0% and 70.6% for B3T patients*

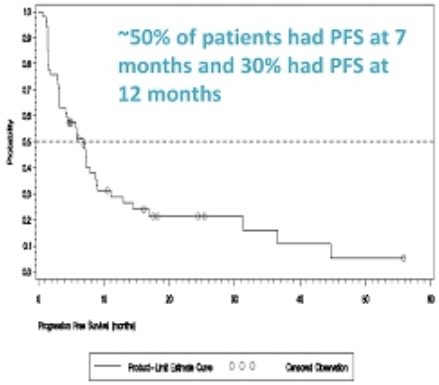
# THYMIC CARCINOMA AND THYMOMA UPDATES

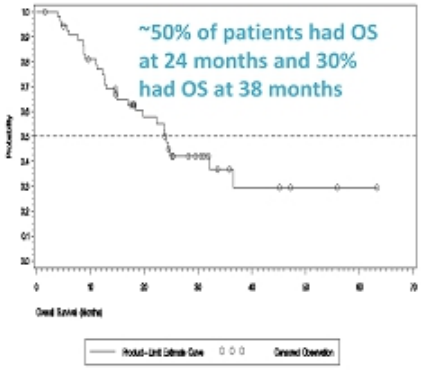
- **Two phase II trials with Milciclib in US, Italy and France**
  - Trial 006: Thymic carcinoma and Thymoma mixed population (72 patients)
  - Trial 007: Thymic carcinoma and Thymoma mixed population (30 patients)
- **Rare cancers with very few cases: Orphan Disease Indications**
- **Positive clinical data**
- **Primary endpoint (PFS) and secondary endpoint (OS) met in both trials**
- **Thymic carcinoma is an aggressive metastatic cancer and has no approved therapy**
- **Milciclib as a single agent met primary as well as secondary endpoints in thymic carcinoma in both trials**

# TWO PHASE 2 TRIALS DEMONSTRATED CLINICAL ACTIVITY AND SAFETY OF MILCICLIB IN THYMIC CARCINOMA AND THYMOMA PATIENTS

**CDKO-125a-006**

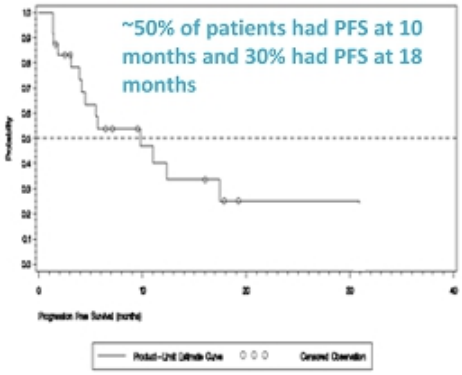
**Thymic Carcinoma and Thymoma mixed population**

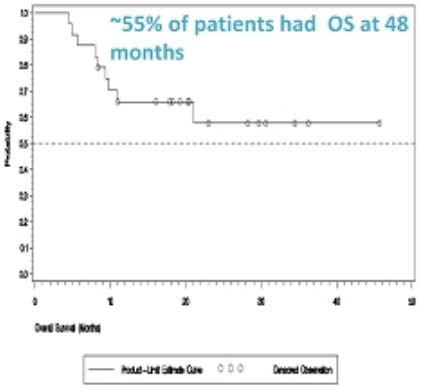



**CDKO-125a-007**

**Thymic Carcinoma and Thymoma mixed population**




Source: (1) TILS press release - Tiziana Life Sciences Announces Safety of Milciclib in a Phase 2a Trial in Unresectable or Metastatic Hepatocellular Carcinoma (HCC) Patients, Dec 8, 2017

# LONG TERM SAFETY OF MILCICLIB

- Five patients from the -006 study and two patients from the -007 study have continued on the Milciclib regimen with good clinical response and safety
- Some patients have been taking Milciclib **since 2012 (6 years)** with few serious adverse events
- More than 20% of the reported symptoms included vomiting, fatigue, anorexia and tremor
- Most of the AEs were mostly low grade 1 or 2
- 150 mg milciclib/day dosing was too high but still safe, minimal AEs
- 7 day ON/7day OFF dosing: Cmax is higher

# INTERIM ANALYSIS DATA FROM MILCICLIB PHASE 2 TRIAL IN SORAFENIB-RESISTANT HCC PATIENTS

- **Why interim analysis:** Since this was the first exposure of Milciclib in HCC patients with, it was important to ensure safety of patient with underlying cirrhosis

- **Trial design**: Oral administration with Milciclib (100 mg/day; 4 day ON/3 day OFF). Total patients 30 to be enrolled. Duration 6 months
  Primary end point: safety
  Secondary end points: PFS, ORR & TTP
  Exploratory: AFP and miRNA profiling
- **Compassionate use**: On request of patients with EC approval

- **Data from 10 sorafenib-resistant HCC patients:**
  1. Four patients completed treatment as per protocol. Three requested to be on compassionate use and are on the drug since September (n=1) and October (n=2) 2017
  2. Two patients are in their $10^{th}$ and $11^{th}$ months of treatment with stabilized disease
  3. Milciclib treatment was well-tolerated
  4. IDMC recommended to continue enrolling patients
  5. Toxicities were manageable

- **Enrollment ongoing:** Enrollment of 30 patients anticipated to be completed by Nov/Dec 2018

- **Anticipated Topline data: 1Q 2019**

# MILCICLIB CLINICAL PROGRAM

| Completed trials | | | | |
|---|---|---|---|---|
| Indication | Phase | Dose | N | Outcome |
| **Advanced metastasis Solid tumors** | 1 | 45-80 mg/m$^2$/day + gemcitabine at 1000mg/m$^2$ | 16 | Complete |
| **B3 Thymoma/Thymic Carcinoma, 2$^{nd}$ line therapy** | 2 | 150mg/day | 72 | Complete |
| **B3 Thymoma/Thymic Carcinoma, 2$^{nd}$ line therapy** | 2 | 150mg/day | 30 | Complete |

**Current focus**

| On-going and Planned Studies | |
|---|---|
| HCC Programs | Phase |
| **Milciclib HCC monotherapy** | 2a |
| **Milciclib HCC combination therapy with Sorafenib** | 2b |
| **Thymic Carcinoma/Thymoma**<br><br>Seek guidance from EMA/FDA to develop next steps for approval | 2 |

**Encouraging clinical data warrant further evaluation in HCC**

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# PRECLINICAL PIPELINE

**TZLS-501, a fully human anti-IL6 receptor mAb, a preclinical candidate**

**Not budgeted.**

- **Multiple Myeloma**
- **Rheumatoid Arthritis**

# TZLS501– ANTI IL-6 RECEPTOR IS A FULLY HUMAN ANTIBODY

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## TZLS-501

Fully human anti-interleukin-6 receptor (IL-6R) monoclonal antibody (mAb)

| Mechanism | Indications | Opportunity | Competitive Edge | IP/Ownership |
|---|---|---|---|---|
| • Interleukin-6 (IL-6) is a potent cytokine regulating cell growth and differentiation as well as immune responses.<br>• Excessive production of IL-6 and its receptor IL-6R are key drivers of chronic inflammation and inflammatory disease | • Multiple Myeloma<br>• Could potentially be used in combination with foralumab for NASH and other inflammatory diseases such rheumatoid arthritis | • Anticipated to exert synergistic effect with Foralumab for inflammatory diseases | • Differs from other anti-IL-6R mAbs (e.g. tocilizumab), by acting not only on membrane-bound IL-6R, but also on soluble IL-6R, and is also able to deplete circulating levels of IL-6 in blood | • Exclusive license from Novimmune (NI-1201)<br>• Method of use in combination with anti-CD3 patent pending |


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IP PORTFOLIO

# INTELLECTUAL PROPERTY PORTFOLIO

| Family | Subject | Priority | Status | Expires | Jurisdiction |
|---|---|---|---|---|---|
| **Foralumab TZLS-401** | Methods of Use (Autoimmune or Inflammatory diseases and disorders) | 2004 | Issued/ Pending | 2025 | Australia, Canada, China, Hong Kong, Israel, Japan, Mexico, Norway, Singapore, South Africa, Ukraine, Armenia, Austria, Azerbaijan, Belgium, Belarus, Switzerland, Germany, Denmark, Spain, France, United Kingdom, Ireland, Italy, Kyrgyzstan, Kazakhstan, Luxembourg, Moldova, Netherlands, Portugal, Russian Federation, Sweden, Tajikistan, Turkmenistan<br>Pending:<br>Norway (divisional) |
| | Composition and methods of use | 2004 | Issued/ Pending | 2025 | US, Armenia, Australia, Austria, Azerbaijan, Belarus, Canada, China, Denmark, France, Germany, Hong Kong, India, Israel, Italy, Japan, Kazakhstan, Kyrgyzstan, Mexico, Moldova, Netherlands, Norway, Republic of Korea, Russian Federation, Singapore, South Africa, Spain, Switzerland, Tajikistan, Turkmenistan, and Ukraine<br>Pending:<br>Brazil, Japan (divisional), Singapore (divisional), US (divisional) |
| | Methods of Use (In combination with anti-IL-6/IL-6R antibodies) | 2011 | Pending | 2032 | US |
| | Formulations and dosing regimen | 2016 | Pending | 2037 | US and PCT |
| **Milciclib TZLS-201** | Composition of matter, methods of use, process of manufacturing | 2003 | Issued | 2024 | US, Europe, Eurasia, Africa, Algeria, Antigua & Barbuda, Argentina, Australia, Barbados, Bosnia & Herzegovina, Brazil, Canada, Colombia, Costa Rica, Croatia, Cuba, Ecuador, Egypt, Georgia, Iceland, India, Indonesia, Israel, Japan, Korea, Kosovo, Malaysia, Mexico, Mongolia, Montenegro, New Zealand, Nicaragua, Norway, Pakistan, Philippines, Serbia, Singapore, South Africa, Sri Lanka, Taiwan, Thailand, Trinidad & Tobago, Tunisia, Ukraine, Uzbekistan, Venezuela, Vietnam |
| | Methods of use (multiple indications) | 2008; 2009 | Issued | 2029; 2030 | US, EU, China, Hong Kong, Japan |
| | Methods of use (combination therapies with cytotoxics) | 2008; 2009 | Issued | 2029; 2030 | US, EU, China, Hong Kong, Japan |
| | Compositions of related entities, formulations and methods of treatment | 2009 | Issued | 2030 | US, EU, China, Hong Kong, Japan |
| | Methods of use (combination therapies with therapeutic antibodies) | 2006 | Issued | 2027 | US, EU, China, Hong Kong, Japan |
| **Anti-IL6R antibody TZLS-501** | Composition of Matter and Methods of use | 2009 | Issued | 2029 | US, Austria, Australia, Belgium, Canada, China, Denmark, France, Germany, Ireland, Italy, Japan Luxembourg, Mexico, Netherland, Spain, Sweden, Switzerland and UK<br>Pending:<br>India |

# NEAR TERM MILESTONES AND USE OF PROCEEDS

**The anticipated proceeds of the proposed offering will be used to accomplish the following in 2019**

- **Foralumab (TZLS-401)**
  - Complete two, Phase 1 trials with oral and nasal administration of foralumab in in healthy volunteers
  - Initiate planning for Phase 2 trials in both indications
- **Milciclib (TZLS-201)**
  - Complete ongoing monotherapy study enrolling a total of 30 HCC patients
  - Initiate a Phase 2b combination study evaluating combination of milciclib and sorafenib in naïve HCC patients
- **StemPrintER™**
  - Continue development and method validation. The cost for this program will be minimal
- **G & A expenses**

  We anticipate that our existing cash resources, together with the net proceeds from the offering, will enable us to fund our operating expenses and capital expenditure requirements to the end of 2019.