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XTL Biopharmaceuticals (NASDAQ: XTLB) (TASE: XTLB.TA)

www.xtlbio.com

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Highlights

- Developing clinical assets for the treatment of autoimmune diseases
 - Address large markets with high unmet clinical needs
 - Well-defined clinical pathway and relatively quick time to market
 - Partner with large Pharma to help fund late stage development
- Initial focus on hCDR1 asset for the treatment of:

Indication	Preclinical	Phase I	Phase II	Phase IIb	Phase III
SLE (lupus)					
Sjogren's Syndrome					

Anticipated Key Development Milestones¹:

Indication	2017	2018	2019
SLE	IND Approval	Last Patient In	Final Data
	Phase 2b trial initiation	Interim Analysis	
SS	IND Approval	Last Patient In	
	Phase 2 trial initiation	Final Data	

1 - Future financing may impact development timeline



Corporate Overview

- Lead product candidate (hCDR1 or Edratide): for treatment of autoimmune diseases
 - Novel compound with unique mechanism of action
 - Clinical data in >400 patients with Systemic Lupus Erythematosus (SLE)
 - Demonstrated favorable safety profile and well tolerated by patients
 - "Demonstrated efficacy in ... clinically meaningful endpoints" (Lupus Science & Medicine Journal – August 2015)



- Encouraging preliminary data in primary Sjogren's Syndrome (pSS) exhibited, similar to data previously obtained in SLE
- Lead indications represent significant unmet medical needs in area of interest
 - GSK acquired HGS in 2012 primarily for its SLE drug Benlysta for \$3 billion
 - No effective therapeutic on the market for either indication and weak competitive pipeline
- Aim to replicate results achieved in previous Phase 2b trial in SLE
 - FDA supports efficacy endpoint based on the BILAG index
 - Improved trial design for SLE based on previous Phase 2b study; FDA "buy in"



hCDR1: Phase II Ready in Two Autoimmune Indications

- Peptide that down-regulates autoimmune processes
- Developed by Prof. Edna Mozes from Weizmann Institute of Science (Israel)
- >40 peer reviewed journal articles; >200 animal experiments
- Three clinical studies completed on hCDR1 treating over 400 SLE patients
- Intellectual Property
 - Minimum of data/regulatory exclusivity
 - US: 6.5 7.5 years from approval (5 years plus variable litigation time)
 - EU: 10 years from approval
 - Recently filed two new U.S. Patent Applications for treatment of SLE covering:
 - 0.5 mg and lower doses
 - Specific patient population and/or treatment regimen
 - Recently filed Provisional U.S. Patent Application for treatment of Sjogren's Syndrome

"First in Class" and "Best in Class" Candidate



hCDR1: Unique Mechanism of Action (MOA)

MOA of hCDR1: Different than existing late stage pipeline candidates

Specific upstream immunomodulation through generation of regulatory T cells



Unique MoA – potential as **standalone** therapy or in **combination** with other lupus drugs



hCDR1: Treatment of SLE/Lupus





SLE: Affected Organs & Symptoms

- Chronic, debilitating inflammatory autoimmune disease
- Resulting in rheumatologic, dermatological and end-organ manifestations



SLE/Lupus: Market Overview

- Prevalence¹
 - 1.5 million patients in U.S. (5 million worldwide) across various ethnicities/geographies
 - Vast majority at onset are women / majority between ages of 15 and 45
- Prognosis
 - Dermatologic & musculoskeletal manifestations are the most common but major organ involvement such as renal, central nervous system and serosal occur frequently
 - Major organs may become involved as disease progresses
 - Most common causes of death
 - Initial active disease or infection
 - Later Renal failure, Cardiovascular disease, CNS disorders
 - 80-90% of patients survive beyond 10 years¹
- Market expected to grow dramatically

¹Lupus Foundation of America





SLE/Lupus: Competitive Landscape

- Current treatments: anti-malarials, corticosteroids, immunosuppressants, cytotoxics
 - Problems with current treatments: severe side effects (hypertension, osteoporosis, bone marrow suppression, increased cancer risk, etc.)
- Benlysta (HGS/GSK): approved by FDA March 2011
 - Only lupus drug approved in the last 50+ years; 2015 sales of £230m (GSK 2015 financials)
- Current pipeline: primarily B-cell inhibitors like Benlysta
 - Recent Phase III failures: UCB/Lilly/Anthera
 - Aurinia "success" in Lupus Nephritis: FDA allows single Phase 3 study (following P2b study); recently raised \$28M to fund Phase 3 program



hCDR1 (Edratide): Clinical Trial History

- Three clinical trials completed (by Teva): Phase Ia, Ib and IIb trials
 - Over 400 patients enrolled in prior trials
 - Well tolerated and demonstrated favorable safety profile
- Phase IIb (PRELUDE) trial (conducted by Teva)
 - Did not meet primary endpoint (SLEDAI)
 - Did not enforce steroid withdrawal algorithm
 - Encouraging results in secondary clinical endpoint, BILAG index (see below)
 - 0.5 mg weekly dose showed a substantial effect
- Opportunity
 - Teva returned to Yeda in 2009 and XTL in-licensed in 2014
 - FDA published revised guidelines in 2010 with BILAG as preferred primary endpoint

Encouraging Phase IIb results based on secondary endpoint (BILAG index) Primary endpoint confirmed by FDA pre-IND written response for planned XTL sponsored trial



PRELUDE - Secondary Endpoint (Pre-defined/ITT Cohort)

BILAG Responder Analysis at LOV Compared to Baseline (Placebo vs. Edratide 0.5 mg)





PRELUDE - Secondary Endpoint (Post Hoc)

BILAG Complete Responder Analysis (Placebo vs. Edratide 0.5 mg)



PRELUDE: Peer-Reviewed Publication (August 2015)

Safety and efficacy of hCDR1 (Edratide) in patients with active systemic lupus erythematosus: results of phase II study

Murray B Urowitz,¹ David A Isenberg,² Daniel J Wallace³

KEY MESSAGES

- Edratide demonstrated efficacy in one and possibly more clinically meaningful endpoints.
- Dose ranging studies demonstrated the 0.5 mg subcutaneous weekly was the most effective dose.
- There were no safety signals in this 26 week study.

Urowitz MB, Isenberg DA, Wallace DJ. Lupus Science & Medicine 2015;2:e000104. doi:10.1136/lupus-2015-000104



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XTL Sponsored Trial: Improve Probability of Success

Proposed trial design based on: (1) FDA written guidance; (2) Benlysta trials; and (3) clinical data from PRELUDE - especially the 0.5 mg results in BILAG endpoint

PRELUDE Trial

Proposed Trial

Primary endpoint	SLEDAI only	BILAG Substantial Responders
Dose	0.5, 1, 2.5 mg	0.5 mg and lower
Steroid Use	< 40 mg daily dose at baseline Steroid sparing not enforced	Lower daily dose at baseline (<15 mg) Defined steroid reduction regimen
Trial duration	26 weeks	26 weeks
Execution	Site discrepancies in disease matrices Suboptimal sample & data handling	Training and monitoring Specialized CRO

FDA Guidance (written response dated January 19, 2016)

- Phase 2 study with a primary efficacy endpoint to be based on BILAG index
- Reduced steroid usage and elevated anti ds-DNA levels in patient population (and other inclusion/exclusion criteria)
- Reasonable number of patients required to prove safety for marketing approval



hCDR1 for SLE: Development Milestones

Milestone	2016	2017	2018
Pre-IND Meeting $$			
Finalize phase 2b trial design $$			
CMC – Drug Product production & testing $$			
New Patent Applications filed $$			
IND Approval		*>	
Trial Enrollment			
Initial Clinical Data			*



hCDR1: treatment of Sjögren's Syndrome (SS)





SS: Affected Organs & Symptoms

Chronic autoimmune inflammatory disorder characterized by diminished lacrimal and salivary gland function that may affect multiple organs/systems

<u>Two types of SS (~50/50)</u>:

- **Primary SS (pSS)**: SS patient who does not have another major rheumatic and/or autoimmune disease
- Secondary SS: secondary to another autoimmune disease





SS: Market Overview

Prevalence

- ~0.7%¹ of U.S. population– estimated 2.5 to 4 million patients²
- Vast majority at onset are women (at least 9:1)²
- Average age at diagnosis: 40-50 years²
- Market expected to grow to 3.5 million cases globally by 2024¹
- Prognosis
 - Hallmark symptoms are dry eyes/mouth, fatigue and joint pain
 - May impact other organs (extra-glandular): kidneys, gastrointestinal system, blood vessels, lungs, liver, pancreas and nervous system
 - Increased risk of non-Hodgkin's B cell lymphoma (relative risk: 13x chance of developing disease vs. general population)¹
 - ~70% of patients have anti-Ro (SS-A); ~40% of patients have anti-La (SS-B)²

¹ Global Data Research 2016

² Sjogren's Syndrome Foundation



SS: Competitive Landscape

- No approved treatment for the systemic manifestations of the disease
- Two approved symptomatic treatments
 - Salagen (pilocarpine; Eisai, 1998) and Evoxac (cevilemine; Daichi, 2000)
- Immunomodulatory treatments (usually for extra-glandular disease)
 - Cyclosporine (ocular inflammation)
 - Hydroxychloroquine (mild inflammatory symptoms of joints, muscles & skin)
 - Corticosteroids (for serious symptoms)
 - Immunosuppressive agents: used to treat serious internal organ manifestations
 - Biologic agents: rituximab (off-label use)
- Competitive pipeline: only 1 Phase III product
 - Orencia (BMS) approved for Rheumatoid Arthritis
 - 1 open-label proof-of-concept study and then straight to Phase 3
 - Other trials off-label use of drugs approved for other autoimmune diseases



Source: Global Data Research 2016



hCDR1: Pre-clinical Study Data on pSS Patients

- Blood mononuclear cells (PBMC) from blood samples of patients with pSS incubated *in-vitro* with hCDR1 and a control peptide
- Promising in-vitro/ex-vivo study results:
 - Significant reduction in gene expression of 3 cytokines considered to be pathogenic in SS
 - Similar to results in SLE patients using same method
- Similar studies in PBMCs of RA and APS patients yielded no significant effect



Reduction in Gene Expression of 3 Cytokines

* P values calculated from % responses of all tested patients (responders and non responders) as compared to medium=100%.



hCDR1: Upcoming (Phase 2) Study in pSS

- Safety of hCDR1 in humans already established in SLE patients
- First clinical trial in pSS will be a controlled Phase 2 study
 - Study objectives: Safety & efficacy of different doses of hCDR1 in pSS patients
 - 3-arm study 2 doses plus control
 - Study duration: 3 months active treatment
 - N≈50 patients

Milestone	2017	2018
Patent Application Filed	*	
IND Approval	*	
Trial Initiation (FPI)		
Clinical Data		*



Management Team



Josh Levine, CEO

CEO, Proteologics; Senior Director, Teva Pharmaceuticals (Innovative Ventures); Partner, Platinum Neurone Ventures; Corporate Finance Head, Patterson Travis; Attorney, WF&G



David Kestenbaum, CPA & MBA, CFO

CFO, ZenithSolar; Finance Director, Colbar Lifescience (division of J&J (NYSE:JNJ)); CFO, ZAG Industries (division of The Stanleyworks (NYSE:SWK)); CFO, Lever Israel (division of Unilever (NYSE:UN)); Sr. Associate, PwC, New York



Dr. Daphna Paran, Medical Director

Senior lecturer: Tel Aviv University; Head of Day Care unit/Deputy Head of the Department of Rheumatology; Tel Aviv Medical Center (Ichilov Hospital); Trained at Rayne Institute, St. Thomas Hospital, London; Published/co-authored >60 articles on rheumatology and lupus



Monique Ben Am, MSc, Clinical Development Lead

VP Clinical Development, BioCancell; Director, Teva Pharmaceuticals Ltd.; VP Clinical, Topspin; Associate Director, Novartis (development of Gleevec[™])



Clinical Advisory Board

- Dr. Daniel Wallace, Cedars-Sinai Medical Center; Largest lupus practice of its kind in the US
 - Former Chairman of the Lupus Foundation of America (LFA), received LFA Award, Lupus Research Institute Achievement Award and others
- Professor David Isenberg, University College London Hospitals
 - Chair of the British Isles Assessment Group (BILAG), President of the British Society for Rheumatology (2004–2006) and Chair of its Biologics Register Committee (2006–2011)
- Dr. Murray Urowitz, University of Toronto; Lupus Clinic at Toronto Western Hospital
 - Established University of Toronto Lupus Clinic and Lupus Databank Research Program.
 - Founding member/president of numerous lupus associations and recipient of numerous awards for his contributions to lupus research.
- Dr. Lee Simon, Former Division Director, US FDA
 - Former US FDA Division Director of Analgesic, Anti-inflammatory and Ophthalmologic Drug Products and practicing Rheumatologist for 36 years.
 - Awarded 2003 ACR Distinguished Service Award and Scientific Leadership Award of the Lupus Research Institute.



Corporate Snapshot

- Headquarters: Raanana, Israel
- Member: Corporate Advisory Council of the Lupus Foundation of America
- ADRs trading on NASDAQ (XTLB) and Ordinary Shares on TASE (XTLB.TA)
- Capitalization (as of December 31, 2016):
 - 274,205,799 Shares Outstanding*
 - Warrants to purchase 961,111 ADRs*
 @ \$2.25 (expire March 2020)
- Member, Corporate Advisory Council, Lupus Foundation of America



Summary

- Lead candidate (hCDR1): for treatment of autoimmune diseases
 - Novel compound with unique mechanism of action
 - Ready for two Phase 2 studies in different autoimmiune indications
 - Clinical data in > 400 SLE patients
 - "Demonstrated efficacy in ... clinically meaningful endpoints"
 - Encouraging preliminary data in primary Sjogren's Syndrome (pSS)
 - Similar to data previously obtained in SLE
- Lead indications represent unmet medical needs in areas of interest
 - GSK acquired HGS/Benlysta in 2012 for \$3 billion
 - No effective therapeutic on the market for either indication
 - Weak competitive pipeline
- Aim to replicate results achieved in previous Phase 2b trial
 - FDA supports efficacy endpoint based on the BILAG index







Thank You

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