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Novel Molecule Development for the Treatment of Leukemia and Other Cancers

High Specificity, Three Mechanism, Low Toxicity, Chimeric Molecules

Overview- M-Life™ is a life sciences company focused on the development of new cancer drugs. The Company's current efforts center on the design of both new *multi-targeting-agents* (MTA's), or chimeras, as well as the advancement of M-Life™ licensed tubulin targeting molecules for use in the treatment of pediatric Acute Myeloid Leukemia (AML). M-Life™ programs leverage the published works of Dr. Peter Crooks, M-Life Chief Discovery Officer and M-Life's *proprietary design platforms*. The initial commercialization strategy is to advance the licensed tubulin molecules novel chimera molecules through IND. Once significant advancement of these molecules is made through the FDA approval process, therapeutic applicability will be expanded to include CNS and many other types of cancer.

Relative to the licensed tubulin molecules, the pool consists of 550 tubulin molecules that are protected by five issued patents. All molecules have been synthesized and tested via the National Cancer Institute's NCI-60 screening regime with roughly 30 percent displaying high performance (see selected references). From these molecules, twelve were identified as potential-high-value-assets using *M-Life's proprietary design platforms*. As a byproduct of the tubulin molecule evaluation, M-Life™ designed new optimal variations of these molecules and multi-targeting chimera molecules. All chimera and licensed molecules were evaluated using M-Life proprietary algorithms for toxicity, selectivity, potency, target docking, drugability and ease of synthesis with summary results reflected herein demonstrate superior efficacy and toxicity profiles compared to the current Standard-of-Care drugs on market.

M-Life™ is seeking $10.0 million in financing to advance licensed tubulin and novel chimera molecules through IND over the next 18 months.

Technical Background-Industry discovery efforts favor botanically derived analogs versus wholly synthetic molecules. Drugs derived from botanicals (*e.g.* the Feverfew plant and South African willow tree) serve as the active pharmaceutical ingredients in many current anti-cancer drugs like, Velcade™ (NF-kB target), Kyprolis™ (NF-kB), and Paclitaxel™ (Tubulin). This botanical basis for synthetically derived analogs has been the source of many standard-of-care anti-cancer agents and also applies to M-Life's™ anti-cancer drug programs.

There are many pathways and potential targets for the development of new cancer drugs. The pathways chosen by M-Life™ are cellular division (tubulin), apoptosis (NF-κB) and glutathione inhibition (inducing ROS toxicity). The rationale for the focus on these three pathways was that they have limited impact on normal functioning cells. And using *M-Life's proprietary design platforms,* the typically problematic toxicities associated with existing drugs were drastically reduced.

NF-κB-This pathway is a family of inducible genetic transcription factors that can, under stress like inflammation, protect cells from undergoing apoptosis (programmed cell death). Unfortunately, cancer cells override this generally constructive cellular capability, resulting in cells that don't die. The immortality feature of cancer cells avails their persistence even under aggressive therapeutic treatment. NF-κB inhibition simply defeats cancer cells' ability to turn off programmed cell death, returning them to the mortal status of normal cells.

Tubulin-Tubulins are intercellular proteins that occur in most cells. They polymerize to form hollow microtubules that can expand or contract forming a flexible scaffold that stabilizes DNA replication during cell division (mitosis). The microtubules serve an essential role in this process, allowing cellular replication of healthy cells.

The inhibition of tubulin affects all cells, but cancer cells differ from normal cells in the *rate* of division, which is much faster for cancer cells, especially aggressive types like leukemia or glioblastoma multiforme (GBM). As a result, cancer cells are much more vulnerable than normal cells to a tubulin inhibition. And, since tubulin inhibition is only relevant during cellular division, other normal cellular function is not impeded. This makes tubulin inhibition a very attractive target for the treatment of certain cancers, because it does not kill cancer cells, but rather, drastically slows their growth.

Glutathione (GSH)-In normal cells GSH serves as a protection against free radicals. Versus normal cells, cancer cells uniquely suffer from a glutathione deficit inhibition of glutathione makes cancer cells highly susceptible to the toxic effects of reactive oxygen species (ROS) yielding cancer selective toxicity/cell death.

Licensed Tubulin Based Anti-Cancer Molecules-M-Life's evaluation included the screening of NCI 60 raw data as well as representative publications across multiple cell-line targets under the CNS and Leukemia categories. A combination of *M-Life's proprietary design platforms, a compendium of M-Life™ proprietary algorithms* for toxicity/efficacy assessment, and a wide range of commercially available tools were used to comprehensively evaluate molecular properties and identify *potential high-value assets*. The table below illustrates this work: the top compounds were screened for efficacy and toxicity and out of 550 NCI tested cancer compounds only 30 percent demonstrated some level of efficacy and of the remainder only 10 percent have favorable toxicity profiles.

Top Tubulin Performers of 550 Evaluated Molecules

	Target		Leukemia/CNS Average		Toxicity				
Compound	Tub IC50 µM	NF-kB IC50 µM	GI50 nm	LC50 µM	QT/Tors	Agran	MitoTox	HepatoTox	Mutagen
ML_LM 001	3.30	5.70	2.23	208.92	0.56	0.41	0.55	0.68	0.39
ML_LM 002a	8.06	1.15	1.02	450.78	0.52	0.39	0.48	0.39	0.43
ML_LM 002b	8.86	1.56	2.27	221.73	0.44	0.21	0.55	0.34	0.50
ML_LM 002c	5.95	1.63	0.93	595.68	0.49	0.32	0.59	0.43	0.42
ML_LM 003a	6.04	1.67	21.68	437.65	0.50	0.25	0.66	0.48	0.40
ML_LM 003b	6.06	2.19	2.64	172.75	0.46	0.20	0.50	0.42	0.39

Key: For any toxicity model, a value > 0.7 is considered significant while 0.8 and above possibly fatal (*e.g.* Torsades, neutropenia, steatosis, etc). The values GI50 and LC50 serve as an indication of efficacy with desired GI50 values below 15nM and LC50 greater than 100mM.

M-Life™ Novel Three Mechanism Chimera Molecules-For the Chimera molecules, both tubulin and NF-κB/glutathione molecular attributes were identified using M-Life*'s* proprietary design platforms *P2L*™ and *MiST*™*.* Various combinations of these attributes were fused. The resulting chimeras were tested in both M-Life and commercial software packages. They were evaluated for efficacy and toxicity and other significant characteristics including receptor docking, drug-ability, ADME and ease of synthesis. M-Life™ also tested

performance across multiple cell lines, including those relevant to leukemia and glioblastoma multiforme (summarized in both tables under the Leukemia/CNS sections), with results indicating efficacy for multiple therapeutic uses. Using the same tools, chimera molecules were further compared to current top performing anti-cancer drugs on market. **M-Life™ Chimeras *were found to be superior to current drugs on market in both efficacy and toxicity - by substantial margins***.

Results for the 'top three' and 'bottom three' performers are summarized in the following table. The M-Life™ molecule MLSCP-CH1002 shows excellent tubulin inhibition and extremely high NF-kB inhibition. In contrast, MLSCP-CH1005/6 (bottom two performers) indicate problematic toxicity profiles (red or pink backgrounds indicate either cardiotoxicity or agranulocytosis and, in both cases, likely hepatotoxicity – drug induced liver injury, DILI). The table below illustrates the classical industry problem wherein molecules with 'Good' efficacy often have 'Poor' toxicity profiles.

Three Top Performers Contrasted by Three Bottom Performers

	Target		Leukemia/CNS Average		Toxicity				
Chimeras	Tub IC50 µM	NFKB IC50 µM	GI50 nM	LC50 µM	QT/Tors	Agran	MitoTox	Hepato Tox	Mutagen
MLSCP-CHI001	5.42	2.43	7.18	34.20	0.52	0.33	0.47	0.45	0.46
MLSCP-CHI002	3.07	0.92	0.16	70.09	0.68	0.14	0.39	0.57	0.50
MLSCP-CHI003	5.09	7.56	2.72	29.91	0.69	0.37	0.42	0.64	0.56
MLSCP-CHI004	2.75	3.96	0.78	32.92	0.82	0.39	0.41	0.72	0.46
MLSCP-CHI005	1.81	1.44	1.17	50.65	0.43	0.86	0.52	0.99	0.56
MLSCP-CHI006	5.11	12.84	0.66	24.59	0.84	0.31	0.43	0.71	0.36

Key: For any toxicity model, a value > 0.7 is considered significant while 0.8 and above possibly fatal (e.*g.* Torsades, neutropenia, steatosis, etc). The values GI50 and LC50 serve as an indication of efficacy with desired GI50 values below 15nM and LC50 greater than 100mM.

Summary-The general advancement of anti-cancer drugs toward a universal therapeutic is linked to lowering toxicity as well as the development of multi-targeting agents (MTA's). Current mainstream, anti-cancer strategies focus on a single target versus multi-targeting agents (MTA's). While MTA's offer a much more attractive approach for cancer treatment (MTA's limit cancer cells ability to biochemically side-step the action of a single targeting drug) they are generally avoided due to potential *toxicity* issues.

M-Life™ resolves both the problem of identifying optimum molecules as well as the development of MTA's through proprietary algorithms which integrate efficacy, toxicity, potency, ADME etc. into a singular non-serial platform that yields optimal molecules. The results of these efforts are:

1. Licensed Tubulin based molecules that have undergone *in vitro* NCI 60 testing wherein performance (*i.e.* efficacy and toxicity) have been vetted by M-Life™ algorithms.
2. Newly designed M-Life™ chimera MTA's for which efficacy and toxicity have been fully assessed.
3. Identification of molecules with therapeutic applicability to multiple types of cancer.

Intellectual Property:

- Tubulin Based Licensed Intellectual Property Includes: US Patent No. 9,957,316; US Patent No. 9,884,842; US Patent No. 10,100,029; US Patent No. 9,938,246; US Patent No. 10,239,844
- M-Life™ New anti-cancer chimera molecules, including testing and synthesis data
- M-Life™ Proprietary Toxicity Predictor algorithms for: Cardio Toxicity (QT Prolongation/Torsades de Pointes), Hepatotoxicity (Drug Induced Liver Injury, DILI), Ocular Toxicity, as well as non-organ- specific models for Mitochondrial Toxicity and Genetic Toxicity
- M-Life™ Platform designed new molecules including: analgesics, anti-parasitic, erectile dysfunction, and male pattern baldness
- Molecular repositories, virtual performance data, and toxicity screens

Proven, Experienced Core Team:

- Ted Moskal Founder, President & CEO; Dr. Peter Crooks, Chief Discovery Officer; Dr. Jon Wilkes, Chief Scientist; Dr. Chris Bojrab, Chief Medical Officer; Dr. John Panos, Director of Translational Discovery; Kai Lo, Chief Financial Officer
- The core team members have worked together for more than a decade
- Extensive ties to leading labs and facilities, and business experience
- Five additional industry experts have committed to join when additional financing is acquired
- Established relationships with CRO's, CMC's, Key Opinion Leaders and Industry Experts

Stage 1 Financing:

The Company has been self-funded to date and has no debt (notwithstanding under $100k in Convertible Debt) or contingent liabilities. M-Life™ seeks USD $10.0 million to sustain operations for 12 to 18 months, advance licensed anti-cancer molecules and novel chimera molecules thru IND.

Further Financing:

USD $25.0 to $50.0 million in 18 months, to advance these new drug molecule programs thru scale-up synthesis, testing, and completion of Phase I Clinical Trials as well as the preparation for advancement of anti-cancer molecules through the completion of clinical trials to NDA.

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Contact Information:

Ted Moskal, President & CEO
Moskal Lifesciences, LLC
tmoskal@m-lifesciences.com
870.680.2141