Active Agent Profile:

Overview; ~ Grounded Truths:

Molecular Pathways

• Up-Regulation of Positive Aging Molecular Pathways

Klotho positively impacts age delaying pathways. Notably, it upregulates SIRT1, Nrf2, PPARy, AMPK and telemorase. These pathways play pivotal roles in enhancing cellular repair mechanisms, promoting lipid metabolism, regulating glucose levels, and combating inflammation. By upregulating SIRT1, Klotho facilitates epigenetic regulation and metabolic adaptation, enhancing cellular defenses against oxidative stress. The activation of Nrf2 and PPARy further reinforces Klotho's antioxidant properties, promoting anti-inflammatory activities and maintaining cellular health. Additionally, by upregulating AMPK, Klotho supports energy regulation and metabolic homeostasis. Collectively, these pathways, facilitated by Klotho's co-receptor function for fibroblast growth factor (FGF), orchestrate a comprehensive anti-aging response, suppressing detrimental processes and enhancing cellular repair and defense mechanisms. By functioning as a gatekeeper and regulator, Klotho plays a pivotal role in maintaining cellular balance and ultimately prolonging healthspan and lifespan.

• Down Regulation of Negative Aging Molecular Pathways

Conversely, Klotho exerts its influence on aging through inhibiting certain pathways associated with advancing aging and promoting pathways that delay aging. Notably, Klotho inhibits five pathways linked to aging: Transforming growth factor β (TGF-β), insulin-like growth factor 1 (IGF-1), Wnt, NF-κB and mTOR. These pathways, unrestrained can induce detrimental cellular processes such as cellular senescence, apoptosis, inflammation, immune dysfunction, fibrosis, and neoplasia, all capable of contributing to the aging process. By down regulating these pathways, Klotho acts as a guardian against age-associated pathologies, preventing the progression of age-related diseases and promoting longevity.

• Additive, Complementary, or Synergistic effects of Active-Agents

An additive effect of a chemical interaction occurs when two or more chemicals combine and produce a chemical with a total effect equal to the sum of the effects of each individual chemical in the reaction. This usually occurs with chemicals that are similar in structure.

This can also occur in drugs that act within the body via a similar mechanism. For additive effect drugs, the same concept occurs in that when two or more drugs are combined, the effect of the combination is the same as what would be expected from the sum of the effects of taking of each drug independently. Moreover, the reaction in this case is called an additive interaction because the additive interaction definition says the effects of the combined drugs is equal to the sum of the effects from each drug taken separately. For example, if a person takes aspirin and Motrin together, they would get an effect of both pain-killing drugs within the body that would be the same as the effects from taking each drug separately.

A synergistic effect ocurrs when two or more drugs (or chemicals) combine to produce a greater effect than the sum of the effects if each drug were given separately. An example of this would be to administer two different chemotherapies (that each work in different ways) together to a patient for treating cancer. For some tumors, the combination enhances efficacy to stop cancer cell growth and is a standard of care.

• **Primary Targeted Active-Agents**

Activated Charcoal	Latanoprost
Adenosine	Ligustilide (Dong Quai)
Adiponectin	Ligustilide >>> Dang Gual
Akkermansia muciniphila	Lipitor (BID)
Alpha-Ketoglutaric Acid Ornithine (AKG)	Lithium
Alpha-Lopic Acid	Losartan
Apigenin	Losartan ((Angiotensin II Receptor Blocker (ARB))
AST-120 (Oral Activated Charcoal)	Luteolin
Astaxanthin	Magnesium
Astragaloside	Manganese
Astragalus Membranaceus	Meditation
Atrasentan	Melatonin
Baicalein	Metadichol, Policosanol
Berberine	Metformin
Bufei Yishen Formula	miR-199b-5p | Atrasentan
Calorie Restriction	miRNA130a
Chrysin	miRNA152/30
Cordycepin	miRNA339
Curcumin / VDR CuraMed	miRNA34a
Curcumin / VDR Quaniol	miRNA556
Diet	Morin
Diosmetin	N-acetyl-L-cysteine

Ellagic Acid	NAD3
Epicatechin gallate (ECG)	Nicotinamide mononucleotide (NMN) (Vit B3)
Epigallocatechin gallate	Nicotinamide riboside
Eplerenone (SARA) blood pressure	Nicotinamide riboside (NR) (Vit B3)
Everolimus	Nobiletin
Exercise	Oleuropein, (Olive polyphenols)
Fasting	Parishin
Fisetin	Pentoxifylline (PTXF)
Fluoride	Pterostilbene
Fluvastatin	Qing'E
Fu-Ti	Quercetin
GABA	Rapamycin
Galangin	Red Ginseng
Genistein	Resveratrol (astragalus triphenol)
Ginkgo Biloba	Rhein >>> Da Huang (Rubarb)
ginsenoside Rg1	RNA, miRNA SiRNA, piRNA
GLP-1-based	Rosiglitazone
Gotu Kola	Rosmarinic acid (RA)
Green Tea Polyphenlys (GTP) EGCG	Salvia miltiorrhiza
Guanosine (ginsenoside Rg1)	Scutellarein
Haikun Shenxi (Chinese approved Drug)	SelInum
Hesperidin	Senolytics
Hibiscus sabdariffa,	Shan Yao (Chinease Yam)
Hyaluronic Acid	Shenkang
l-Histidine	Sinensetin
Intermedin	Sodium butyrate
Ketone:	Spermidine

Klotho	Sulforaphane (broccoli, broccoli sprouts)
L-carnitine tartrate	Tangeritin
L-carnitine tartrate (18.65%)	Taurine
L-Cystine	Troglitazone
L-Isoleucine (bcaa)	Ursolic Acid (Rosemary Acid (GABA agnost)
L-Leucine (bcaa)	Valsartan
L-Lysine	Valsartan (Angiotensin II Receptor Blocker (ARB)
L-Methionine	VIT A
L-Phenylalanine	VIT B (Complex)
L-serine	VIT B12
L-serine (61.75%),	Vit C
L-theanine ++ memory in Klotho -/- mice	VIT D / (VDRAs)
L-Threonine	VIT E {39}
L-Triptophan	VIT K
L-Tyrosine	Wogonin
L-Valine (bcaa)	Zinc

• **Primary Targeted Molecular Pathways**

Adenosine Monophosphate-Activated Protein Kinase (AMPK)
Angiotensin-Converting Enzyme 2 (ACE2)
Cyclic Adenosine Monophosphate pathway (cAMP)
endothelial nitric oxide synthase (eNOS)
Epigenetic Modification Pathway (Epigenetics)
Fibroblast Growth Factor 19 pathway (FGF19)
Fibroblast Growth Factor 21 Pathway (FGF21)
Fibroblast Growth Factor 23 Pathway (FGF23)
Insulin
Insulin Signaling Pathway (ISP)

Insulin-Like Growth Factor 1 Pathway (IGF-1)
Interferon Gamma Pathway (INF-γ)
Interleukin-6 (IL-6)
Klotho Signaling Pathway (KLP)
Mammalian Target of Rapamycin pathway (mTOR)
Mitogen-Activated Protein Kinase Pathway (MAPK)
Nuclear factor erythroid 2-related factor 2 pathway (Nrf2)
Nuclear factor-kappa Beta (Light-chain-enhancer of activated B cells) pathway, (NF-κB)
Peroxisome Proliferator-Activated Receptor Gamma (PPAR-γ)
Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1-Alpha
Phosphatidylinositol 3-Kinase/Protein Kinase B pathway, (PI3K/Akt)
Protein Kinase C (PKC)
Renal Outer Medullary Potassium Channel (ROMK1)
Renin-Angiotensin System (RAS)
Sirtuin 1 Pathway (SIRT1)
Sodium-Potassium Adenosine Triphosphatase Pathway (Na+/K+-ATPase)
Specificity Protein 1 Pathway (Sp1)
Transforming Growth Factor-beta (TGF-β)
Transient Receptor Potential Cation Channel Subfamily V Member 5 Pathway
Tumor Narcoisis Factor alpha
Tumor Protein p53 and Cyclin-Dependent Kinase Inhibitor 1 Pathway (p53/p21)
Vitamin D Receptor Element (VDRE)
Wingless/Integrated Signaling Pathway (Wnt)

PROMPT QUERIES:

Title = 1) Biological / Pharmacological / Pharmacokinetics Profile

Please provide a biological / pharmacological / pharmacokinetics profile of the Active-Agent.

Title = 2) Molecular Pathways

Please provide a list of all known molecular pathways modulated, activated or down-regulated by this active agent. Pay special attention to the target list provided in the Overview.

Title = 3) Impact on Klotho

Please indicate if this active-agent directly or indirectly up-regulates Klotho.

Title = 4) Safety Profile

Please provide the known safety profile of this active-agent.

Title = 5) Oral Bioavailability

Please provide the oral bioavailability of this active-agent.

Title = 6) Plasma Half-Life

Please provide the half-life of this active-agent.

Title = 7) Additive, Complementary, or Synergistic

Please provide a list of any know agents that are additive, complementary, or synergistic with this active agent. Profile is also provided in the overview.

Title = 8) Antagonistic

Please indicate any of the other active agents identified in in the overview that this active agent has an antagonistic effect upon when concomitantly administered.

Title = 9) Diseases Impacted by Active Agent

Please identify all known diseases that this agent has demonstrated therapeutic benefit or activity in.

Title = 10) Human Clinical Trials of Active Agent

Please list any human clinical trails that included this active-agent.

Title = 11) Known Anti-Aging Effects Attributable to Active-Agent

Please identify all known anti-aging effects attributable to this active agent.

- **Response Key - Triggering Prompt Activation**

Respond **“Ready for Klotho Target Pathway?”** and I will paste the Active Agent name for you to analyze?

Please replace the “active-agent” text with the name of the entered active agent. Please use the Text that follows “Title =” as the header for each section. Please indent the response to each prompt below each Title header. Do not include the “Title =” portion of each Title Header. Thank you.