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## KEY ADVANTAGES

- Proven success in drug discovery
- Flexibility for a wide variety of biological targets
- Produces drug-like compounds with good metabolic stability and aqueous solubility
- Favorable pharmacokinetic profiles, including oral bioavailability
- Potent activity demonstrated in clinically relevant animal models
- Provides strong IP position
- Accelerated, resource efficient lead optimization

## WHO TO CONTACT

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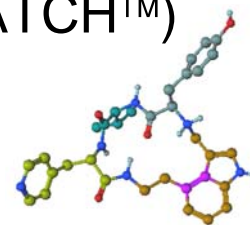
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tranzyme<sup>®</sup>  
pharma

# Macrocytic Template Chemistry (MATCH™)

## Proprietary Small Molecule Technology for Drug Discovery and Development



Tranzyme Pharma's **Macrocytic Template Chemistry (MATCH)** is a proprietary drug design and medicinal chemistry technology which exploits a distinct class of low-molecular weight compounds, **macrocycles**, with proven activity on a wide range of extracellular and intracellular targets. MATCH is a particularly rich potential source for novel drug candidates as it maintains the favorable characteristics exhibited by large biomolecules, such as tight receptor binding for high potency and selectivity, while eliminating the drawbacks associated with peptide and protein drugs, i.e. poor metabolic stability, low oral bioavailability, lack of membrane permeability, high manufacturing costs, and antigenicity.

Tranzyme Pharma has successfully used MATCH to discover and develop its pipeline of novel drugs.

## APPLICATIONS OF MATCH

MATCH is broadly applicable for:

- **Screening amenable to any pharmaceutical target type**, including G protein-coupled receptors (GPCRs), protein kinases, enzymes, ion channels and nuclear receptors
- **Transformation of peptide and peptidomimetic leads into viable small molecule drugs**
- **Rapid hit-to-clinic progression** through simultaneous investigation of chemical and spatial requirements.

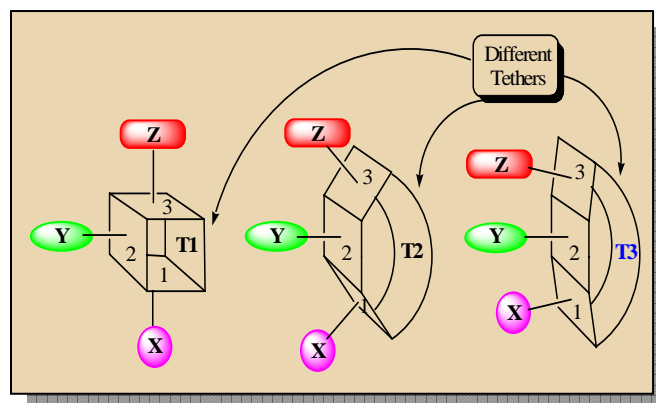
MATCH makes available for the first time a library of macrocycles ready for discovery screening (**HitCREATE™ Library**). Tranzyme has designed the HitCREATE Library as a knowledge-based or "smart" library in order to access structures of greater interest for pharmaceutical development. This library contains a unique set of drug-like compounds with distinct topologies and diverse functionalities. It has consistently produced information-rich primary hits with high potency and selectivity (**hit validation rate >50%**;  $K_i < 500$  nM).

MATCH enables lead to clinic optimization faster than the industry average through (1) proprietary, robust and efficient assembly methods for all building blocks, (2) rapid SAR profiling, (3) concurrent modification of activity and physicochemical properties, and (4) cost-effective larger scale manufacturing processes. MATCH has proven particularly useful for identifying lead **agonists and antagonists** in the major pharmaceutical target class – GPCRs.

## CHARACTERISTICS OF TRANZYME'S MACROCYCLES

Tranzyme's macrocycles are a unique class of small molecules with defined, three-dimensional shapes. Macrocyclic molecules are preorganized for **potent binding specificity** and **improved ADME/Tox properties**. Although compounds from this class have been successfully developed as drugs by several pharmaceutical companies, they have either originated from natural sources or have been synthesized individually. MATCH allows, for the first time, the construction of synthetic libraries of these molecules in a highly efficient manner. Further, Tranzyme's design approach results in compounds with **significant initial activity** and **high selectivity** for a biological target. The molecular rigidity of the molecules additionally favors **high oral bioavailability, metabolic stability** and **good aqueous solubility**.

Tranzyme's macrocycles incorporate four elements of diversity—three recognition sites (X, Y, Z) to modify chemical properties and a proprietary tether (T) to control spatial diversity. MATCH enables the variation of these tethers in order to modulate the compounds' spatial orientation. While the recognition elements interact with the targeted receptor, the tether *locks* the recognition elements in a unique conformation, ensuring tighter binding and improved potency. In addition, MATCH enables the simultaneous variation of all these sites of diversity, accelerating what is typically the very resource intensive task of lead optimization. The result is more rapid identification of a high quality clinical candidate.



Proprietary tethers (M.W. 100-200) enable controlled modulation of molecular shape and interacting functionality