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Verner

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(54) **INHIBITORS OF BRUTON'S TYROSINE KINASE**

(75) Inventor: **Erik Verner**, San Mateo, CA (US)

(73) Assignee: **Pharmacyclics, Inc.**, Sunnyvale, CA (US)

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(51) **Int. Cl.**

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C07D 497/00	(2006.01)
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(52) **U.S. Cl.** **514/262.1**; 514/789; 544/184; 544/262; 544/350; 435/194

(58) **Field of Classification Search** ..... None
See application file for complete search history.

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Primary Examiner—James O Wilson
Assistant Examiner—Jeffrey H Murray
(74) *Attorney, Agent, or Firm*—Wilson Sonsini Goodrich & Rosati

(57) **ABSTRACT**

Disclosed herein are imidazo[1,5-f][1,2,4]triazine compounds that form covalent bonds with Bruton's tyrosine kinase (Btk). The imidazo[1,5-f][1,2,4]triazine compounds described are irreversible inhibitors of Btk. Methods for the preparation of the imidazo[1,5-f][1,2,4]triazine compounds are disclosed. Also disclosed are pharmaceutical compositions that include the imidazo[1,5-f][1,2,4]triazine compounds. Methods of using the imidazo[1,5-f][1,2,4]triazine Btk inhibitors are disclosed, alone or in combination with other therapeutic agents, for the treatment of autoimmune diseases or conditions, heteroimmune diseases or conditions; cancer, including lymphoma, and inflammatory diseases or conditions.

12 Claims, 7 Drawing Sheets

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BTK	I	T	E	Y	M	A	N	G	C	L	L
BMX	V	T	E	Y	M	A	R	G	C	L	L
TEC	V	T	E	F	M	E	R	G	C	L	L
TXK	V	T	E	F	M	E	N	G	C	L	L
ITK	V	F	E	F	M	E	H	G	C	L	S
EGFR	I	T	Q	L	M	P	F	G	C	L	L
ErbB2	V	T	Q	L	M	P	Y	G	C	L	L
ErbB4	V	T	Q	L	M	P	H	G	C	L	L
JAK3	V	M	E	Y	L	P	S	G	C	L	R
BLK	V	T	E	Y	L	P	S	G	C	L	L
LCK	I	T	E	Y	M	E	N	G	S	L	V
LYN	I	T	E	Y	M	A	K	G	S	L	L
SYK	V	M	E	M	A	E	L	G	P	L	N

Fig. 1

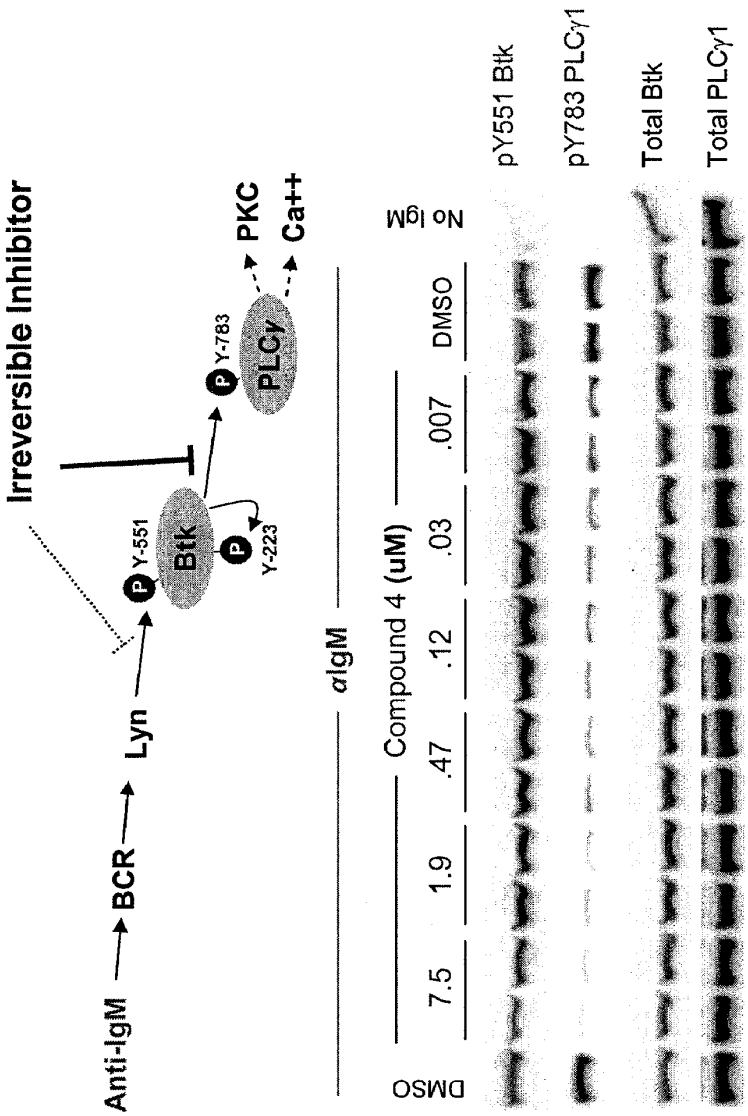

Fig. 2

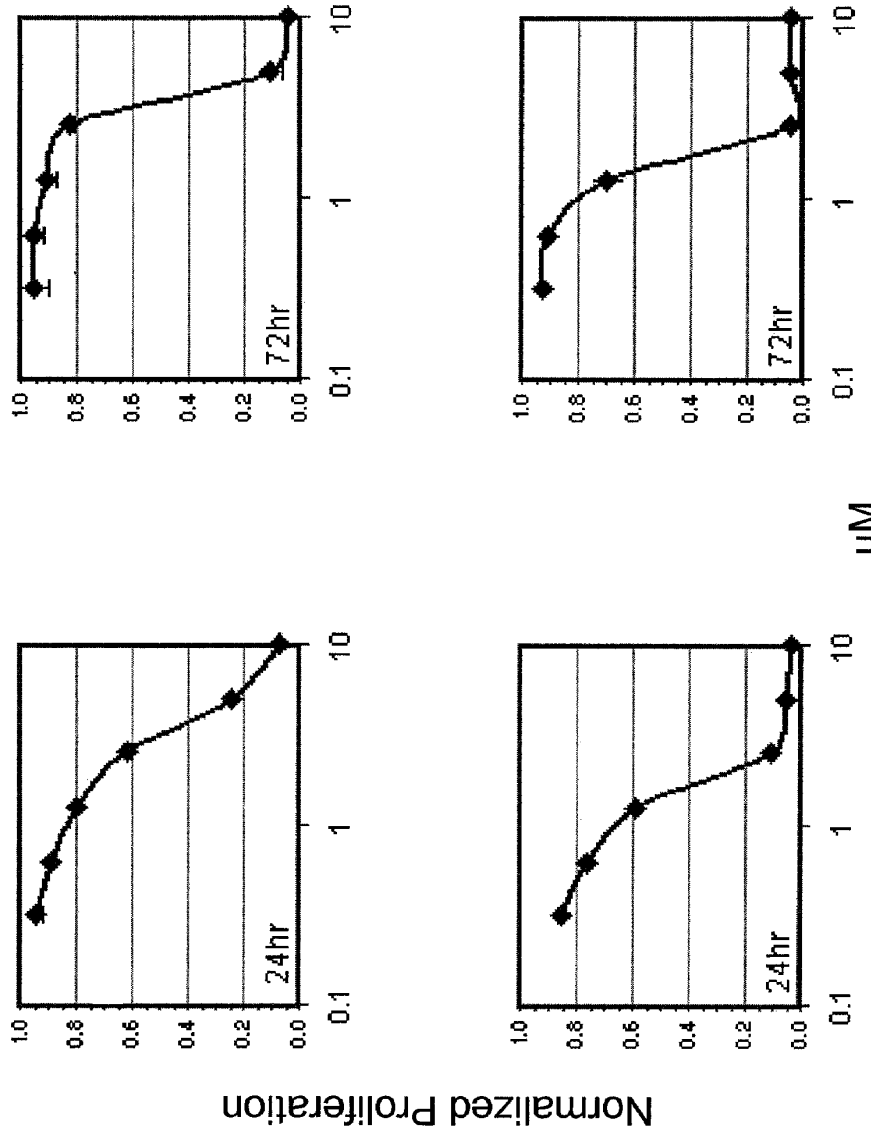

Fig. 3

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