## SUPPLEMENTARY FIGURE AND TABLE

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PIM1 129 YQVGPLLGSGGFGSVYSGIRVSDNLPVAIKHVEKDRISDWGELPNGTRVPMEVVLLKKVS
PIM2  32 YRLGPLLGKGGFGTVFAGHRLTDRLQVAIKVIPRNRVLGWSPLSDSVTCPLEVALLWKVG
PIM3  40 YQVGAVLGSGGFGTVYAGSRIADGLPVAVKHVVKERVTEWGSL-GGATVPLEVVLLRKVG

PIM1 189 S--GFSGVIRLLDWFERPDSFVLILERPEPVQDLFDFITERGALQEELARSFFWQVLEAV
PIM2  92 AGGGHPGVIRLLDWFETQEGFMLVLERPLPAQDLFDYITEKGPLGEGPSRCFFGQVVAAI
PIM3  99 AAGGARGVIRLLDWFERPDGFLLVLERPEPAQDLFDFITERGALDEPLARRFFAQVLAAV

PIM1 247 RHCHNCGVLHRDIKDENILIDLNRGELKLIDFGSGALLKDTVYTDFDGTRVYSPPEWIRY
PIM2 152 QHCHSRGVVHRDIKDENILIDLRRGCAKLIDFGSGALLHDEPYTDFDGTRVYSPPEWISR
PIM3 159 RHCHSCGVVHRDIKDENLLVDLRSGELKLIDFGSGALLKDTVYTDFDGTRVYSPPEWIRY

PIM1 307 HRYHGRSAAVWSLGILLYDMVCGDIPFEHDEEIIRGQVFFRQRVSSECQHLIRWCLALRP
PIM2 212 HQYHALPATVWSLGILLYDMVCGDIPFERDQEILEAELHFPAHVSPDCCALIRRCLAPKP
PIM3 219 HRYHGRSATVWSLGVLLYDMVCGDIPFEQDEEILRGRLLFRRRVSPECQQLIRWCLSLRP

PIM1 367 SDRPTFEEIQNHPWM
PIM2 272 SSRPSLEEILLDPWM
PIM3 279 SERPSLDQIAAHPWM
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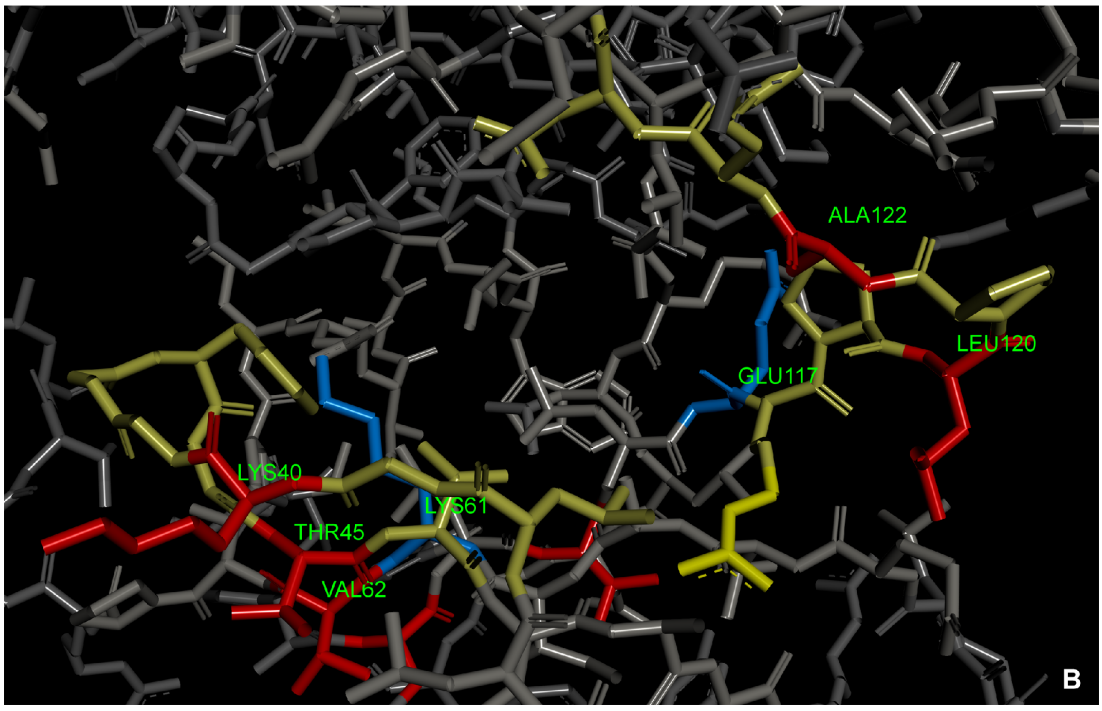
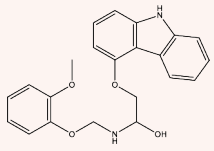
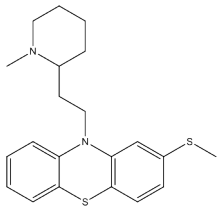
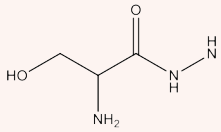
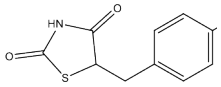
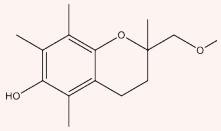
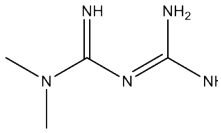
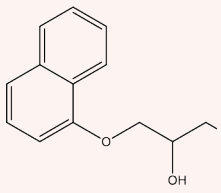
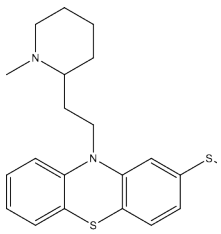
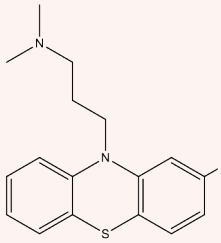
A

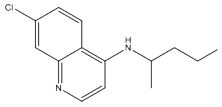
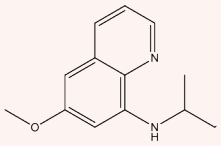
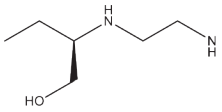
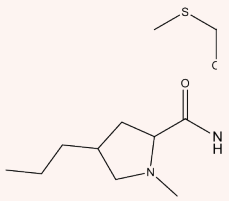
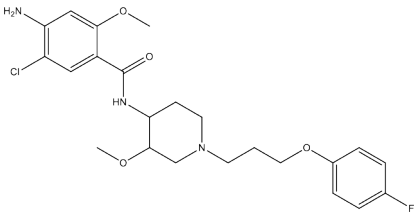
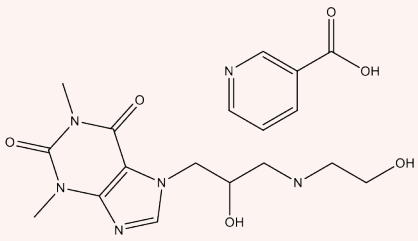
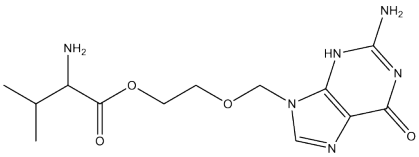
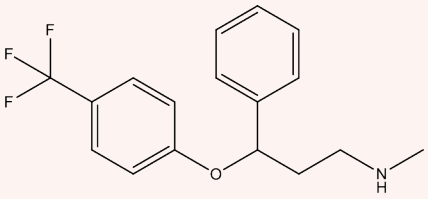
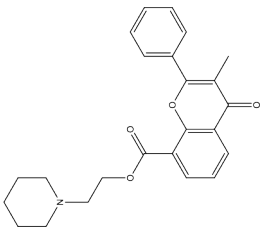



**Supplementary Figure S1: Sequence alignment of kinase domains and structure-based differences between PIM1 and PIM2. (A)** Sequence alignment of kinase domains of PIM1, PIM2 and PIM3, the differences are underlined with red background or words. The amino acids that form part of the ATP binding are marked with blue boxes; **(B)** The active side (yellow) of PIM2, LYS40, THR45, VAL62, LEU120 and ALA122 (red) are differences in the protein sequence. LYS61 and GLU117 (blue) are amino acids with conformational differences between PIM1 and PIM2, which influence the effect on PIM2 of PIM1 inhibitors with crystallographic structure.

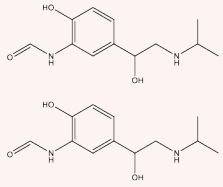
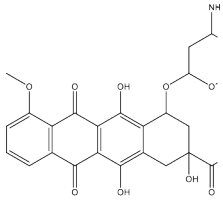
**Supplementary Table S1: The MTT assay of candidate small-molecule PIM inhibitors from Drugbank**

| Number | Name | CAS NO. | Structure | Inhibitory ratio (%) |
|---|---|---|---|---|
| P1 | Carvedilol | 72956-09-3 |  | 51.77537144 |
| P2 | Lansoprazole | 103577-45-3 |  | 22.66431629 |
| P3 | Benserazide hydrochloride | 14919-77-8 |  | 10.12339461 |
| P4 | Rosiglitazone hydrochloride | 302543-62-0 |  | 46.81440443 |
| P5 | Troglitazone | 97322-87-7 |  | 6.925207756 |
| P6 | Metformin HCL | 1115-70-4 |  | 11.20624528 |
| P7 | Propranolol Hydrochloride | 318-98-9 |  | 3.878116343 |
| P8 | thioridazine hydrochloride | 130-61-0 |  | 59.12868295 |
| **P9** | **Chlorpromazine** | **50-53-3** |  | **93.95618232** |

(*Continued*)

| Number | Name | CAS NO. | Structure | Inhibitory ratio (%) |
|---|---|---|---|---|
| P10 | Hydroxychloroquine sulfate | 747-36-4 |  | |
| P11 | Primaquine diphosphate | 63-45-6 |  | 39.56182322 |
| P12 | Ethambutol Hydrochloride | 1070-11-7 |  | 10.75295895 |
| P13 | Lincomycin Hydrochloride | 859-18-7 |  | 29.84134979 |
| P14 | cisapride | 81098-60-4 |  | 38.10123395 |
| P15 | xantinol nicotinate | 437-74-1 |  | 11.45807101 |
| P16 | Valaciclovir | 124832-26-4 |  | |
| P17 | Fluoxetine hydrochloride | 56296-78-7 |  | 12.36464367 |
| P18 | Flavoxate Hydrochloride | 3717-88-2 |  | −1.284311257 |

(*Continued*)

| Number | Name | CAS NO. | Structure | Inhibitory ratio (%) |
|---|---|---|---|---|
| P19 | Formoterol Fumarate | 43229-80-7 |  | 0.138504155 |
| P20 | Daunorubicin hydrochloride | 23541-50-6 |  | 91.26164694 |