

Figure S1. A heatmap showing the hit rates percentages for the Malaria Box compounds against several piroplasm parasites (*B. divergens*, *B. bovis*, *B. bigemina*, *T. equi*, and *B. caballi*), *Toxoplasma gondii*, *Entamoeba histolytica*, *Schistosoma mansoni*, and *Cryptosporidium parvum*. *B. divergens* exhibited the highest hit rate %.* data adopted from [2], # data adopted from [22], ** data adopted from [23], ## data adopted from [24].

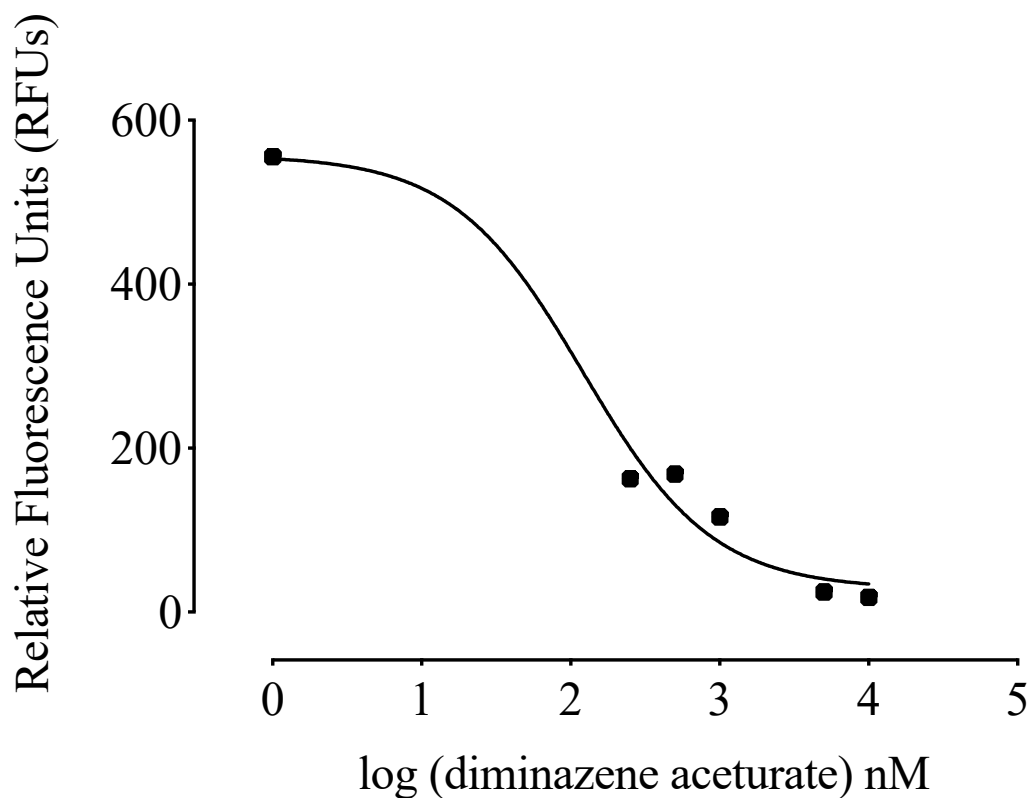


Figure S2. Fluorescence-based monitoring of diminazene aceturate-induced growth inhibition of *B. divergens*. Correlation between RFUs (y-axis) and log concentration of diminazene aceturate (nM) (x-axis). Each value represents a mean of triplicate wells after subtraction of the background fluorescence for non-parasitized RBCs.

Table S1. Characterization and IC₅₀ values of malaria box compounds number 2 to 21 from plate (A) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC ₅₀ (μM) ^b |
|--------------|--------------------------|------------------|------------------------------------|
| A-2 | MMV665915 | Drug-like | 10.53 |
| A-3 | MMV666023 | Probe-like | 7.34 |
| A-4 | MMV665876 | Drug-like | 15.97 |
| A-5 | MMV019406 | Probe-like | 10.52 |
| A-6 | MMV019871 | Drug-like | 1.45 |
| A-7 | MMV666596 | Probe-like | 9.07 |
| A-8 | MMV006309 | Probe-like | 1.87 |
| A-9 | MMV000642 | Probe-like | 1.98 |
| A-10 | MMV396672 | Drug-like | 10.15 |
| A-11 | MMV001038 | Drug-like | 3.04 |

| | | | |
|-------------|-----------|------------|-------|
| B-2 | MMV665916 | Drug-like | 2.88 |
| B-3 | MMV666101 | Probe-like | 10.27 |
| B-4 | MMV665841 | Probe-like | 10.51 |
| B-5 | MMV007695 | Probe-like | 10.55 |
| B-6 | MMV020788 | Probe-like | 5.72 |
| B-7 | MMV009063 | Drug-like | 10.12 |
| B-8 | MMV007384 | Probe-like | 1.72 |
| B-9 | MMV006429 | Drug-like | 1.16 |
| B-10 | MMV007116 | Drug-like | 1.71 |
| B-11 | MMV396703 | Drug-like | 2.62 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S2. Characterization and IC₅₀ values of malaria box compounds number 22 to 41 from plate (A) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| C-2 | MMV665785 | Probe-like | 10.46 |
| C-3 | MMV665805 | Drug-like | 4.51 |
| C-4 | MMV020492 | Drug-like | 7.60 |
| C-5 | MMV006937 | Drug-like | 1.53 |
| C-6 | MMV666693 | Drug-like | 2.47 |
| C-7 | MMV007686 | Probe-like | 9.94 |
| C-8 | MMV019066 | Drug-like | 1.74 |
| C-9 | MMV000662 | Drug-like | 3.50 |
| C-10 | MMV007839 | Drug-like | 10.19 |

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|-------------|-----------|------------|-------|
| C-11 | MMV396680 | Probe-like | 11.33 |
| D-2 | MMV665782 | Drug-like | 3.07 |
| D-3 | MMV665874 | Drug-like | 6.35 |
| D-4 | MMV011567 | Drug-like | 10.33 |
| D-5 | MMV006278 | Drug-like | 3.33 |
| D-6 | MMV085583 | Probe-like | 10.11 |
| D-7 | MMV020885 | Probe-like | 1.42 |
| D-8 | MMV006457 | Probe-like | 2.70 |
| D-9 | MMV020549 | Drug-like | 1.67 |
| D-10 | MMV011259 | Drug-like | 1.18 |
| D-11 | MMV396679 | Probe-like | 1.66 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S3. Characterization and IC₅₀ values of malaria box compounds number 42 to 61 from plate (A) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| E-2 | MMV665941 | Probe-like | 5.29 |
| E-3 | MMV665878 | Drug-like | 9.70 |
| E-4 | MMV000448 | Probe-like | 10.51 |
| E-5 | MMV666691 | Probe-like | 10.55 |
| E-6 | MMV006455 | Drug-like | 5.72 |
| E-7 | MMV666600 | Probe-like | 10.12 |
| E-8 | MMV006558 | Probe-like | 1.72 |

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|-------------|-----------|------------|-------|
| E-9 | MMV020548 | Drug-like | 1.16 |
| E-10 | MMV011256 | Drug-like | 1.71 |
| E-11 | MMV396678 | Probe-like | 2.62 |
| F-2 | MMV666021 | Probe-like | 10.46 |
| F-3 | MMV665820 | Drug-like | 4.51 |
| F-4 | MMV085203 | Probe-like | 0.83 |
| F-5 | MMV008956 | Drug-like | 1.53 |
| F-6 | MMV007907 | Drug-like | 2.47 |
| F-7 | MMV666601 | Probe-like | 9.94 |
| F-8 | MMV000570 | Probe-like | 1.74 |
| F-9 | MMV001246 | Drug-like | 3.50 |
| F-10 | MMV396797 | Drug-like | 10.21 |
| F-11 | MMV006087 | Drug-like | 13.19 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S4. Characterization and IC₅₀ values of malaria box compounds number 62 to 81 from plate (A) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID^a | Set[*] | IC₅₀ (μM)^b |
|---------------------|--------------------------------|------------------------|---|
| G-2 | MMV666062 | Probe-like | 5.40 |
| G-3 | MMV665827 | Probe-like | 2.23 |
| G-4 | MMV666688 | Probe-like | 4.86 |
| G-5 | MMV008416 | Probe-like | 1.22 |
| G-6 | MMV006172 | Probe-like | 1.56 |
| G-7 | MMV007160 | Probe-like | 5.65 |
| G-8 | MMV006427 | Drug-like | 1.74 |
| G-9 | MMV019258 | Drug-like | 10.58 |

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|-------------|-----------|------------|------|
| G-10 | MMV011099 | Drug-like | 6.67 |
| G-11 | MMV019110 | Drug-like | 7.16 |
| H-2 | MMV665977 | Probe-like | 1.04 |
| H-3 | MMV665831 | Probe-like | 1.61 |
| H-4 | MMV006203 | Probe-like | 1.08 |
| H-5 | MMV020500 | Drug-like | 1.11 |
| H-6 | MMV006861 | Probe-like | 3.45 |
| H-7 | MMV008294 | Probe-like | 5.88 |
| H-8 | MMV020439 | Drug-like | 1.16 |
| H-9 | MMV666607 | Probe-like | 1.03 |
| H-10 | MMV008138 | Drug-like | 4.09 |
| H-11 | MMV396693 | Probe-like | 0.78 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S5. Characterization and IC₅₀ values of malaria box compounds number 82 to 101 from plate (B) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| A-2 | MMV665929 | Drug-like | 0.42 |
| A-3 | MMV665917 | Drug-like | 0.28 |
| A-4 | MMV665979 | Drug-like | 0.53 |
| A-5 | MMV666116 | Drug-like | 0.05 |
| A-6 | MMV666081 | Drug-like | 0.06 |
| A-7 | MMV665906 | Drug-like | 0.04 |
| A-8 | MMV665891 | Drug-like | 0.07 |
| A-9 | MMV009060 | Drug-like | 0.05 |

| | | | |
|-------------|-----------|-----------|------|
| A-10 | MMV019313 | Drug-like | 0.16 |
| A-11 | MMV000648 | Drug-like | 0.36 |
| B-2 | MMV665939 | Drug-like | 0.25 |
| B-3 | MMV665789 | Drug-like | 0.16 |
| B-4 | MMV665961 | Drug-like | 0.21 |
| B-5 | MMV666067 | Drug-like | 0.05 |
| B-6 | MMV666093 | Drug-like | 0.05 |
| B-7 | MMV665890 | Drug-like | 0.11 |
| B-8 | MMV665826 | Drug-like | 1.05 |
| B-9 | MMV142383 | Drug-like | 0.05 |
| B-10 | MMV007564 | Drug-like | 0.25 |
| B-11 | MMV000653 | Drug-like | 1.43 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S6. Characterization and IC₅₀ values of malaria box compounds number 102 to 121 from plate (B) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| C-2 | MMV665935 | Drug-like | 0.23 |
| C-3 | MMV665799 | Drug-like | 0.08 |
| C-4 | MMV666009 | Drug-like | 0.14 |
| C-5 | MMV666071 | Drug-like | 0.16 |
| C-6 | MMV666075 | Drug-like | 0.23 |
| C-7 | MMV665817 | Drug-like | 0.24 |
| C-8 | MMV665902 | Drug-like | 0.32 |
| C-9 | MMV006188 | Drug-like | 0.25 |

| | | | |
|-------------|-----------|-----------|------|
| C-10 | MMV019780 | Drug-like | 0.33 |
| C-11 | MMV008149 | Drug-like | 0.45 |
| D-2 | MMV665928 | Drug-like | 0.20 |
| D-3 | MMV665800 | Drug-like | 0.07 |
| D-4 | MMV665953 | Drug-like | 0.15 |
| D-5 | MMV666110 | Drug-like | 0.19 |
| D-6 | MMV666103 | Drug-like | 0.18 |
| D-7 | MMV665899 | Drug-like | 0.15 |
| D-8 | MMV665888 | Drug-like | 0.13 |
| D-9 | MMV019758 | Drug-like | 0.05 |
| D-10 | MMV019746 | Drug-like | 1.35 |
| D-11 | MMV019662 | Drug-like | 1.59 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S7. Characterization and IC₅₀ values of malaria box compounds number 122 to 141 from plate (B) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| E-2 | MMV665909 | Drug-like | 0.31 |
| E-3 | MMV665803 | Drug-like | 0.27 |
| E-4 | MMV665946 | Drug-like | 1.19 |
| E-5 | MMV665954 | Drug-like | 0.39 |
| E-6 | MMV666105 | Drug-like | 1.33 |
| E-7 | MMV665857 | Drug-like | 0.37 |
| E-8 | MMV007617 | Drug-like | 1.48 |

| | | | |
|-------------|-----------|-----------|------|
| E-9 | MMV019074 | Drug-like | 1.20 |
| E-10 | MMV000788 | Drug-like | 0.14 |
| E-11 | MMV001255 | Drug-like | 0.35 |
| F-2 | MMV665918 | Drug-like | 0.36 |
| F-3 | MMV665796 | Drug-like | 0.29 |
| F-4 | MMV666070 | Drug-like | 0.21 |
| F-5 | MMV666057 | Drug-like | 0.16 |
| F-6 | MMV666108 | Drug-like | 1.28 |
| F-7 | MMV665901 | Drug-like | 0.19 |
| F-8 | MMV000248 | Drug-like | 0.26 |
| F-9 | MMV000498 | Drug-like | 0.18 |
| F-10 | MMV000620 | Drug-like | 0.15 |
| F-11 | MMV001230 | Drug-like | 0.62 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S8. Characterization and IC₅₀ values of malaria box compounds number 142 to 161 from plate (B) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| G-2 | MMV665914 | Drug-like | 0.24 |
| G-3 | MMV665798 | Drug-like | 0.17 |
| G-4 | MMV666069 | Drug-like | 1.17 |
| G-5 | MMV666072 | Drug-like | 0.22 |
| G-6 | MMV666102 | Drug-like | 0.02 |
| G-7 | MMV665879 | Drug-like | 0.001 |
| G-8 | MMV000563 | Drug-like | 0.21 |
| G-9 | MMV019064 | Drug-like | 1.17 |

| | | | |
|-------------|-----------|-----------|------|
| G-10 | MMV019738 | Drug-like | 0.13 |
| G-11 | MMV007571 | Drug-like | 0.33 |
| H-2 | MMV665913 | Drug-like | 0.29 |
| H-3 | MMV665948 | Drug-like | 0.15 |
| H-4 | MMV666061 | Drug-like | 0.25 |
| H-5 | MMV666080 | Drug-like | 0.26 |
| H-6 | MMV665807 | Drug-like | 0.01 |
| H-7 | MMV665850 | Drug-like | 0.01 |
| H-8 | MMV665940 | Drug-like | 0.18 |
| H-9 | MMV000561 | Drug-like | 2.18 |
| H-10 | MMV000634 | Drug-like | 0.22 |
| H-11 | MMV011944 | Drug-like | 0.39 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments.*The set data are provided in the supporting information for the malaria box.

Table S9. Characterization and IC₅₀ values of malaria box compounds number 162 to 181 from plate (C) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| A-2 | MMV665904 | Drug-like | 3.78 |
| A-3 | MMV019762 | Drug-like | 0.01 |
| A-4 | MMV019700 | Drug-like | 2.86 |
| A-5 | MMV019202 | Drug-like | >25 |
| A-6 | MMV009108 | Drug-like | 0.12 |
| A-7 | MMV018984 | Drug-like | >25 |
| A-8 | MMV000972 | Drug-like | >25 |
| A-9 | MMV396719 | Drug-like | >25 |

| | | | |
|-------------|-----------|-----------|------|
| A-10 | MMV006820 | Drug-like | >25 |
| A-11 | MMV396705 | Drug-like | 5.99 |
| B-2 | MMV665883 | Drug-like | 4.40 |
| B-3 | MMV011576 | Drug-like | 1.74 |
| B-4 | MMV000760 | Drug-like | 3.03 |
| B-5 | MMV020505 | Drug-like | 0.79 |
| B-6 | MMV019670 | Drug-like | 0.59 |
| B-7 | MMV007808 | Drug-like | 7.52 |
| B-8 | MMV306025 | Drug-like | >25 |
| B-9 | MMV396715 | Drug-like | 0.57 |
| B-10 | MMV396744 | Drug-like | 0.55 |
| B-11 | MMV396704 | Drug-like | 0.57 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set are provided in the supporting information for the malaria box.

Table S10. Characterization and IC₅₀ values of malaria box compounds number 182 to 201 from plate (C) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| C-2 | MMV665806 | Drug-like | 0.57 |
| C-3 | MMV000848 | Drug-like | 2.13 |
| C-4 | MMV020700 | Drug-like | 0.95 |
| C-5 | MMV000911 | Drug-like | 0.79 |
| C-6 | MMV020490 | Drug-like | 1.28 |
| C-7 | MMV020651 | Drug-like | 1.76 |
| C-8 | MMV403679 | Drug-like | 13.09 |
| C-9 | MMV396681 | Drug-like | 0.15 |

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|-------------|-----------|-----------|------|
| C-10 | MMV305841 | Drug-like | >25 |
| C-11 | MMV006587 | Drug-like | >25 |
| D-2 | MMV665843 | Drug-like | 0.38 |
| D-3 | MMV007881 | Drug-like | 1.47 |
| D-4 | MMV020942 | Drug-like | 1.18 |
| D-5 | MMV001344 | Drug-like | 4.69 |
| D-6 | MMV020275 | Drug-like | 1.02 |
| D-7 | MMV007906 | Drug-like | 2.04 |
| D-8 | MMV007374 | Drug-like | 2.63 |
| D-9 | MMV396595 | Drug-like | 2.91 |
| D-10 | MMV396794 | Drug-like | 0.19 |
| D-11 | MMV006706 | Drug-like | 0.03 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set are provided in the supporting information for the malaria box.

Table S11. Characterization and IC₅₀ values of malaria box compounds number 202 to 221 from plate (C) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| E-2 | MMV665897 | Drug-like | 1.96 |
| E-3 | MMV007430 | Drug-like | 10.24 |
| E-4 | MMV006767 | Drug-like | 9.74 |
| E-5 | MMV001318 | Drug-like | 1.65 |
| E-6 | MMV000483 | Drug-like | 3.49 |
| E-7 | MMV008212 | Drug-like | 4.79 |
| E-8 | MMV008127 | Drug-like | 6.75 |
| E-9 | MMV007875 | Drug-like | 2.00 |

| | | | |
|-------------|-----------|-----------|-------|
| E-10 | MMV396632 | Drug-like | >25 |
| E-11 | MMV667487 | Drug-like | 10.30 |
| F-2 | MMV000839 | Drug-like | 1.85 |
| F-3 | MMV011795 | Drug-like | 7.04 |
| F-4 | MMV019918 | Drug-like | 4.44 |
| F-5 | MMV008270 | Drug-like | 2.74 |
| F-6 | MMV007977 | Drug-like | 4.03 |
| F-7 | MMV007978 | Drug-like | 2.68 |
| F-8 | MMV056726 | Drug-like | 1.87 |
| F-9 | MMV000356 | Drug-like | 6.23 |
| F-10 | MMV396633 | Drug-like | 2.33 |
| F-11 | MMV000963 | Drug-like | 2.03 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set are provided in the supporting information for the malaria box.

Table S12. Characterization and IC₅₀ values of malaria box compounds from 222 to 241 from plate (C) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set[*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|------------------------|--|
| G-2 | MMV019266 | Drug-like | 0.46 |
| G-3 | MMV007363 | Drug-like | 0.46 |
| G-4 | MMV666599 | Drug-like | 0.72 |
| G-5 | MMV019124 | Drug-like | 0.01 |
| G-6 | MMV075490 | Drug-like | 0.10 |
| G-7 | MMV019127 | Drug-like | 0.13 |
| G-8 | MMV396736 | Drug-like | 0.14 |
| G-9 | MMV396669 | Drug-like | 0.11 |

| | | | |
|-------------|-----------|-----------|-------|
| G-10 | MMV274073 | Drug-like | 0.20 |
| G-11 | MMV006319 | Drug-like | 0.34 |
| H-2 | MMV020654 | Drug-like | 0.50 |
| H-3 | MMV020660 | Drug-like | 0.98 |
| H-4 | MMV001049 | Drug-like | 0.61 |
| H-5 | MMV006913 | Drug-like | 0.001 |
| H-6 | MMV007791 | Drug-like | 0.12 |
| H-7 | MMV000481 | Drug-like | 0.24 |
| H-8 | MMV019017 | Drug-like | 0.22 |
| H-9 | MMV084940 | Drug-like | 0.02 |
| H-10 | MMV396749 | Drug-like | 0.61 |
| H-11 | MMV006704 | Drug-like | 0.63 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S13. Characterization and IC₅₀ values of malaria box compounds number 242 to 261 from plate (D) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set[*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|------------------------|--|
| A-2 | MMV666025 | Probe-like | 0.28 |
| A-3 | MMV666123 | Probe-like | 7.34 |
| A-4 | MMV665944 | Probe-like | 0.69 |
| A-5 | MMV666026 | Probe-like | 0.51 |
| A-6 | MMV666079 | Probe-like | 2.36 |
| A-7 | MMV007574 | Probe-like | 5.81 |
| A-8 | MMV000304 | Probe-like | 1.50 |
| A-9 | MMV019555 | Probe-like | 0.56 |

| | | | |
|-------------|-----------|------------|------|
| A-10 | MMV007181 | Probe-like | 0.52 |
| A-11 | MMV498479 | Probe-like | 0.41 |
| B-2 | MMV006787 | Probe-like | 0.07 |
| B-3 | MMV666124 | Probe-like | 5.88 |
| B-4 | MMV665994 | Probe-like | 1.06 |
| B-5 | MMV666020 | Probe-like | 2.58 |
| B-6 | MMV009127 | Probe-like | 9.98 |
| B-7 | MMV666597 | Probe-like | 9.63 |
| B-8 | MMV007127 | Probe-like | 4.12 |
| B-9 | MMV000442 | Probe-like | 9.69 |
| B-10 | MMV008474 | Probe-like | 4.47 |
| B-11 | MMV007577 | Probe-like | 0.88 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S14. Characterization and IC₅₀ values of malaria box compounds number 262 to 281 from plate (D) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| C-2 | MMV001241 | Probe-like | 2.47 |
| C-3 | MMV665908 | Probe-like | 1.14 |
| C-4 | MMV665987 | Probe-like | 0.67 |
| C-5 | MMV665972 | Probe-like | 5.59 |
| C-6 | MMV085471 | Probe-like | 0.07 |
| C-7 | MMV000917 | Probe-like | 2.24 |
| C-8 | MMV000326 | Probe-like | 0.51 |
| C-9 | MMV000443 | Probe-like | 0.01 |

| | | | |
|-------------|-----------|------------|------|
| C-10 | MMV019741 | Probe-like | 0.48 |
| C-11 | MMV007396 | Probe-like | 0.40 |
| D-2 | MMV665934 | Probe-like | 0.05 |
| D-3 | MMV665797 | Probe-like | 0.02 |
| D-4 | MMV665969 | Probe-like | 0.02 |
| D-5 | MMV666109 | Probe-like | 0.07 |
| D-6 | MMV019241 | Probe-like | 0.03 |
| D-7 | MMV007224 | Probe-like | 0.03 |
| D-8 | MMV006753 | Probe-like | 2.15 |
| D-9 | MMV000445 | Probe-like | 0.02 |
| D-10 | MMV000787 | Probe-like | 1.55 |
| D-11 | MMV019995 | Probe-like | 0.01 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S15. Characterization and IC₅₀ values of malaria box compounds number 282 to 301 from plate (D) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set[*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|------------------------|--|
| E-2 | MMV665936 | Probe-like | 0.10 |
| E-3 | MMV665783 | Probe-like | 0.33 |
| E-4 | MMV665949 | Probe-like | 0.19 |
| E-5 | MMV665943 | Probe-like | 0.09 |
| E-6 | MMV007273 | Probe-like | 0.07 |
| E-7 | MMV000699 | Probe-like | 0.01 |
| E-8 | MMV000720 | Probe-like | 0.02 |
| E-9 | MMV007199 | Probe-like | 0.15 |

| | | | |
|-------------|-----------|------------|------|
| E-10 | MMV000604 | Probe-like | 0.12 |
| E-11 | MMV008173 | Probe-like | 0.10 |
| F-2 | MMV665923 | Probe-like | 2.68 |
| F-3 | MMV665786 | Probe-like | 1.36 |
| F-4 | MMV666022 | Probe-like | 0.14 |
| F-5 | MMV666060 | Probe-like | 1.92 |
| F-6 | MMV007228 | Probe-like | 1.53 |
| F-7 | MMV666604 | Probe-like | 0.65 |
| F-8 | MMV006250 | Probe-like | 0.17 |
| F-9 | MMV019690 | Probe-like | 0.74 |
| F-10 | MMV000617 | Probe-like | 0.37 |
| F-11 | MMV020912 | Probe-like | 0.05 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S16. Characterization and IC₅₀ values of malaria box compounds number 302 to 321 from plate (D) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| G-2 | MMV666125 | Probe-like | 0.25 |
| G-3 | MMV665794 | Probe-like | 0.50 |
| G-4 | MMV666054 | Probe-like | 0.001 |
| G-5 | MMV666095 | Probe-like | 0.38 |
| G-6 | MMV006389 | Probe-like | 0.66 |
| G-7 | MMV007113 | Probe-like | 1.52 |
| G-8 | MMV006882 | Probe-like | 22.17 |

| | | | |
|-------------|-----------|------------|-------|
| G-9 | MMV007208 | Probe-like | 0.08 |
| G-10 | MMV000619 | Probe-like | 0.03 |
| G-11 | MMV007557 | Probe-like | 0.51 |
| H-2 | MMV665924 | Probe-like | 16.92 |
| H-3 | MMV665980 | Probe-like | 2.63 |
| H-4 | MMV665971 | Probe-like | 15.81 |
| H-5 | MMV666106 | Probe-like | 0.42 |
| H-6 | MMV000444 | Probe-like | 0.47 |
| H-7 | MMV007275 | Probe-like | 0.20 |
| H-8 | MMV006513 | Probe-like | 0.69 |
| H-9 | MMV008455 | Probe-like | 0.52 |
| H-10 | MMV000621 | Probe-like | 1.89 |
| H-11 | MMV006764 | Probe-like | 1.45 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S17. Characterization and IC₅₀ values of malaria box compounds number 322 to 341 from plate (E) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| A-2 | MMV665813 | Probe-like | 3.32 |
| A-3 | MMV665852 | Probe-like | 2.11 |
| A-4 | MMV665810 | Probe-like | 0.47 |
| A-5 | MMV007654 | Probe-like | 9.71 |
| A-6 | MMV073843 | Probe-like | 1.50 |
| A-7 | MMV000340 | Probe-like | 0.78 |
| A-8 | MMV396723 | Probe-like | 1.94 |
| A-9 | MMV007020 | Probe-like | 2.23 |

| | | | |
|-------------|-----------|------------|-------|
| A-10 | MMV007041 | Probe-like | 2.82 |
| A-11 | MMV638723 | Probe-like | 15.95 |
| B-2 | MMV665927 | Probe-like | 1.66 |
| B-3 | MMV665898 | Probe-like | 3.75 |
| B-4 | MMV665814 | Probe-like | 1.83 |
| B-5 | MMV009015 | Probe-like | 10.28 |
| B-6 | MMV019881 | Probe-like | 1.60 |
| B-7 | MMV086103 | Probe-like | 10.41 |
| B-8 | MMV396663 | Probe-like | 10.46 |
| B-9 | MMV020243 | Probe-like | 2.61 |
| B-10 | MMV667489 | Probe-like | 10.37 |
| B-11 | MMV080034 | Probe-like | 10.97 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S18. Characterization and IC₅₀ values of malaria box compounds number 342 to 361 from plate (E) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| C-2 | MMV665894 | Probe-like | 10.55 |
| C-3 | MMV665840 | Probe-like | 10.39 |
| C-4 | MMV666686 | Probe-like | 9.86 |
| C-5 | MMV008160 | Probe-like | 1.45 |
| C-6 | MMV009085 | Probe-like | 1.07 |
| C-7 | MMV011832 | Probe-like | 2.73 |
| C-8 | MMV006303 | Probe-like | 2.37 |
| C-9 | MMV396665 | Probe-like | 10.44 |

| | | | |
|-------------|-----------|------------|-------|
| C-10 | MMV667490 | Probe-like | 1.96 |
| C-11 | MMV001041 | Probe-like | 1.17 |
| D-2 | MMV665881 | Probe-like | 0.95 |
| D-3 | MMV665824 | Probe-like | 2.58 |
| D-4 | MMV666687 | Probe-like | 1.98 |
| D-5 | MMV008829 | Probe-like | 10.38 |
| D-6 | MMV000478 | Probe-like | 9.903 |
| D-7 | MMV084434 | Probe-like | 10.10 |
| D-8 | MMV396664 | Probe-like | 10.18 |
| D-9 | MMV396770 | Probe-like | 6.00 |
| D-10 | MMV667491 | Probe-like | 1.88 |
| D-11 | MMV667492 | Probe-like | 1.85 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S19. Characterization and IC₅₀ values of malaria box compounds number 362 to 381 from plate (E) evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| E-2 | MMV665836 | Probe-like | 2.16 |
| E-3 | MMV665830 | Probe-like | 2.02 |
| E-4 | MMV007474 | Probe-like | 2.27 |
| E-5 | MMV000753 | Probe-like | 3.49 |
| E-6 | MMV007591 | Probe-like | 2.52 |
| E-7 | MMV020750 | Probe-like | 11.71 |
| E-8 | MMV000704 | Probe-like | 2.15 |
| E-9 | MMV006169 | Probe-like | 2.06 |

| | | | |
|-------------|-----------|------------|-------|
| E-10 | MMV396717 | Probe-like | 12.08 |
| E-11 | MMV645672 | Probe-like | 10.69 |
| F-2 | MMV665882 | Probe-like | 5.12 |
| F-3 | MMV665809 | Probe-like | 6.30 |
| F-4 | MMV011895 | Probe-like | 9.947 |
| F-5 | MMV020403 | Probe-like | 6.45 |
| F-6 | MMV666692 | Probe-like | 12.25 |
| F-7 | MMV006962 | Probe-like | 10.68 |
| F-8 | MMV396594 | Probe-like | 10.45 |
| F-9 | MMV396726 | Probe-like | 4.71 |
| F-10 | MMV396652 | Probe-like | 10.20 |
| F-11 | MMV006522 | Probe-like | 3.22 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box.

Table S20. Characterization and IC₅₀ values of malaria box compounds number 382 to 401 from plate (E) and diminazene aceturate evaluated for *Babesia divergens* parasites

| Compound No. | Compound ID ^a | Set [*] | IC₅₀ (μM) ^b |
|---------------------|---------------------------------|-------------------------|--|
| G-2 | MMV665812 | Probe-like | 3.91 |
| G-3 | MMV665864 | Probe-like | 0.57 |
| G-4 | MMV011436 | Probe-like | 2.23 |
| G-5 | MMV128432 | Probe-like | 10.19 |
| G-6 | MMV007092 | Probe-like | 1.94 |
| G-7 | MMV001239 | Probe-like | 10.32 |
| G-8 | MMV667486 | Probe-like | 2.56 |

| | | | |
|-------------|-----------|------------|-------|
| G-9 | MMV000986 | Probe-like | 2.55 |
| G-10 | MMV011522 | Probe-like | 2.93 |
| G-11 | MMV396635 | Probe-like | 1.95 |
| H-2 | MMV665875 | Probe-like | 2.29 |
| H-3 | MMV665886 | Probe-like | 3.25 |
| H-4 | MMV011438 | Probe-like | 10.06 |
| H-5 | MMV666689 | Probe-like | 4.65 |
| H-6 | MMV007764 | Probe-like | 2.30 |
| H-7 | MMV006656 | Probe-like | 10.27 |
| H-8 | MMV007285 | Probe-like | 3.39 |
| H-9 | MMV667488 | Probe-like | 2.85 |
| H-10 | MMV019199 | Probe-like | 10.26 |
| H-11 | MMV006825 | Probe-like | 4.19 |
| - | DA | Drug-like | 0.13 |

^a Compounds are designated by their MMV identifier codes; ^b IC₅₀ values for each drug were calculated on the fourth day based on the growth inhibitions determined by fluorescence- based method. Results are means from triplicate experiments. *The set data are provided in the supporting information for the malaria box. DA, diminazene aceturate (positive control drug)

Table S21. Viability test results of potent MMV hits evaluated for *Babesia divergens*

| Compound ID ^a | Drug concentrations (μM) ^b | | | |
|--------------------------|---------------------------------------|----|---|-----|
| | 25 | 10 | 1 | 0.1 |
| MMV665807 | - | - | - | - |
| MMV665850 | - | - | - | - |
| MMV019124 | - | - | - | - |
| MMV006913 | - | - | - | - |
| MMV019995 | - | - | - | - |
| MMV000699 | - | - | - | - |
| MMV666054 | - | - | - | - |

^a Compounds are designated by their MMV identifier codes. ^bany value calculation was dependent on the fluorescence assay in three different treatment of experiments. Every concentration was done in triplicate in each experiment. + = viable; - = dead

